NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"The Factor Inducing Bystander Effect of E1A Gene Therapy"

Description:
The human adenovirus type 5 early region 1A (E1A) tumor suppressor gene has been widely studied. The E1A gene transcribes two mRNA species (13S and 12S) related to two separate proteins (289R and 243R). The E1A proteins bind to other cellular proteins (e.g. P300, pRB family, Ap-1 and cyclin A) to mediate transactivational transcription of various cellular genes. E1A has been shown to repress the Her-2/neu promoter and down-regulate Her-2/neu p185 resulting in suppression of tumorigenecity. The use of liposomes- or adenovirus-mediated E1A gene therapy for experimental cancer has successfully resulted in tumor suppression, regression and prolongation of life. Further studies have shown that cells unmodified by the gene therapy experience suppression of tumor growth. "Bystander effect" is a term used to describe this toxic effect that gene modified tumor cells have on nearby unmodified tumor cells. Through continued experimentation, a soluble factor, which may be responsible for this activity, has been identified and isolated. The characterized factor could result in the development of a new therapeutic agent for various cancer types.

Market:
It is anticipated that the technology has broad applications in gene therapy, primarily in lung cancer, breast cancer, and ovarian cancer. As reported in the POV, Inc. publication, "Cancer 2000…Evolving Long-Term Business Opportunities and Threats in Cancer Therapeutics in the US – 1995 Edition," the prevalence of these diseases exceeds:

	Prevalence	New Cases	Deaths
Breast Cancer	715,000	184,000	46,000
Lung Cancer	320,000	170,000	158,000
Ovarian Cancer	68,000	266,000	14,500
Total	1,103,000	620,000	218,500.

In addition, the current and forecasted sales of prescription cancer products through 2005 exceed $3 billion and $9 billion, respectively. Should this technique prove efficacious and penetration into these lucrative markets occurs, a substantial return on investment may result.

MDA Reference Number: IDR98-17/JJS/0698

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NON-CONFIDENTIAL DESCRIPTION
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"RAPID ANALYSIS OF GENE EXPRESSION (RAGE)"

Description:

There are currently several methods of determining changes in gene expression. Most of them depend on selecting a small subset of the transcribed genes, developing specific probes for each of these genes and estimating mRNA levels by either hybridization methods or RT-PCR. New technologies are being developed at several fronts, including gene chip hybridization at Affymetrix; gene expression microarray technologies pursued by several companies; and SAGE being developed by Genzyme Molecular Oncology, Inc. and others.

Among them, RAGE offers a unique approach to determine the frequency distribution of virtually all polyadenylated mRNAs in a cell population or tissue at a selected point in time. It is best suited for determined global chances in gene expression patterns subsequent to some stimulus, but can also be applied to comparisons of tissue samples, e.g. tumor vs. normal tissue. In addition to providing quantitative global data, it can be tailored to look at a particular subset of the transcriptome, and it can be used for gene discovery. Compared to other methods, RAGE requires fewer and less complicated molecular manipulations and no cloning. The modular nature of RAGE allows one to analyze the entire genome in a manageable number of experiments, or to concentrate on selected portions. It allows both a quantitative global description of expression patterns and possibility of discovering new genes based on changes in their expression in response to a given stimulus. Initial feasibility studies have been successfully conducted in a human breast cancer cell line.

Potential products include kits containing the hardware, chemical reagents, and software to collect and analyze data. In addition to utilities mention above, such products would be useful in basic reassert, defining pathophysiological conditions, defining patient response to therapy, etc.

Availability: exclusive license

Reference: MDA IDR 98-11 (KQ2/98)

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Description:

The major cause of death from cancer is metastasis that is resistant to conventional therapies. In the majority of cancer patients, metastasis to regional lymph node and/or distant organs has occurred by the time of diagnosis of the primary tumor. Understanding the critical determinants of cancer metastasis should suggest new approaches to cancer therapy. Among them, activation of inducible nitric oxide syntheses (iNOS) gene appears to be promising.

Previous studies have strongly suggested that NO is associated with cell death, suppression of tumor development, and inhibition of metastasis. To take the discovery further, a team of scientist at MD. Anderson has successfully cloned iNOS gene into retroviral vectors with an inducible promoter. In *in vitro* studies, a highly metastatic melanoma cell line, which expressed low level of iNOS, was transfected with an enzymatically active iNOS. The active iNOS transfected cells produced high level of NO and underwent apoptosis, while control cell did not. In vivo studies in melanoma also showed strong anti-metastasis activities in active iNOS transfected cells.

In addition, similar results were observed in liver metastasis studies. Both in vitro and in vivo results showed direct correlation between iNOS expression and NO production. Increased level of NO induced apoptosis in metastatic cells, while decreased level of NO significantly diminished antitumor activities.

Collectively, these data strongly suggest the activation of iNOS by the retroviral vectors can be a potential approach for treatment of cancer metastasis. The technology appears to have broad applications in treating a wide variety of cancers, such as prostate carcinoma, ovarian carcinoma, melanoma, renal cancer, liver and lung cancer.

Availability: Exclusive license

Reference: MDA IDR: 97:03, UTSC: 534

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NON-CONFIDENTIAL DESCRIPTION
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"IMPROVED METHODS FOR TRANSDUCING CELLS IN GENE THERAPY"

Description:

One of major technical obstacles to successful gene therapy is low transudation efficiency, or the low efficiency of the insertion and expression of the selected transgene in host cells. Although transgene expression can be increased by administration of a high dose of vectors, the accompanying severe local inflammatory responses limit the effectiveness of increasing dosage.

The present invention seeks to overcome the limitations of current gene transduction methods through a reduction of the endogenous expression of interferon b in the cells which are targeted for transduction. Studies showed that infection of murine macrophage with Ad5cmv-lacZ produced increased expression of endogenous IFN-b. Neutralization with anti-IFN-b antibody during infection with the vector enhanced expression of LacZ. In contrast, IFN gene expression was not detected in readily transduced NIH 3T3 cells, and the tranduction efficiency of NIH 3T3 cells was unaffected by the antibody. LacZ gene expression in NIH 3T3 cells was decreased when cocultured with macrophages or in the presence of exogenous IFN-b. The addition of the anti-IFN-b antibody reversed this inhibition.

These results demonstrated that endogenous and exogenous IFN-b can significantly reduce the expression of the LacZ gene transduced *in vitro* by a recombinant Ad vectors. Because viral infection can induce expression of INF-b in many cell types, including epithelial cells, fibroblasts and macrophages, the data suggested that INF-b contributed to the low transduction efficiency in vivo. Based on above discoveries, the invention further provided compositions and methods for the efficient transduction of cells with nucleic acid constructs administered to host cells.

It is believed that increased transduction efficiency will have significant impact on a wide variety of gene therapy applications, including genetically based diseases, cancers, and other major live threatening diseases.

Patent(s): US and foreign patents pending

Availability: exclusive license

MDA IDR: 97-03, UTSC: 516

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NON-CONFIDENTIAL DESCRIPTION
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"BIOACTIVE BIODEGRADABLE NERVE CONDUIT"

Description:

Tumor removal, traumatic injuries and congenital anomalies often result in injuries to or sacrifice of critical nerves. Failure to restore injured nerves can result in the loss of muscle function. Functional nerve defects have traditionally been reconstructed by the surgical transfer and sacrifice of healthy normal nerves from an uninjured location to the injured site. The current technology involving nerve repair is limited by the availability of donor tissue and the morbidity related to the sacrifice of donor nerve.

The technology is based on the concept of an engineered, biodegradable polymer conduit that would provide physical and physiological structures to restore nerve regeneration. This bioactive and biodegradable nerve conduit will be seeded with support cells and induction factors through a novel timed delivery system, to reproduce all the necessary components of a nerve graft, thus avoiding the morbidity of autografts.

A number of technological milestones have been accomplished in the past few years, including:

- Establishment of a reproducible model for the functional and histomorphologic evaluation in the rat posterior tibial nerve
- Axonal growth through the biodegradable conduits in pilot studies
- Assessment of major properties in controlled drug release
- Technical fabrication of support cells to promote axonal proliferation

Market Information:

Markets for this technology include patients with peripheral nerve injuries, reconstructive surgery patients (500,000 patients in the US annually) and surgical patients with excessive scarring or surgical adhesion. (Scarring and adhesion may interfere with nerve function.)

Availability: Exclusive or non-exclusive Licensing
MDA Ref. No.: IDR 97-12 (KF) (12/12/97MBL)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"A METHOD TO PREVENT SIGNAL-PILE UP IN SCINTILLATION DETECTORS"

Description:
When a radiation particle such as gamma ray is detected in a scintillation detector, the detector will emit light, which is then converted into electronic signal by a photo-sensor. When the incoming radiation flux is high, signal pileup may occur as the next radiation particle arrives while the present event is still emitting light. As a result, the identity of each particle will be lost, and several particles will merge into a larger signal. Therefore, the performance of conventional scintillation detectors is greatly inhibited as they are not capable of taking a higher count of signal.

The invention relates to a novel hybrid processing method to prevent and correct signal pile up. It is an improvement over the delay line pulse clipping techniques since more scintillation light is collected and there is less signal pile-up. An electronic prototype to prevent pileup in energy measurement was developed and tested in a NaI(TI) detector. The tests showed a significant improvement in measuring gamma energy at very high count-rates even when pileup approaches 86%. A 10 to 12 fold improvement in count-rate capability over conventional detector was observed with the new method, and most of the scintillation light is collected. Additionally, the new method allows the use of a 10x stronger radiation source, which enables the data collection time to be reduced by 90%.
The conventional integration method (and its equivalent pulse-shaping method) has been the gold standard in nuclear physics and nuclear medicine for the past 40 years. The new method represents a significant breakthrough, which has great impacts over a broad spectrum of industrial applications:

- Medical uses including gamma cameras, PET, bone scanners, thyroid probes, monitors and dosimeters.

- Surveying uses such as oil field logging, nuclear reactor monitoring, airport luggage scanning, etc.

- Industrial gauging including thickness, level and density gauging.

- Research applications in nuclear physics, high energy physics and medicine.

Availability: Exclusive or non-exclusive license
MDA Ref No.: UTSC: 531 (KQ/0297) (MBL 1/8/98)

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NON-CONFIDENTIAL DESCRIPTION
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"SUBCUTANEOUS ENDOSCOPIC DISSECTOR"

Description:

The dissector is designed to allow minimally invasive surgery in anatomic locations not amenable to the usual endoscopic techniques. For an example, in order to operate subcutaneously, one must have surgical instruments that are capable of 1) retraction, 2) irrigation, 3) suction, 4) cautery for dissection and coagulating small blood vessels, and 5) visualization. To date, all these functions require separate instruments.

The invention works by allowing the various components of a surgical operation to be concentrated at the small space located at the end of the instrument. It provides a mean for the surgeon to use a single hand and control retraction, visualization, suction, irrigation, and electrocautery in the deep tissue. There are multiple channels down the shaft of the instrument which allows introduction of endoscopic cameras and other instrumentation. At the operating end of the instrument there are expanding jaws which retract the tissue and allow a dissection to occur in the tissue planes. The retractor can be activated by the hand piece. Additional components can be activated by adding other control surfaces to the instrument.

The dissector permits video guided minimally invasive surgery to be perform in a more efficient manner by the surgeon. It has been successfully used in an experimental domestic pig to dissect muscle flaps and other tissues. The primary products which may result from this invention are a variety of specialized surgical instruments for these purposes.

Availability: Exclusive license

MDA Ref No: 549 (KQ/0497)

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NON-CONFIDENTIAL DESCRIPTION
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"INHIBITION OF BCL-2 PROTEIN EXPRESSION"

Description:
Bcl-2 is an oncogene with tumorigenic potential due to its capacity to block programmed cell death. By blocking the production of the bcl-2 protein, the tumor cells are able to regain the capacity to enter programmed cell death. More than 90% of follicular lymphoma patients have a translocation of the bcl-2 gene from its normal location on chromosome 18 to the immunoglobulin heavy chain gene locus on chromosome 14. Therefore, the bcl-2 gene is under the influence of the immunoglobulin heavy chain enhancer, and is consequently overexpressed. Antisense oligos specific for the translation initiation site of the human bcl-2 mRNA are incorporated into liposomes and transported into the cellular cytoplasm. These liposomal oligos inhibited the proliferation of cell lines derived from human B-cell lymphomas. Phosphorothioate oligos are known to be more potent than phosphodiesters in inducing growth inhibition, but when used with the cationic lipids even less oligo concentrations are necessary.

Several human lymphoma and human leukemia cell lines were tested. A cell line which does not overexpress the bcl-2 protein was used as a negative control cell line. A dose-dependent growth inhibition was found in cells bearing the t(14:18) translocation and expressing very high levels of bcl-2. Liposomal control oligos showed no growth inhibition, and non-specific toxicity was not observed.

Market:
Follicular lymphoma is the most common lymphoid malignancy in Europe and the U.S. Although the response to chemotherapy is initially good, relapses are inevitable with the transformation to more aggressive histological type and the development of drug resistance. There is a great need for new methods and compositions to treat bcl-2 associated diseases like this. Between leukemia and lymphoma there are about 80,000 new cases annually in the U.S., and 400,000 existing cases with the risk of recurrence. The market for non-Hodgkins lymphoma alone is expected to be $185 M by the year 2000.

Patentability: Patent pending

MDA Ref. No.: UTSC:504/KVF/0996

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"A MULTIPURPOSE ANTIMICROBIAL SILASTIC SHEATH"

Description:
Catheter-related septicemia represents the most frequent life-threatening complication of vascular catheters. This new device will allow for replenishment of the antimicrobial/anticoagulant agents along the path of the catheter as frequently as needed in order to maintain the potency and efficacy of the preparation. This new design will also allow for very prolonged and safe use of indwelling catheters, thereby eliminating the infectious and thrombotic complications that presently result from the use of long-term catheters.

The invention consists of encasing existing catheters or modified ones with a silastic "sheath" filled with antibiotics or anticoagulants, such as minocycline, rifampin, and EDTA. The antibiotic layer under the silastic sheath can be introduced in a powder form, or impregnated in silastic as a layer underneath the silastic sheath. The choice of the silastic sheath thickness will determine how rapidly the antimicrobial agent will be released from the depot underlying the sheath. Both the powder preparation and the silastic impregnated preparation will allow the catheter devices to be used for long periods of time.

Market:
It is estimated that vascular catheters are inserted in more than 20 million patients in hospitals each year. The predicted U.S. market in 1995 for central intravenous catheters will be about $272 million.

Patentability: Patent pending

MDA Ref. No.: 385/KFV/1196

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NON-CONFIDENTIAL DESCRIPTION
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"TUMOR-SPECIFIC CELL SURFACE BINDING MONOCLONAL ANTIBODY"

Description:
The detection of gynecological tumors at an early stage is an essential element in the successful control of these cancers, and early treatment of these tumors can be determinative of the progression of the disease. With the capability to duplicate immune system responses, monoclonal antibodies can be used to identify and destroy cancer cells and other invading agents. A human monoclonal IgM antibody (CR4E8) reactive to specific cervical associated tumor antigens has been cloned and characterized. Its specificity has been analyzed in vitro with panels of human tumor cell lines and on histological sections of normal and malignant tissues of human patients.

The CR4E8 monoclonal antibody was developed by fusing SPATZ 4 cells with peripheral blood lymphocytes from a patient with cervical cancer who was immunized intralymphatically with a viral oncolysate allogeneic tumor vaccine. The CR4E8 monoclonal antibody recognizes a cell surface antigen expressed on cervix, melanoma, breast, colon, and other carcinomas, and immunoprecipitates from cervical tumor cells a 55 kD polypeptide. The antibody has little or no reactivity with most normal tissues. Sequence analysis showed that the variable region of the antibody had 98% homology to the human Ig germline heavy chain.

Market:
This technology has the potential to be used as both a diagnostic and a therapeutic agent for certain cancers. It is considered a potentially important means of delivering safer chemotherapeutic drugs. The availability of purer forms of antibodies have been made possible by using hybridoma cell lines. The market for monoclonal-based therapeutics is large and should be $240 M by the year 2000, and $500 M in sales by 2007. More specifically, 500,000 women are diagnosed with cervical cancer each year in the U.S., and 70 M cervical smears are performed annually.

Patentability: Patent pending

MDA Ref. No.: 461/KFV/0996

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NON-CONFIDENTIAL DESCRIPTION
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"Optoacoustic Imaging With Pulsed Laser"

Description:
The field of optoacoustics is currently undergoing a renaissance. Since the development of laser technology, interest and applications have blossomed. New techniques for non-contact ultrasonic measurements based on the use of laser optics are being pursued. Scientists here have developed an invention which allows imaging of a complex tissue structure on the basis of optical contrast. It uses a pulsed laser to slightly but suddenly heat any region within a tissue which has increased optical absorption relative to its surroundings. This can be blood vessels or melanin or any other pigment. The slight heating converts to a pressure wave which propagates outward from the source of heating, and a piezoelectric transducer at the surface detects the time, magnitude and shape of arriving pressure waves.

This system will allow for the imaging of tissue structures with high spatial resolution within turbid media such as biological tissues. It could be used to image the depth and structure of a portwine stain lesion before and after clinical treatment, and it could be used to image hematomas. In addition, it could be used to image the pigmented retinal epithelium and the underlying choroid plexus. In diagnostic radiology, it can be used to image a highly perfused tumor of the breast.

MDA Ref. No.: ID96-01/KVF/0796

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NON-CONFIDENTIAL DESCRIPTION
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"AEROSOLIZED LIPOFECTION"

Description:
This invention describes a non-toxic, non-immunogenic, cationic lipid formulation that can be used to transfect specific genes in the bronchial epithelium by aerosolization. It is intended to be used to correct genetic defects in premalignant lesions in the bronchial epithelium of patients at risk of lung cancer, and as a result, delay or prevent lung cancer. Compared to other gene delivery systems, this new method is an improvement. Viruses are more efficient than liposomes in transfecting cells but are also more toxic and immunogenic, therefore, repeated administration is unrealistic. Liposome composition and size are major determinants of the transfection efficiency. Specific liposome formulations have been identified to have a higher transfection efficiency and, therefore, a greater potential as therapeutic agents. The invention has been successfully tested in models of endobronchial human lung cancer in nude mice.

Market:
There are over 150,000 deaths per year in the U.S. related to lung cancer. There is a huge population at risk of lung cancer that would benefit from strategies aimed at delaying the carcinogenic process; the same way that controlling cholesterol levels delays ischemic heart disease. Because of its increasing incidence, lung cancer incidence may actually plateau and the introduction of new agents, the market for drugs is expected to increase tremendously over the next ten years to more than $750M by the year 2007.

MDA Ref. No.: ID96-41/KVF/0796

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NON-CONFIDENTIAL DESCRIPTION
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"Novel Human cDNA, *SKB1Hs*"

Description:
ras genes are highly conserved in evolution and encode small, monomeric G proteins that regulate cell growth and differentiation in a broad spectrum of eukaryotic organisms. *ras* genes are of substantial medical significance, as oncogenic mutant *ras* genes can be detected in 40% or more of all human cancers. The fission yeast *Schizosaccharomyces pombe* possesses a single known *ras* homolog, *ras1*, the product of which is required for at least two distinct cellular functions: (1) regulation of a peptide mating pheromone-induced mitogen-activated protein kinase (MAPK) module and (2) control of cellular morphology. A Ras-related small G protein, Cdc42, is an essential component of the Ras1p signaling complex in *S. pombe*. The functions of Ras1p in fission yeast are highly analogous to known functions of Ras proteins in mammalian cells.

Previously, it was demonstrated that the protein kinase Shk1, a homolog of mammalian $p21^{Cdc42/Rac}$-activated kinases (PAKs), is a downstream target for Cdc42 in *S. pombe* (Marcus et al., 1995, *PNAS*, 92:6180). By conducting a genetic screen for proteins that physically associate with Shk1, my laboratory has identified a novel gene, *skb1*. Genetic analyses indicate that the *skb1* gene product, Skb1, is a component of the Ras1/Cdc42-dependent morphological control pathway in *S. pombe* and that it positively modulates Shk1 function. Skb1 is the first non-Ras-related protein to be directly implicated as a PAK regulator.

Searches of the computer data bases revealed that homologs of Skb1 are encoded by uncharacterized open reading frames in the genomes of the budding yeast, *Saccharomyces cerevisiae*, and the nematode *Caenorhabditis elegans*, and by a set of overlapping EST sequences encompassing a partial human cDNA. My laboratory has now cloned the full length human cDNA, which we have named *SKB1Hs*. Efforts are underway to characterize *SKB1Hs*, including functional studies using yeast and mammalian cell-based assays, biochemical analyses, and mapping studies to determine whether the *SKB1Hs* gene is associated with a known disease locus.

Various lines of evidence indicate that PAKs in both yeasts and mammals are likely to participate in regulating diverse cellular functions. PAKs have been shown by us and others to induce ERK and JNK/SAPK MAPK cascades, which control cell growth, differentiation, apoptosis, and other processes in higher organisms. We propose that proteins such as Skb1 could define functional specificity for distinct PAK isozymes, which all interact with Cdc42 and Rac proteins. Our current work is aimed at determining whether Skb1Hs proteins play a significant role in Ras/Cdc42-dependent signal transduction pathways in mammalian cells, as does Skb1 in fission yeast.
MDA Ref. No.: ID96-42/KVF/0896

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"Glutathione S-Transferases (GSTs)"

Description:
A major cause of therapeutic failure in many human cancers, such as breast, brain and leukemia is the resistance of the tumor cells to the cytotoxic action of the anticancer agents. Current agents are often poorly tolerated by patients because they require high dosage levels and repeated administrations to override tumor resistance and prevent recurrence. The glutathione S-transferases (GSTs) are enzymes frequently found elevated in tumor cells. Drug resistance mediated by the glutathione mechanism is a significant clinical problem, and interfering with this mechanism can render tumor cells more susceptible to chemotherapy.

Glutathione S-transferase-pi (GST-pi), the protein encoded by variant genes, facilitates the inactivation of many types of anticancer agents, particularly alkylating agents and platinum

analogues, by catalyzing their conjugation with glutathione. Consequently, most drug resistant tumors have been shown to contain high GST-pi levels. Down-regulation of the expression of GST-pi genes and/or inhibition of the activity of GST-pi proteins will increase the therapeutic efficacy of current chemotherapy by decreasing the ability of the tumor cells to inactivate the drugs, and by decreasing therapy-associated normal tissue toxicity. These genes have been cloned and characterized, and can be targeted in many different ways towards the cancer.

Market/Products:
The products and applications of polymorphic variant glutathione S-transferase-pi genes are numerous. They encompass diagnosis, prognosis, and therapy of human cancers. Small molecule GST-pi inhibitors can be designed to target the active site pockets and other structural components of the variant GST-pi peptides. Because the active site pockets of the peptides encoded by the different genes are significantly different, small molecules ligands with different affinities for the various peptides can be designed. Antisense deoxyribonucleotides and ribozymes can block translation or cause cleavage of GST-pi RNA. Vectors, such as plasmids, and other delivery systems, such as liposomal, can be used to accomplish this. Antibodies can be developed for use in diagnostic and prognostic agents. Reagents and assays to identify and to quantitate the level of expression of the genes in tumors and other tissues can be used as a tool for early detection and/or screening for cancers.

Patentability: Patent filed

Availability: Available for exclusive license

MDA Ref. No.: UTSC:492 (ID96-25) 0796/KVF

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NON-CONFIDENTIAL DESCRIPTION
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"Cell Type-Specific Anticancer Gene Therapy"

Description:
This invention relates to the construction of tissue-specific promoter/enhancer driven genetic constructs which target DNA polymerases, topoisomerases, and transcription factors. A novel myeloid specific gene and its promoter have been cloned. This gene is not expressed in normal tissues, and is only expressed in very low levels occasionally in AML patients. High levels of the gene messages can be induced in lymphoblasts by juxtaposing the gene to the enhancer of the immunoglobin heavy chain gene. These findings suggest that the gene promoter combination could be used to induce high levels of genetic products solely in lymphoid cells. By inhibiting cell proliferation, these products could result in specific growth inhibition of lymphoid cells without affecting other organs.

Several cell lines, including three human prostate cancer cell lines, were transfected with the genetic constructs, and the control plasmid by a lipofection-mediated method. No growth inhibition was observed in cells of non-prostatic origin. In contrast, viabilities of the prostate cancer cells were impaired by the PSAP-driven constructs targeting the transcription factor.

The advantages of this approach are that it should enhance expression of the therapeutic gene in the tissue where the cancer is located, and by limiting drug expression in other tissues it should therefore limit toxic effects.

Market:
The gene therapy market is quite large, and the commercial interest in this area is considerable. Many companies continue to support research and development in this area, and clinical trials are currently in progress.

Availability:
Available for exclusive or non-exclusive license

MDA Ref. No: ID96-15 (KVF05/96)

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NON-CONFIDENTIAL DESCRIPTION
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"Heparin Interaction Protein (HIP) And HIP-Peptide"

Description:
A novel peptide capable of discriminating a biologically important heparin fraction has been identified and cloned. This heparin interaction protein has been shown to selectively bind with high affinity to a subset of heparin species, the form that binds with highest affinity to antithrombin-3. When added to in vitro clinical assays for blood coagulation activity, the HIP peptide has been shown to block heparin's anticoagulant activity, presumably by preventing heparin from binding to and activating anti-thrombin-3. The HIP peptide and parent protein could be used to isolate anticoagulant species of heparin thereby generating sub-fractions of this anticoagulant factor that are greatly enriched with desired activity and depleted of undesired side effects. Current procedures to do this are expensive and tedious, and result in relatively low yields. There is also the possibility of using the peptide or parent protein in bandages and/or wound coverings to stimulate blood coagulation.

Market:
Heparin dominates the market for injectable anticoagulants.The dollar value of the heparin market is approximately $100 million, and consists of two distinct components. "Therapeutic" heparin is used systemically to reduce the coagulability of the patient's blood, and the lock-flush or heparin-lock formulations are used to prevent coagulation and blockage of in-dwelling catheters where flow is intermittent. The lock-flush formulations should enjoy continued gradual growth, undisturbed by any major new product introductions. Low Molecular Weight Heparin is a new product and the market is very competitive. Fractions, or parts of the heparin molecule are being developed, as the entire heparin molecule is not needed to achieve an anticoagulant effect. LMW Heparin's greater effectiveness over traditional heparin should establish this product as the coagulant of choice over the next few years because of the drug's ability to reduce costly patient monitoring and to minimize serious bleeding problems.

Availability: Available for exclusive or non-exclusive license

MDA Ref. No: ID96-14 (KVF/0196)

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NON-CONFIDENTIAL DESCRIPTION
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"SYSTEM FOR PERFORMING CLOSED STABILIZATION OF METASTATIC BONE LESIONS"

Description

The current standard procedure to fixation of metastatic bone lesions includes: exposing the metastatic deposit, curetting the tumor tissue under direct vision, inserting a rod or other fixation devices, and filling the tumor cavity with polymethylmethacrylate. The necessity for open exposure of the tumor increases intraoperative blood loss and potential morbidity due to wound infection, tumor contamination, and wound complications (hematoma, dehiscence).

The researcher at MD. Anderson Cancer Center has conceived a system that will allow for adequate closed treatment of metastatic bone lesions without surgical exposure of the lesion. The system consists of: 1) a set of special instruments to facilitate intramedullary tumor debulking utilizing a closed technique; 2) a set of intramedullary nails; 3) the use of polymethylmethacrylate. The system allows for appropriate positioning of an intramedullary nail within the bone after the tumor tissue has been removed, but before cementation. Low viscosity PMMA is introduced into the nail using a cement pressurizer. An expandable cutter is providede for closed removal of tumor tissue. Compared with the conventional method, this closed technique should decrease perioperative morbidity and decrease total hospital days attendant on treatment of this condition.

MD. Anderson Cancer center is seeking a corporate partnership to take the technology into the commercial stage. The system is well designed and has high successful rate. We firmly believe it is a unique technology with significant market potential, relative low developmental risk and short product development time.

Availability: Exclusive licensing

MDA Ref No: 96-02 (KQ/11/95)

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"MOUSE ADVANCED RESTRAINT SYSTEM"

Description:

The invention relates to a mouse restraint device that can be used in a variety of experimental and surgical procedures in research and veterinary laboratories.

The unique design of the restraint system allows non-anesthetized mouse (with tail or not) to be restrained in a gentle and secure way. Applied values of the forces on the head, neck, shoulders, and tension on the legs and tail are small, but strong enough to completely secure mouse position. The restraint time can be from 30 seconds up to 30 minutes. All system parts are made with plastic or stainless steel that can be easily clean and sterilized. During restraining operation, hands are well guarded and free for other procedures as needed.

It has the following unique features that make it an excellent tool to restrain mice:

- The Anterior Should Holder with a flexible Neck Protector is carefully designed for gentle and secure restraint of the mouse neck, breast and shoulders.
- The Rear Restraint Unit has a unique approach to secure the mouse position in the most flexible and gentle way.
- The Tail Support is a unique design for easy positioning the mouse back.
- The Tail Holder uniquely attached to the Sliding Board, which allows for better tail blood circulation and longer monitoring period.
- The Rear Leg Holder is designed for managing different mouse strains.

The system is also designed to accommodate different usages in various experimental environment: an Examination Table is designed for microscopic observation, photography or videotaping; a Surgical Board allows for injection or taking blood samples; Shaving and Tattooing Board are also available; Anterior Shoulder Holder comes with right-hand or left-hand version.

The system has been tested extensively in Science Park Research Division of MD. Anderson Cancer Center. To date, over 4000 mouse restraint operations have been performed successfully.

Availability: Available for exclusive license.

MDA Ref. No.: 96-13 (KQ/0196)

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

" A SIMPLE DEVICE TO REMOVE ENDOTRACHEAL TUBES AND NASAL TRUMPETS FROM FIBEROPTIC ENDOSCOPES IN AIR WAY MANAGEMENT"

Description:
Fiberoptic manipulation of the airway by practicing clinicians is easily accomplished and generally well tolerated by the patient. During routine nasotracheal fiberoptic intubation, it is customary to perform fiberoptic laryngoscopy through a nasal trumpet with the endotracheal tube preloaded on the fiberoptic bronchoscope. However, a dilemma exists for such procedures: the nasal trumpet must be removed from the fiberoptic bronchoscope prior to placing the endotracheal tube in the airway. Traditionally, The are two methods to the problem. One is to cut the nasal trumpet off the fiberoptic scope and then advance the tube into the airway. This technique is somewhat cumbersome and uncomfortable to patients because nasal trumpets are difficult to cut off. The second alternative is to precut the nasal trumpet prior to it being placed in the nose. The major drawback is that nasal trumpets usually do not stay aligned and collapse once they are placed in the nose, resulting in insufficient lumen to perform a fiberoptic laryngoscopy. In addition, another common difficulty encountered in airway management is that endotracheal tube sometimes has to be replaced. The same problem occurs since polyvinyl chloride tubes are very difficult to cut. This may result in significant patient hypoxemia and discomfort during the tube changes.

Having recognized the problems, the physician at M.D. Anderson has successfully developed a simple device that can cut off nasal trumpet and endotracheal tube easily and safely. The device has a replaceable cutting surface that is easily to obtained and is common to all operating rooms. The device is easily cleaned and sterilized after each patient use. The main advantage of the device is that it can easily remove a nasal trumpet or endotracheal tube off a fiberoptic scope without losing the airway with minimal patient discomfort.

Market:
It is estimated that 5% of the patients receiving surgical operations every year needs airway management in their anesthesia. This device makes the removal of trumpet and tubes much easier and comfortable to the patients. When applied in an anesthesia procedure, as much as 50% of time consumed in the process can be saved, which would translate into significant amount of savings.

Availability: Available for exclusive license

MDA Ref. No.: 96-05 (KQ/0895)

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"A SYSTEM THAT INCREASES THE PERFORMANCE OF COMPRESSION METHODS WHEN COMPRESSING SETS OF SIMILAR IMAGES"

Description:
The invention relates to a technique, Set Redundancy Compression (SRC) that can be used to enhance the performance of other compression methods for compressing sets of similar images.

This technique takes advantage of the large amount of set redundancy, the common information existed in a set of similar images. When the images are pre-processed with SRC, this common information is extracted and is used to "smooth" the images in a lossless way, therefore increasing their compressibility. To recover the original images, the same procedures are simply reversed.

Significantly improved compression can be achieved by coupling SRC with any other currently existing compression methods. To date, SRC has been tested with two compression methods, Huffman Encoding and Lempel-ZIv Compression. The results show an average of two-fold improvement in the compression ratios. Furthermore, the pre-processing of image with SRC is lossless, meaning that there is absolutely no loss in image quality. In addition to 2-D image processing, the technology has potential in 3-D data processing.

Better compressibility means smaller storage requirements and smaller transmission times, which can be translated into great financial savings from reduced communication and storage costs. Significant commercial value and broad applications are expected for this invention, including medical imaging and transmission, educational and industrial archiving; aerospace imaging databases, and the like.

Availability: Available for exclusive license.

MDA Ref. No.: 95-60 (KQ/1195)

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"RETINOID THERAPY FOR THE TREATMENT OF VASCULAR RESTENOSIS"

Description

Retinoid therapy has been used successfully in the treatment of a variety of human cancers including acute promyelocytic leukemia, squamous cell carcinoma of the neck, and melanoma. Vascular proliferative diseases, particularly atherosclerosis and iatrogenic restenosis, involve the aberrant growth of smooth muscle cells (SMC).These cells phenotypically resemble neoplastic cells in that they lose their normal differentiated function and display proliferative/migratory properties. To date, no effective drugs exist for treating acute vasculoproliferative diseases.

Researchers here have shown that two retinoids can effectively block vascular SMC proliferation in vitro, thereby demonstrating their potential clinical utility. The retinoid therapy could be used as a preventative measure against acute restenosis following percutaneous transluminal coronary angioplasty, atherectomy or bypass graft surgery.
These retinoids have been shown to inhibit cell proliferation by at least 50%, and this growth inhibition is fully reversible, and is not due to toxicity or apoptosis.

Market

The potential market for any possible therapeutic drugs is quite large. At least 300,000 patients undergo balloon angioplasty each year and thousands more have bypass graft surgery to alleviate clinical symptoms associated with pre-existing vascular disease. Between coronary artery bypass grafting (CABG) and percutaneous transluminal coronary angioplasty (PTCA), there were greater than 828,000 procedures performed in the U.S. in 1994. Despite their widespread use, the effectiveness of these procedures is significantly reduced by acute and chronic complications, mainly reocclusion and restenosis. Restenosis occurs in 25-50% of patients who undergo coronary angioplasty.

Availability

Available for exclusive license

MDA Ref No.: ID95-61/KVF/1095

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"WATER SOLUBLE TAXOL PRODRUGS"

Description:
Paclitaxel has shown remarkable anti-neoplastic effect in human cancer, primarily in advanced ovarian and breast cancer. A major difficulty in the development of paclitaxel for clinical trial use has been its insolubility in water. The amount of Cremophor EL necessary to deliver the required doses of taxol is significantly higher than what is administered with other marketed drugs that use the same formulation. Several toxic effects are also attributed to Cremophor, including vasodilation, dyspnea, hypotension, and hypersensitivity.

By conjugating taxol to metal chelators, researchers here have greatly improved its aqueous solubility. In addition, this taxol conjugate has been shown to be much more stable than other water-soluble taxol derivatives. Also, this new conjugate has demonstrated very strong antitumor activity in a variety of different cell lines both in vitro and in vivo.

This taxol analogue can also be radiolabelled and used to image the tumor and to determine the tumor uptake of taxol by single photon emission computed tomography or positron emission tomography. This imaging technique allows for the determination of in vivo pharmacokinetic properties of taxol. This radiolabelled analogue is able to detect tumors and to quantify the uptake of taxol in the tumors. This new technique can assist in the selection of patients for taxol treatment. By combining with paramagnetic and ferromagnetic materials, the analogue can also be used as a selective MRI imaging agent.

Market:
The market for taxol is tremendous. It has the highest dollar sales of all the anti-cancer drugs currently on the market, and is the second order of treatment for ovarian and breast cancer patients. In addition, it is used in the treatment of lung cancer, head and neck cancers, and in metastatic melanoma. Industry analysts estimate that Taxol sales in the U.S. will reach $180 million by 1995.

Availability:
Available for exclusive license

MDA Ref No.: ID95-51/KVF/0695

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"FIBER OPTIC PROBE FOR THERMAL INJURY DETECTION"

Description:
This fiber optic based device will detect and monitor the full extent of deep lethal thermal injury in living biological tissues during or within seconds of heating by various sources such as laser irradiation, heated solid materials, radiofrequency or microwave heating sources and/or electrosurgical devices. Use of this device coupled to the heat source will allow control of the size and/or extent of lethal thermal damage deep in the tissue during any thermal coagulative treatments using any of these sources. Up until now, the full extent of deep lethal thermal damage could only be detected one or more days after heat treatment by observation of tissue necrosis using pathologic techniques on tissues removed from the body.

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Web Page: www.mdanderson.org/~otd/

Well defined, measurable concentric zones of thermal damage characteristically form around single volume heat sources in several biologic tissues. Two visibly distinct zones develop within seconds of heating. These zones include a central white zone of coagulation and an outer red zone of blood (hemoglobin) accumulation due to thermally-induced hemostasis, hemorrhage and hyperemia. The boundary of lethal thermal damage is determined by measurements of changes and rates of change of back-reflected light intensity due to increased light absorption by hemoglobin accumulating at the outer boundary of the red thermal damage zone.

Market:
The potential marketable products would be the fiber optic detection device and the coupling system for automatic control of the heating source. Thermal coagulation of tissues is a medical application that can be improved with real-time control of lesion size. This treatment technique, has not enjoyed wide acceptance because clinicians have not been able to control the extent of lethal thermal damage. The detection device/control system will increase the use of localized thermal coagulation of benign and malignant tumors. This system can be applied to surface, percutaneous, endoscopic and open operative procedures.

Availability:
Available for exclusive or non-exclusive license.

MDA Ref No.: ID95-50/KVF/0695

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"QUANTIFICATION OF LIGAND/RECEPTOR COMPLEXES"

Product Description:
The activity of nuclear receptors is primarily regulated by their interaction with a specific ligand. The binding of ligand to receptor results in reduced sensitivity to protease digestion. Our studies have shown that the sensitivity of receptor to proteolytic digestion is directly proportional to ligand concentration. Both synthetic and cellular receptors have similar ligand binding properties, therefore the traditional receptor binding assays and this protease sensitivity assay yield similar results. The protease sensitivity assay has several advantages over the traditional "radioreceptor" assay, and can be used to test the affinity and stability of new synthetic ligands with unknown binding properties. It can also be used to test the receptor binding activity of metabolites, and to quantify the levels of receptor-binding steroid hormones in body fluids.

The advantages of this assay include a shorter time and cheaper cost to prepare the receptor. The radioisotope cost and assay time are much less than the traditional assay, and the actual labor time invested to do the assay is dramatically decreased. In addition, this assay is highly reproducible and has been proven to be far more sensitive than the traditional radioreceptor assay. It is a direct method to test receptor binding activity of metabolites and unknown ligands.

Market:
Basic researchers, large commercial laboratories, and hospital clinics can use this rapid and sensitive assay. Its reduced cost and sensitivity will be specifically appreciated in: 1) diagnostic tests of 1,25-dihydroxyvitamin D_3 in patients with disorders in calcium metabolism and bone remodeling, and 2) diagnostic tests of estradiol 17-beta in pregnancy or in patients with fertility disorders.

Availability:
Exclusive or non-exclusive license

MDA Ref No.: ID95-49(003GA)/KVF/0196

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"CERAMIDE'S EMERGING ROLE AS A PATHWAY REGULATOR"

Product Description:
Studies have shown that tumor necrosis factor and interleukin-1 both use the sphingomyelin pathway to effect signal transduction, which is initiated by hydrolysis of sphingomyelin in the plasma membrane to ceramide. Ceramide appears to act as a potential mediator of the effects of these extracellular agents on cell growth, differentiation, and apoptosis. A novel ceramide-dependent pathway of signal transduction is beginning to emerge. Research work here have shown that cell-permeable ceramides will cause cytotoxicity in a broad spectrum of human adherent tumor cell lines, irrespective of their TNF sensitivity. Expression of MDR or HER-2/neu does not affect the susceptibility of the human tumor cell lines to ceramide. Chemoresistance associated with HER-2/neu over-expression has been linked to poor therapeutic response and prognosis, particularly in breast cancer. Therefore, the cell-permeable ceramides could be used to induce apoptosis and/or cytotoxicity in solid tumors in vivo. In addition, liposomal ceramide has also been shown to induce cytotoxicity in these cell lines. The liposomal formulation delivers ceramide to the target cell via one or more possible mechanisms, and overcomes the problem of low solubility of hydrophobic ceramides in aqueous systems, including plasma. It also offers the possibility for passive or active tumor targeting of the ceramide in vivo.

Market:
The potential market for pathway and/or apoptotic regulators is enormous. Scientists have traditionally been most successful with cytotoxic agents, but now they are seeking to interfere with other growth mechanisms and signals that are unique to cancer cells. They are developing new and more accurate means of directing therapeutics at cancer cells by turning off and on regulators of cell growth and/or cell differentiation. The world market for anticancer drugs now exceed $5 billion and should top $10 billion by 1998. Given the degree of failure seen with currently used drugs, opportunity and profit clearly await new technologies to treat and perhaps cure cancer, even if they only capture a small portion of the market.

Availability:
Exclusive license

MDA Ref No.: 004GA (ID95-48)/KVF/0695

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"OVARIAN CANCER VACCINE"

Description:
Ovarian cancer affects a large number of women. Disease progression calls for novel therapeutic opproaches based on molecular reactions that mat control tumor development. Overexpression of HER-2/neu (HER-2) gene product on tumors is believed to play a central role in tumor progression.

The invention relates to a small peptide-based vaccine for cancer which is designed to function by inducing a tumor reactive cytotoxic T-cell response (CTL). Researchers from M.D. Anderson Cancer Center identified CTL epitopes of 15-20 amino acids from within the Her-2 protein and then enhance their immunogenecity by amino acid substitution at key anchor positions within the peptide epitope so as to incrase increase their affinity for the HLA transmembrane receptor. HLA-A2 is an immunodominant human lymphocyte antigen which is expressed in 45% of the caucasian population. He synthesized a series of 9-amino acid analogs of the HER-2 neu peptides and showed in an *in vitro* assay that these peptides can sensitize CTLs and cause lysis of ovarian tumor cells.

Market:
Gynecologic malignancies (comprised largely of carcinomas of the ovary, cervix, and endometrium) result in over 20,000 deaths in the U.S. per year. Annually, 70,000 patients are diagnosed with these malignancies.

Patent Status: Patent pending

Availability: Available for exclusive license

MDA Ref No.: UTSC:390/FSR/0395

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"ANTIMICROBIAL COATING OF CATHETERS AND OTHER MEDICAL DEVICES"

Description:
Catheter-related septicemia represents one of the most life-threatening complications of all catheters. Several surfactants and methods have been developed over the years to coat the surfaces of catheters with antimicrobial agents and other compounds. Most of these commonly used agents are very costly and often lead to phlebitis when used on vascular catheters. Scientists here at M.D. Anderson, in collaboration with others at Baylor College of Medicine, have developed a very simple and inexpensive method for coating catheters.

This new method allows for better binding of antimicrobial or anticoagulant agents, and could be very useful in coating several different kinds of catheters, including those made of polyurethane, silicone and polyethylene. Both vascular and urological catheters can be coated by this new technique. In addition, this new invention has been shown to bind much higher concentrations of antibiotics than the traditional methods. Also, the antimicrobial agents bound by this method maintain their efficacy against microbial agents in urine and in serum for a much longer period when compared to the same agents bound by the generally accepted procedure. The organisms used in the testing include the most common catheter-related bacteria and fungi.

Market:
Aging populations and an increasing emphasis on treatment of cardiovascular disease and cancer are spurring growth in the world catheter market. Sales are expected to grow 9% per year to reach $3,700 million by 1998, with the U.S. being by far the largest and one of the fastest-growing regional segments in the catheter market. The world urological catheter market is expected to reach approximately $276 million by 1998, and the central venous market is expected to be even bigger - $537 million by 1998. With these two market segments alone, the catheter market looks very promising, and any innovative technology that is able to command a portion of the market will be a sales booster for its company.

Availability: Available for non-exclusive or exclusive license

MDA Ref. No.: 432/KVF/0295

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"SUSCEPTIBILITY TESTING OF MYCOBACTERIA TO DRUGS"

Description:
Mycobacterial infections are on the rise, and this is partly due to the lack of an effective cure for both mycobacterial diseases and AIDS. Infections due to Mycobacterium avium-intracellular complex (MAC) are the most frequent and fatal complications in AIDS patients. Susceptbility testing of these microorganisms have been quite problematic and controversial. Either they take too long, are insensitive, or require the use of radioactive materials or other expensive equipment. Inventors here at M.D. Anderson Cancer Center have developed a technique which has considerable advantages over other methods currently in use for susceptibility testing.

Reducing the time for susceptibility testing of mycobacteria will enable clinicians to start therapy earlier than the time period presently used. This test is based on a colorimetric assay that is measured by simply reading the absorbance. Furthermore, this new method is rapid and can easily be standardized for many different drugs, without the use of expensive material and/or specially trained people.

Market:
Opportunistic infections are the major cause of morbidity and mortality in immunosuppressed individuals, particularly patients with cancer and AIDS. In addition, according to the World Health Organization, it is estimated that approximately one-third of the world's population is infected with the TB organism with 20 million individuals suffering from active TB. Therefore, the market for detecting mycobacterial diseases is thought to be quite substantial, with the potential for some 500,000 - 750,000 tuberculosis tests required worldwide.

Availability: Available for non-exclusive or exclusive license

MDA Ref No.: UTSC:459/KVF/0295

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"PACLITAXEL EXTENDED STABILITY INJECTION"

Description:
Paclitaxel, or Taxol as it is commercially known, is one of the most commonly used anti-cancer drugs today. It is approved for ovarian and breast cancers that do not respond to other treatments. Unfortunately, paclitaxel is very insoluble in aqueous solution and presently is formulated for injection in equal parts of a surfactant and dehydrated alcohol. The maximum stability time from preparation is about 27 hours, which is brief but adequate for one-day infusions.

Recently, several clinical protocols have called for multi-day continuous infusion of paclitaxel. This becomes a problem because the drug begins to crystallize out of solution after 48 hours. Also, the intravenous bags must be changed daily, requiring the patient either to remain in the hospital or make daily visits. This also increases the risk of systemic infection from contaminated iv lines. The result is increased cost and an inconvenience to the patient.

Researchers at M.D. Anderson Cancer Center have developed a formulation that modifies the existing, FDA approved, formulation. This "new" formulation has demonstrated extended stability in aqueous solution at much higher concentrations, and for at least 9 days without crystallization. This formulation could also be used with other drugs to increase their stability for multi-day use.

Market:
The market for taxol-based anti-cancer drugs is getting increasingly crowded, especially since Bristol-Myers Squibb will lose its exclusive marketing rights in the U.S. in December 1997. Of all the anti-cancer drugs presently used, taxol commands one of the biggest markets. Worldwide sales of this anti-cancer drug continues to increase each year.

Patent Status: Patent pending

Availability: Available for exclusive license

MDA Ref. No.: UTSC:394/0994/KVF

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NOVEL LIPOSOMAL FORMULATIONS OF CAMPTOTHECIN (CPT)"

In clinical trials conducted several ago, Camptothecin (CPT) was shown to be highly active against tumors particularly of the colon, lung, breast and ovary. However, use of this compound fell out of favor due to dose limiting toxicities and difficulties with solubility. Recently, interest in this drug has rekindled following the finding that the target for the compounds' cytotoxic activity is DNA topoisomerase I. Several analogues of CPT are currently being evaluated by others to overcome the aforementioned shortcomings associated with the parent drug.

This technology offers an alternative approach using a novel liposomal formulation of CPT as a means of reducing systemic toxicity while maintaining potency. The formulation has been shown to be stable and possess *in vitro* anti-tumor activity comparable to free drug. *In vivo* studies using a mouse model, demonstrated that liposomal CPT treatments increased the survival of inoculated animals as compared to those treated with free drug. These studies when taken together indicate that this technology has therapeutic potential. In addition, the use of the parent drug is substantially less costly as compared to analogues and is generally believed to possess a broader range of anti-tumor activity.

If you are interested in obtaining further information about this technology, please contact the U. T. M. D. Anderson Office of Technology Development.

MDA Ref No.: 333/0694

FSR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"PARTICULATE CONTRAST MEDIA FOR CT ENHANCEMENT OF LIVER TUMORS"

This disclosure relates to a new particulate contrast media derived from currently used water soluble, non-ionic contrast agents (lohexol, loxilan, lopromide) for hepatic tumors. The modifications to the currently used contrast agents make them more lipophilic, thus allowing one to apply established methods to produce particulate suspensions. The invention is essentially a "prodrug", that is targeted to the kupffer cells of the liver and is quickly degraded to the non-ionic contrast agent and CO_2, and cleared from the body.

Current products on the market have several disadvantages. The liposome encapsulated contrast agents have short half lives and other non-biodegradable contrast agents produce liver and chronic toxicities. This invention solves these problems by designing a particulate contrast media that is targeted to the liver, less toxic, more rapidly eliminated from the body, and can be sold in a lyophilized powder formulation-resulting in a longer shelf life.

Approximately 170,000 new cases of primary liver tumors are diagnosed each year in the US, while the incidence of metastatic liver disease is common in advanced cases of most solid tumors. In Africa and Asia hepatic tumors comprise between 10 and 50% of all malignancies. Worldwide sales of contrast agents for CT use reached $1.65 billion in 1991 and is expected to reach $1.79 billion in 1996.

MDA Ref No.: 006RA/0694

FSR

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Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"NOVEL RADIOLABELLED ANTIBODIES FOR THERAPY AND IMAGING "

Description

Treating and imaging cancer with radioimmunoconjugates is of particular importance because of its ability to target and deliver radiation directly to tumor cells without hurting surrounding normal tissues. Unlike conventional systemic cytotoxic therapy, systemic imaging therapy, and external beam radiation therapy, immunoconjugates are supposed to target tumor cells without harmful side effects.

Not all radiolabelled monoclonal antibodies are the same. Some are unstable, too large, or elicit an immune response and never reach the tumor. Others employ sub-optimal radioisotopes for either therapy or imaging. Still others are expensive and cannot utilize the same chelater to bind both diagnostic and therapeutic isotopes. Each of these reasons have hindered the use of monoclonal antibodies in the clinical setting.

Researchers at MD Anderson have developed a new method for preparing radiolabelled monoclonal antibodies that overcomes these obstacles. The model combines a unique chelater to a human immunoglobulin fragment that shows faster tumor uptake and reduced binding to normal tissues. The immunoglobulin fragment clears rapidly from the circulation to be a safe method for tumor imaging, binds long enough to the tumor to deliver the optimal amount of therapeutic radiation, and is small enough not to elicit an immune response. Furthermore, the chelate binds to both yttrium-90 and indium-111 for therapeutic and imaging purposes.

Early mouse, beagle and human clinical studies of radiolabeled antiferriten immunoglobulin in Hodgkin's Disease have shown excellent results in heavily pre-treated patients. Their experience has encouraged the scientists to pursue an IND and next generation products in other tumors using their established radioimmunoconjugate technology.

Market

The market for imaging Hodgkins Disease grows by 7900 people each year. The market for treating relapsed Hodgkin's Disease patients is smaller, but would fall under an orphan drug status. Other uses of their current antibody is in Kaposi Sarcoma and neuroblastoma. Furthermore, the market for using their technique to image and treat other cancers safely and effectively is enormous. If you are interested in receiving additional information about this technology, please contact the M.D. Anderson Office of Technology Development.

MDA Ref. No.: 406/1194-FSR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"METASTASIS ASSOCIATED BREAST CANCER GENE "

Breast Cancer is the most common form of cancer in the US and the third most deadly. In 1992 alone, there were 46,300 deaths and 180,000 new cases diagnosed. In the past two years breast cancer overtook lung cancer as the most common form, increasing at a rate of 26%. Breast Cancer has been on the rise primarily due to earlier detection as well as a growing population. Many scientists even think diet is involved. The mortality and morbidity associated with breast cancer will also most likely increase into the 21st century and place an even heavier burden on our healthcare system.

The development of diagnostic tools for early detection and treatment is paramount to our goal to reduce health care costs and to improve survival. Researchers at M.D. Anderson have discovered a gene associated with the metastasis of breast cancer cells. Therefore, it can provide a method for screening cells for metastatic potential. We are seeking patent protection for the gene, its protein product and methods of using the invention for diagnostic and research purposes. For example the DNA sequence will find utility as a probe or primer in nucleic acid hybridization experiments.

With approximately one out of every nine women at risk for breast cancer, the market for this technology is enormous. Any technology that could assist physicians diagnose and better treat their patients would be seen as a cost saver and in demand. If you would like further information regarding this technology, please contact M.D. Anderson Office of Technology Development.

MDA Ref No.: 387/FSR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"NON-INVASIVE BILIRUBIN MONITORING DEVICE"

Clinical jaundice occurs in about 10% of the 3.7 million newly born infants each year, and places them at risk of serious neurological damage. These infants receive blue light phototherapy to oxidize bilirubin and facilitate systemic clearance. Serum bilirubin levels are monitored by lab analysis of repeated blood samples from the baby, which places a burden on the limited blood volume of a premature infant and fails to continuously monitor the fluctuations and kinetics of the therapy. Most physicians are reluctant to draw blood from neonates and would favor a bilirubin monitor that offers the advantage of quick and noninvasive diagnosis to be used in the clinic or Neonatal Intensive Care Unit.

In the past, reflectance bilirubinometers have failed to give satisfactory correlations between transcutaneous and serum bilirubin concentrations in heterogeneous populations due to variations in skin pigmentation and therefore have not been widely accepted. Today, researchers at MD Anderson have developed a novel optical fiber-based monitor for bilirubin measurement. Clinical *In viv*o studies of 86 infants have shown the device reliably monitors bilirubinemia despite variations in skin pigmentation, blood volume, skin layer thickness, hydration, age, and health, all which influence skin optics and *in vivo* spectroscopy.

The efficacy and safety concerns surrounding the use of invasive monitoring indicate that there is a need for an effective and less dangerous alternative. In this regard, the market opportunities appear to be substantial. The total world market for clinical testing is estimated to be about $6.5 billion per year. The U.S. market for the bilirubin monitor is estimated to be about $50 million per year suggesting a significant commercial potential for this technology. If you would like further information regarding this technology, please contact M.D. Anderson Office of Technology Development.

M.D. Anderson has an issued patent for this technology.

MDA Ref No.: 254/0394 FSR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"SITE-SPECIFIC TOPICAL CONTRACEPTIVE"

Topically applied spermicides such as those containing nonoxynol-9 are somewhat effective agents in neutralizing sperm and thus preventing conception. Although these agents can be used alone, maximum birth control effectiveness can be achieved when used in conjunction with barrier methods of contraception such as condoms, diaphragms, and sponges. As a group, these forms of birth control which rely on preventing sperm from interacting with the unfertilized egg, are popular alternatives to hormonal based oral contraceptives. For many women, non-hormonal contraceptive methods are the only option due to either personal preferences or because of the well known side effects associated with birth control pills. Other women who usually tolerate oral contraceptives, often choose spermacides for their short term use, such as after childbirth.

Today, the FDA is currently raising questions over the efficacy of spermacidal products such as nonoxynol-9. Although studies show they are safe to use OTC, their active ingredients lose some of their efficacy in humans. Furthermore these agents, which are detergents, nonspecifically solubilize cellular membranes and have been associated with several toxic reactions both topically and systemically.

Scientists at M.D. Anderson have recently discovered a biochemical mechanism which has lead to the development of a more effective, novel and safe alternative to conventional contraceptive spermicide. The technology is based on the inhibition of specific cell surface receptors that mediate primary sperm-egg binding. These scientists have shown that certain enzymes exist on the surface of sperm where they function in gamete binding by interacting with specific oligosaccharide molecules on the egg coat. Animal studies have demonstrated that inhibition of these sperm enzymes can prevent sperm-egg binding. Thus, this site-specific technology can serve as the basis for methods to prevent fertilization. The proposed contraceptive composition can be formulated into lotions, creams, lubricants and therefore can be used in applications similar to current usages of spermicides: alone or as coatings for condoms, diaphragms and sponges.

The efficacy and safety concerns surrounding the use of detergent based spermicides indicate that there is a need for a more effective and less toxic alternative. In this regard, the market opportunities appear to be substantial. The US OTC market for female contraceptives reached $62 million in 1993 and U.S. sales of condoms with spermicide amounted to $228.5 million in 1991, suggesting a significant commercial potential for this technology. M.D. Anderson is pursuing patent protection for this technology.

MDA Ref No.: 325 04/94-FSR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"MEDICAL IMAGE MANAGEMENT SYSTEM"

Description

A new medical image management software system is currently being developed at M.D. Anderson and is designed to be used by radiologists, pathologists, surgeons, medical oncologists, and internists.

We expect the imaging system to provide tremendous benefits to M.D. Anderson and to other hospitals and institutions. Simultaneous access to pathology and radiology images for all physicians for diagnostic and therapeutic purposes is one goal of the project. Achieving a paperless radiology and pathology department would reduce costs and improve patient care by improving physician response time to diagnosis and treatment. The system also has the capability of displaying CD-ROM based video images which could be used for showing surgeries. In addition, we have plans that can potentially image-link M.D. Anderson to smaller community hospitals and other academic institutions around the country. These outside users could access valuable medical information for diagnostic, therapeutic, or educational purposes.

The software is designed to be compatible with macintosh, IBM, and SUN Microsystem operating systems for the desktop computer and is user friendly. It is not designed to replace a PAC system. M.D. Anderson's MIMS is designed to be an image storage and retrieval system.

Market:

The applications for this technology is widespread: 1)The medical decision support field in the hospital environment, 2) the medical education field centered on image-based teaching files, 3) the scientific research field also based on a catalog of medical photography for papers and talks, 4) telemedicine applications, and 5) image based research.

This system can be used in its entirety and because of its modular design can be broken into useful subsystems.

Availability: Available for exclusive or non-exclusive license

MDA Ref No.: ID94-18/FSR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"NOVEL TISSUE OPTICAL MEASUREMENT DEVICE"

This year over 500,000 new cases of skin cancer (squamous cell carcinoma, basal cell carcinoma, and melanoma) will be detected and one out of 500,000 moles will become malignant. These skin lesions are distinguished generally by subjective visual inspection and their definitive diagnosis requires time-consuming histopathological evaluation of exisional or incisional biopsies.

Since the optical properties of many diseased tissues are different than those of normal tissues, researchers at MD Anderson have developed a unique diagnostic device that offers a non-invasive method for differentiating the optical properties of tissue. This device can be used to distinguish diseased tissues from normal tissues earlier than conventional methods. Therefore, it can facilitate early screening and detection of skin cancers to maximize cure and reduce or even avoid unnecessary biopsies. When used in conjunction with an endoscope, the device can detect gastrointestinal diseases as well.

Currently there is no other device available to measure tissue optical properties *in vivo* efficiently and accurately. Furthermore, this device is portable and cost effective.

MDA Ref No.: 005RA
FSR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"NOVEL RADIATION THERAPY EYE SHIELD"

Researchers at MD Anderson have developed a superior and more efficacious eye shield to protect patients undergoing electron beam radiotherapy around the eye and eyelid. Conducting comparative studies on phantoms in the laboratory, they discovered the current eye shields on the market do not provide sufficient blockage to electron energies greater than 6MeV. These eye shields were designed primarily for orthovoltage x-ray.

Concerned for their patients' safety, the researchers designed and tested a new eye shield that possesses the following characteristics:

- Safer-- improves chances for preserving vision, fewer side effects, and fewer infections.
- Greater applications-- protects ocular structures against electron energies up to 9MeV.
- Claims of efficacy are supported by data.
- Product is as comfortable as existing eye shields.

While a patent is being pursued, MD Anderson is searching for the appropriate licensee. High demand is predicted once the product is advertised. More than ten hospitals have already called MD Anderson to place orders.

Three prototypes are already being clinically tested and the experimental phantom designed in the laboratory can be sold separately as a quality control test kit to the manufacturer. Please contact The Office of Technology Development if you are interested in licensing this technology.

MDA Ref No.: 003RA
FSR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"LOW COST, NOVEL HYBRIDIZATION UNIT"

Trained molecular biologists and technicians have many safety concerns when performing procedures that involve hazardous materials in the laboratory. In the past scientists were forced to manipulate rudimentary heat sealable plastic bags to perform hybridization techniques, cognizant of the risks involved. An alternative then came on the market -- the hybridization cassette, specifically designed for hybridizations and elimination of radioactive exposure from spillage. However, its cost $225-$375 per unit, was prohibitively expensive for the average scientist.

Today, an MD Anderson scientist has developed a third generation device that not only enables the molecular biologist and technician to perform hybridization procedures hazard-free, but also can be manufactured for pennies per unit. It can withstand temperatures from -80^{0}C to100^{0}C, is water tight, and allows one to introduce and remove hazardous materials safely. Furthermore, the device may be used for many other procedures needing a liquid containing closed system and where cost is an issue.

If you are interested in licensing and manufacturing this technology that would be used daily in over 40% of all molecular biology labs nationwide, please call MD Anderson's Office of Technology Development. A patent is being pursued.

MDA Ref No.: 373/FSR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"NOVEL FIELD ABUTMENT EDGE-WEDGE"

One of the major problems with giving fractionated radiation treatment to large treatment areas is the possibility of under or overdosing at the field's edges due to either a gap or overlapping of treatments. Despite the careful matching techniques by radiation oncologists, an open beam mismatch of +/- 1 cm could result in an overdose or underdose of +/- 100%. With the moderately sloped edge-wedge designed at MD Anderson, a similar mismatch of +/- 1 cm would result in an overdose or underdose of only +/- 15%. Certainly everyone could appreciate this improved safety profile.

The unique design of MD Anderson's edge-wedge allows for superior treatment performance over other wedges on the market:

- treatment fields of up to 40cm long in any fractional incremental step
- the possibility of shaping two simultaneous penumbra-- either two wide or one wide and one sharp penumbra
- the ability to position the wedge in any 90^0 angle orientation due to attachment of the device downstream of the standard beam.

Medical linear accelerators comprise a growing market for use in radiation therapy with approximately 2000 medical linear accelerators in operation around the country. The edge wedge is designed to be an accessory to the linear accelerator and therefore M.D. Anderson is looking to license the technology to a manufacturer familiar with the medical linear accelerator market.

MDA Ref No.: 94-03/1193
FSR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"SMART LAPAROSCOPIC DISSECTING DEVICE"

One of the major problems in advancing laparoscopic surgery is the loss of tactile sensation which is indispensable for surgeons to dissect in the abdominal cavity. This is especially important when surgeons have to dissect blood vessels. If laparoscopic surgeons could hear blood vessels as they dissect, we could replace tactile sensation with hearing.

A surgeon at M. D. Anderson has developed a novel laparoscopic instrument which would benefit any laparoscopic or thorascopic procedure that required dissection around major blood vessels. Its novel construction and additional features would be useful for alerting the surgeon of major blood vessels during a laparoscopic resection and identifying their location, thereby preventing the surgeon from lacerating the vessels. Furthermore, its novel construction provides benefits unlike any other disposable doppler probe currently on the market.

Any laparoscopic device that increases accuracy, improves safety, and decreases the time of any laparoscopic procedure will gain a competitive edge over existing devices. Currently the laparoscopic market is very strong and analysts estimate it will explode in growth over the next few years, reaching 2.4 billion dollars worldwide by 1995. Please contact us if you are interested in learning more about this exciting technology.

MDA Ref No.: 93-007/0993
FSR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"NOVEL DEVICE FOR BRACHYTHERAPY"

Local-regional control of tumors of the head & neck, chest, pelvis, and extremities can be treated by chemotherapy, surgery, or radiation, alone or in combination. In particular, radiation therapy for cancer treatment has been used successfully for curative or palliative intent and is administered via external beam, internal irradiation or both depending on the patient's tumor.

Internal irradiation, or brachytherapy refers to the placement of a radioactive source, usually contained in a specially designed applicator, inside the body. This method allows for a concentrated dose of radiation to reach the tumor site without damaging nearby tissue and thus provide a targeted form of radiation. Today brachytherapy devices utilize different radioactive isotopes (gold, palladium, iodine) and applicators to best match the dosage and duration of radiation that is needed for a specific treatment regimen.

Researchers at M. D. Anderson have designed a new brachytherapy device aimed at overcoming the disadvantages with current brachytherapy. The radioisotope used emits low energy x-rays and possesses a shorter half-life than iodine-125, thereby reducing unnecessary patient exposure. The casing for the radioisotope does not absorb the radiation like conventional titanium welded tubing, but rather provides a superior distribution for the radiation. Still in the pre-prototype stage, this new device once developed, would provide a more uniform distribution of radiation, safer toxicity profile for patients than iodine-125 seeds, and safer handling for radiation therapists than gold seeds. If marketed effectively, this new device could replace gold and iodine-125 seeds currently available.

MDA Ref No.: 93-036/0893
FSR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"DACH PLATINUM COMPLEXES"

Description

The University of Texas M.D. Anderson Cancer Center has obtained a series of composition of matter and method of use patents on a class of compounds that represents the next generation of platinum cancer chemotherapy agents.

Platinum compounds have been used in anticancer therapy for 20 years despite their high degree of toxicity such as irreversable nephrotoxicity, ototoxicity, and peripheral neurotoxicity. Although new platinum drugs, such as carboplatin have been developed that have safer profiles, these drugs are less potent and not as active against the same resistant cell lines as cisplatin.

To overcome these drawbacks, researchers at The University of Texas M.D. Anderson Cancer Center have developed a new generation of potent platinum anti-cancer compounds over the past few years.

These new water soluble 1,2 - Diaminocyclohexane (DACH) platinum complexes demonstrate a broader spectrum of activity, increased antitumor activity, and reduced toxicity in mouse models.

Other highly water soluble analogs show a distinct superiority over existing platinum complexes by virtue of overcoming more than one mechanism of resistance. In animal models they have been shown to be active against cisplatin and tetraplatin resistant cell lines (DDP-resistant L1210, DACH-resistant L1210, and M5076). No other analog appears to have activity against both resistant cell lines.

Market

Clinicians and researchers at M.D. Anderson strongly believe that these compounds have significant potential as potent anti-tumor agents and represent a fertile area for drug development. World-wide sale of metal-complex anticancer chemotherapeutic pharmaceuticals is approximately $220 million and are expected to grow to $380 million by 2000. Thus, there appears to be substantial commercial opportunities for novel platinum analogs with improved clinical performance.

Patents

U.S. patents 5,011,959; 5,041,578; 5,132,323; 5,288,887; 5,318,962; and others pending. International patent protection is also being sought.

Availability: For exclusive license
MDA Ref. No.: 099/040/214/294/308/369 FSR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"ENTRAPPED WATER-INSOLUBLE THERAPEUTIC AGENTS"

Drug delivery systems for water insoluble therapeutic substances is considered one of the most fertile areas for medical product development, with an estimated world wide market potential of $4 billion in the 1990s. Biodegradable microencapsulation has been identified as the most promising of the many new drug delivery systems currently under investigation. M.D. Anderson has applied for patent protection on just such a delivery system for new potent anticancer agents comprised of formulations of non-water soluble drugs such as retinoic acid or anthracycline analogs entrapped within a biodegradable polymeric microparticle. The resulting pharmaceutical formulation permits the intravenous delivery of otherwise unstable drugs. It provides a stable formulation for the intravenous injection of a highly potent but previously unstable anticancer agent, increasing its antitumor activity and decreasing its toxicity.

MDA Ref No.: 086-0490

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"CYCLIC IMMUNOAUGMENTING PEPTIDES"

Based on the immunoaugmenting peptide Tuftsin, this invention is cyclic peptides that are anticipated to have therapeutic value while resisting degradation.

Tuftsin is a natural hormone-like peptide that enhances the immune response to disease. It was characterized in the early 1970's as the portion of the human leukokinin molecule responsible for stimulating white blood cells. These two cyclic analogues to Tuftsin were synthesized rationally to have the following advantages: greater potency than Tuftsin itself; and conservation of activity when administered orally due to their cyclization.

These analogues should be useful as immunoaugmentors in AIDS, cancer, sickle cell disease, splenectomy, and trauma. A gauge of the potential market for these peptides is the market for other immunoaugmenting growth factors such as Granulocyte Stimulating Factor (G-CSF), estimated to have a 1992 market of $500 million or more.

MDA Ref No.: 277-0792/TLR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"HIGHLY ACTIVE IMMUNOAUGMENTING PEPTIDE" (TUFTSIN ANALOG)

This invention is a pharmaceutically active peptide that is a non-toxic therapeutic product with wide ranging applications. The peptide is a natural substance which is an immuno-augmenting agent for treatment and prophylaxis of cancer and infections. A gauge of the potential market for this product as an anti-infective therapeutic is the market for other immuno-augmenting growth factors such as Colony Stimulating Factors (CSFs), estimated to have a market of between $225 million to $250 million in the United States by 1993 and $600 million by 1998.

The peptide was derived from Colony Stimulating Factors in an effort to develop an analog of tuftsin with improved biologic activity. Tuftsin is a natural hormone-like peptide that enhances the immune response to disease. It was characterized in the early 1970's as the portion of the human IgG molecule responsible for stimulting white blood cells. A U.S. patent has been issued to The University of Texas System for an analog of tuftsin that is more biologically active and is easier to chemically synthesize. Foreign patent applications for the analog are pending.

In vitro studies show that the analog is taken up by white blood cells more easily than tuftsin, stimulates the proliferation of white cells better than tuftsin, and show a great enhancement over tuftsin of the disease fighting capacity (cytotoxicity) of the immune system. It is anticipated that that analog will retain the extremely low toxicity of tuftsin (LD10 4g/Kg in mice; LD50 in mice of intravenous tuftsin is 2.4g/Kg body weight, which is 5,000 times highter than the optimum antitumor dose). In fact, no acute or chronic toxic effects have been observed with tuftsin. Tuftsin has been administered to humans intravenously or by injection, although other formulations may be possible.

Like tuftsin, the analog also has potential for the treatment of infections including sickle cell anemia related infections, post-splenectomy sepsis, post-trauma infections, and systemic lupus erythematosus-related infections. Tuftsin has been shown to have anti-cancer and anti-AIDS activities in human clinical trials in Israel.

Patent Status: U. S. Patent obtained
Availability: For exclusive license
MDA ID#: 124-0490 - (MEB)

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"GENE THERAPY FOR TREATMENT OF BREAST AND OVARIAN CANCER"

This invention is a possible gene therapy method for the treatment of breast and ovarian cancer. According to The American Cancer Society, there are approximately 176,000 new cases of breast cancer per year. As one indicator of the U.S. market size for breast cancer therapeutics, the market for tamoxifen is about $115 million. This invention involves the use of one gene (E1A) to suppress the cancer-causing properties of another gene (Neu).

The Neu oncogene is a cancer-causing gene originally isolated from rat neuro/glioblastomas. The human counterpart of Neu (also called HER-2 or c-erbB2) is amplified in 25-30% of human primary breast and ovarian cancers. Neu overexpression in breast cancer is a prognostic factor in that patients which overexpress Neu have a significantly shorter survival rate and a shorter time to relapse than non-overexpressing patients.

E1A is an adenovirus gene which activates other adenovirus genes by modifying the host cell transcriptional apparatus. Introduction of the E1A gene into Neu-transformed cells results in reduced expression of the Neu gene product, suppression of tumor formation, and suppressed metastatic progression.

When E1A is introduced in Neu-containing cancer cells ("transformed cells") the transformed cells become normal (non-transformed, flat morphology and contact inhibited growth). There was no observable effect of E1A on non-transformed control cells (NIH 3T3). Nude mice injected with Neu transformed cells rapidly develop large, highly metastatic tumors. Introduction of E1A into the nude mouse system results in no detectable tumors or dramatically smaller tumors with greatly reduced metastatic progression.

To confirm that E1A is a transformation suppressor for human cancer cells overexpressing Neu, experiments to extend these results into human breast and ovarian cells are on-going. Ultimately, E1A could be constructed into a retroviral vector as a therapeutic modality for breast cancer patients with poor prognosis. At least one retroviral vector has been approved by the FDA for human experimental use, and has been used at NIH for gene therapy of ADA deficiency. Gene therapy, while not without risk, does hold the promise of truly effective, long term therapeutic benefit to poor prognosis patients.

MDA Ref No.: 203-1291 MEB

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"OVARIAN CANCER: DIAGNOSTIC AND THERAPEUTIC HUMAN MONOCLONAL ANTIBODY"

Background
This invention is the first human monoclonal antibody that has been determined to be reactive with the cell surface of human ovarian carcinomas. Most other reported human monoclonal antibodies are reactive with internally located cellular antigens, thereby precluding such antibodies from reaching their target in the clinical situation. M.D. Anderson's antibody is also reactive with certain other malignancies such as colon, breast, and some melanomas, but has little or no reactivity with most normal tissues. Intraperitoneal administration of the radiolabelled human monoclonal antibody to nude mice with transplanted human ovarian tumors resulted in radioimaging of the

transplanted growing tumors with excellent results. This has encouraged the investigators to prepare an IND for the product and prepare for a clinical trial in 15 patients.

The nucleotide sequence of the antibody and the antibody itself has been characterized and is produced by a reasonably stable hybridoma cell line that was generated over four years ago. The antibody has been immortalized by sequencing variable portions of the antibody that include a segment that binds specifically to an antigen on the target cell.

The antibody will be useful for imaging and treating tumors in direct or antibody guided therapy with isotopes, chemotherapy, or other cytotoxic agents. Most recently this antibody has been successfully used in the clinic with a unique chelator that binds to both diagnostic (yttrium-90) and therapeutic (indium-111) isotopes and shows faster tumor uptake and reduced binding to normal tissues. Furthermore, we have studies to show that the immunoglobulin fragment clears rapidly from the circulation to be a safe method for tumor imaging, binds long enough to the tumor to deliver the optimal amount of therapeutic radiation, and is small enough not to elicit an immune response.

Market
M.D. Anderson believes this technology has very promising clinical potential. Gynecologic malignancies (comprised largely of carcinomas of the ovary, cervix, and endometrium) result in over 20,000 deaths in the U.S. per year. Annually 70,000 patients are diagnosed with these malignancies. The projected U.S. market for a diagnostic and therapeutic antibody for ovarian cancer alone is $50 million.

Patent Protection: A patent to the monoclonal antibody has been allowed.
Availability: Available for exclusive license
MDA Ref. No.: 216/436-04/95 (FSR)

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"CELL-CELL ADHESION IMAGE ANALYSIS SYSTEM"

The invention is a hardware/software system based on video-microscopy digital image analysis technology. The system measures the adhesion mechanism of cellular interactions by quantifying the morphology of cell-cell aggregates. Specifically, it compares adhesion kinetics, population distribution, size distribution and aggregate morphology. Although initially designed to measure the cell-cell adhesion of lymphocytes, it can measure any cell-cell adhesion mechanism.

Adhesion is the initial step required for most lymphocytic functions. T lymphocytes are the critical cells responsible for breakdown or lysis of foreign cells by the immune system. The ability to quantify the reaction of T cell adhesion is important in studying immune system dysfunctions such as autoimmune diseases and cancers.

Currently, methods used to describe and compare the adhesion of cells exposed to various conditions are subjective. Methods involve double-blind experiments using technicians who view the reactions microscopically and grade the adhesion on a scale of one plus (1+) to five plus (5+).

Potential applications for this system include: differentiating leukemic cells from normal cells; estimating the probability of repeat heart attacks through measure platelet aggregation rates; and non-radioactive assays for measuring B- and T-cell proliferation. Basic Science researchers would find the invention especially useful in studying immunological and metastatic mechanisms. The market for this system would thus include research laboratories in cell biology, immunology and tumor biology, and diagnostic laboratories that serve oncology and cardiology hospitals.

MDA Ref No: 157-0490 (MEB)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"ENDOGLYCOSIDASE ASSAY"

Metastasis, or metastatic cancer, refers to the change in a tumor from being localized in a particular organ, to being dispersed through out the body. When a tumor becomes metastatic, the tumor cells spread to other organs, where they colonize, resulting in a new tumor taking hold in other colonized organs.

A simple blood test to detect metastases has been a long sought after diagnostic goal. Early detection of metastases is critical to treatment strategies and survival. Researchers at M.D. Anderson have developed a simple assay that can be performed on the blood serum of cancer patients to determine whether their cancer has metastasized. The assay detects the presence of an enzyme that is strongly associated with metastases. A patented solid phase substrate has also been developed to be used with the assay. This rapid and sensitive assay can be used with tissues, cell extracts, blood, or serum, and it can be used to monitor cancer patients for the presence of highly malignant cells before these cells can be detected by imaging techniques or routine examination.

This as a diagnostic product in the form of a kit to detect or predict metastasis.

Although the market for tumor marker diagnostics in the United States alone is estimated at $170 million, the technology will require some development before a product can enter this market. Less development would be necessary for a detection kit that would have a market in biological research laboratories. The assay might be adaptable to automation, adding value to the product in all markets.

MDA Ref No.: 27/58/152-0190

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"METHODS AND COMPOSITIONS FOR THE IDENTIFICATION OF METASTATIC HUMAN TUMORS"

This product is a diagnostic blood test in the form of a kit to detect or predict metastasis. The test has been used with breast cancer, but may also be useful with other cancers. U.S. and foreign patents have issued and additional patent applications are pending. Much of the product development has already been accomplished at M.D. Anderson, so relatively little effort should be required to complete the development to product form. No blood test is currently on the market for the specific detection of metastasis. The U.S. market for tumor marker diagnostics is estimated at $190 million.

Breast cancer is the leading cause of death in middle aged women in the United States and Western Europe. Almost all women that die of breast cancer succumb when their cancer spreads to other sites (metastasis). A simple blood test for the early detection of metastasis has been a long sought after diagnostic goal because early detection of metastasis is so critical to treatment strategies and survival.

Researchers at M.D. Anderson have developed a simple assay that can be performed on the blood serum of cancer patients to determine whether their cancer has metastasized or to assess their risk of metastasis. The assay uses antibodies to detect the presence of an enzyme that is specifically associated with metastasis. Antibodies are molecules that bind only to very specific molecular features, called antigens, of a cell or of another molecule. In this case, the antigen is a particular fragment of the enzyme. The antigen is used both to generate antisera and to purify high affinity antibodies from the antisera by affinity chromatography.

Monoclonal antibodies are currently available for detecting breast cancer cells. However, the specific features to which they bind have not been determined and, as a result, most of them also bind to normal breast tissue and benign breast tumors. None of these antibodies preferentially bind to metastatic cells. The limitations of these breast cancer detecting antibodies have been overcome by using a well defined antigen specific for metastasis to purify specific high affinity antibodies.

The antibodies developed here can be used to (1) detect the presence of malignant breast cancer cells with high amounts of the indicator enzyme; (2) detect the presence of the indicator enzyme, or its fragments, in blood or sera; (3) reveal the location of metastatic tumors by linking the antibodies with easily detectable labels; and (4) develop specific treatments against metastases.

MDA Ref No.: 28/58/115/193-0590

Related technology has also been developed, including an enzymatic assay using a patented solid phase substrate to detect or predict metastasis, and a purified metastasis-indicator enzyme from a different enzyme family than that described above, from which immunologic and enzymatic assays for metastasis will be developed.

MDA Ref No.: 28/58/115/193-0590

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"RECOMBINANT B-CELL GROWTH FACTOR"

B-cells play an important role in the immune system. Among other things, they are responsible for secreting antibodies into the blood as part of the immune response to disease or infection. When B-cells become activated in response to the presence of disease, they proliferate very rapidly.

This invention is a DNA sequence (a "gene") that encodes for a polypeptide (a small protein) that stimulates B-cell proliferation. The invention also includes a method for cloning the DNA sequence using recombinant DNA techniques. The cloned DNA sequence has been shown to produce active B-cell growth factor, that is, the cloned gene "expresses" the factor that stimulates B-cell proliferation. The ability to clone and express the gene for B-cell growth factor will allow large scale production of the factor for both experimental and therapeutic purposes.

The initial market for this invention is research products. Such products would be useful in immunology, cell biology, and tumor biology laboratories. Eventually, second stage markets will develop in therapeutic products to treat immuno-compromised patients (a common complication of AIDS) or to enhance the immune response to diseases such as cancer or to viral diseases such as the common cold or herpes.

MDA Ref No.: 063-0490
(MEB)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"ORGAN GROWTH STIMULATION AND INHIBITION FACTORS"

Metastases, or metastatic cancer, refers to the change in a tumor from being localized in a particular organ or clump, to being dispersed through out the body. When a tumor becomes metastatic, the tumor cells spread to other organs, where they colonize, resulting in the cancer taking hold in the colonized organ. The metastatic cells do not, however, spread to other organs at random. They preferentially spread to particular organs. The preferred organ of colonization depends on the nature of the tumor and the organ of tumor origin. For example, when a cancer of mammary gland becomes metastatic, the metastases preferentially colonizes the lung.

This invention is a growth factor, purified to homogeneity, that stimulates the growth of lung-metastatic rat and other species of mammary tumor cells. Until now, no differential growth stimulating, or inhibiting, factor for metastatic cells had ever been purified and characterized. The isolation and characterization of this factor will contribute to understanding the mechanism of metastatic spread. The invention may be used to develop methods to inhibit the growth of metastases. It is possible that the invention might be similar to the substances that cause the regeneration of damaged organs, and could be used for this purpose, or, alternatively, it could be used to develop growth inhibitory factors that might be useful in hyperplastic diseases.

The initial market for this invention is for laboratory research products. Such products would be useful in cell biology, tumor biology, and biochemistry research laboratories. As the invention is better characterized, and corresponding inhibitory factors are developed from it, second stage markets will appear in therapeutic products to treat cancer, organ regeneration and hyperplastic diseases.

MDA Ref No.: 073/268-0490

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"GROWTH ARREST OF PROLIFERATING CELLS"

This invention is a method for stopping the growth of proliferating cells. Most agents that prevent cell proliferation are directed toward the DNA synthesis that occurs during cell division. The method of this invention, however, is directed toward intervening in the cell growth processes catalyzed by an enzyme, at a stage in the cell cycle prior to DNA synthesis. The method is based on the use of enzyme inhibitors to block the action of an enzyme that stimulates cell proliferation.

Two situations of particular interest where cells proliferate are cancer and the immune response. Cancer is a disease where cells are rapidly proliferating in an uncontrolled way. The immune system responds to disease by causing the proliferation of specialized immune cells. One type of immune cell, the T-cell, proliferates and kills diseased cells. Another type of immune cell, the B-cell, proliferates and secretes antibodies against the disease.

A line of special B-cells exists that is dependent on a substance called B-cell Growth Factor (BCGF). In the absence of BCGF, these cells do not proliferate, but, in the presence of BCGF, they proliferate readily. The invention has been shown to arrest the proliferation of these B-cells in the presence of BCGF (the invention does not act on BCGF). The invention has also proven effective against a variety of rapidly proliferating malignant cell strains.

The initial market for this invention is in research products to screen for inhibitors of the growth stimulating enzyme. Such products would be useful in cell biology, tumor biology and immunology research laboratories. As scientific advances continue, second stage markets will develop for therapeutic products to treat cancer, autoimmune diseases, and allograft rejection, as well as diagnostic products to screen patients receiving enzyme inhibitor therapy. The invention has particular advantages as a chemotherapeutic agent against cancer. Most chemotherapy regimes use agents directed toward DNA, and are therefore toxic to normal cells, not just malignant cells. This invention, when used in combination with other chemotherapeutic agents not targeted at DNA replication, has the potential for great effectiveness against malignancy with much lower toxicity than conventional chemotherapy.

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(MEB)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"METHOD FOR DNA ISOLATION"

Cloning, genetic engineering, and probes are important tools in biotechnology. These techniques involve the manipulation of genetic material, either DNA or RNA. The need for isolated quality genetic material has increased considerably in recent years. This invention is an inexpensive, easy and rapid method to isolate large, intact genetic material from a wide variety of sources, free from degrading contaminants and suitable for use in experimental or industrial systems. The key to the method is a reagent that dissolves the cell for extraction of the material while at the same time removing protein contaminants and inactivating denaturing components of the cell.

Although different techniques for isolating genetic material from cells have been used for many years, the method of this invention is a breakthrough. Up to now, state of the art techniques required more steps, some requiring great skill, such as density gradients, and frequently involved harsh treatment such as ultracentrifugation. This method has fewer steps and less handling, allowing for greater recovery of large strands of material intact. It requires no expensive equipment and can be performed without any special skills or training. No restrictions have yet been found on the types of cells or tissue that may be used as the source of genetic material. The method is equally suitable for small scale bench-top applications as for large scale production applications. The method can easily be adapted for automation or for packaging as a kit.

The initial market for this invention is primarily in entities that manipulate genetic material. Such entities include academic and industrial basic research laboratories in fields such as molecular biology, biochemistry, virology and cellular biology, as well as biotech companies involved in cloning or genetic engineering. The human genome project is anticipated to greatly enhance the research market for this invention.

The forensic use of DNA fingerprinting is expected to be a sizable market for this technology. A market already exists in companies that provide diagnostic or screening services using DNA probes. It has been projected that this market will exceed a billion dollars world-wide by 1995. Therapeutic markets may develop in gene therapy for genetic diseases.

MDA Ref No.: 133-0490
(MEB)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"INHIBITORS OF TUMOR INVASIVENESS OR METASTATIC PROFUSION"

Metastasis, or metastatic cancer, refers to the change in a tumor from being localized in a particular organ or clump, to being dispersed through out the body. When a tumor becomes metastatic, the tumor cells spread to other organs, where they colonize, resulting in the cancer taking hold in the colonized organ. Metastasis is the most lethal form of cancer and is the most difficult to treat effectively. A method to inhibit the spread of a potentially metastatic tumor is a critical goal in the war against cancer.

Metastasis occurs in discrete steps. One of the earliest steps is the invasion by the tumor of the surrounding tissues from the organ of origin. This step requires that metastatic cells penetrate the barrier membrane that separates organs and other tissues in the body. Metastatic cells produce an enzyme that degrades the barrier.

Researchers at M.D. Anderson Cancer Center have developed chemical derivatives that inhibit the action of this enzyme. Therefore, metastasis can be inhibited at a very early stage of its progression. Administration of any of the derivatives was shown to dramatically reduce metastasis in a variety of tumors both in tissue culture and in mice. The derivatives are suitable for the development of therapeutic products for the treatment of cancer patients to reduce the chances of, or prevent entirely, the metastatic spread of their tumors.

The most promising market for products using the derivatives is therapeutic products for health care providers.

MDA Ref No.: 143-0490

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"INHIBITION OF SYSTEMIC HYPOTENSION PRODUCED BY BIOLOGICAL RESPONSE MODIFIERS"

The University of Texas M.D. Anderson Cancer Center and Cornell Medical School have developed a proprietary compound and method of use to prevent or treat septic shock and hypotension.

Hypotension is low blood pressure. It is frequently lethal. Septic shock, an acute form of hypotension, is the leading cause of death in hospital Intensive Care Units. Septic shock is caused by endotoxin produced by bacterial infection. In response to the presence of bacterial endotoxin, the body produces biological response modifiers (BRMs) which cause the blood pressure to drop, often to a critical level.

In the treatment of cancer, pharmaceutically available BRMs similar to those produced by the body in response to endotoxin, can be administered as chemotherapy. Hypotension is a dose limiting toxic side effect of chemotherapy with BRMs such as gamma-interferon, tumor necrosis factor (TNF), and interleukin-2. BMR chemotherapy would be more effective if toxic hypotension could be eliminated as a side effect without inhibiting anti-tumor activity.

BRMs induce hypotension by activating certain types of cells to produce nitric oxide (NO), a transient, highly reactive molecule that causes loss of blood pressure. Production of NO requires the presence of arginine. This invention inhibits arginine-dependent NO production and has been shown to block NO production by endothelial cells in vitro, and to restore normal blood pressure in hypotensive dogs treated with toxic doses of TNF. The invention suppresses BRM-induced hypotension without inhibiting BRM anti-tumor activity. It is superior to monoclonal antibody stragtegies against shock because 1) it does not prevent the therapeutic effect of the BRM, and 2) it acts immediately to reverse hypotension without the lag time required for monclonal antibody action.

The principal and most immediate market for this technology is in therapeutic products to treat septic shock. It has been estimated that the U.S. market for biological products to treat septic shock will be in the $500 to $750 million range and one billion dollars world wide by the early 1990's. There is also a sizable potential market in therapeutic products as adjuncts to BRM chemotherapy of cancer.

MDA Ref No.: 158-0490

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"LIPOSOMAL CHEMOTACTIC PEPTIDES"

The University of Texas M.D. Anderson Cancer Center has patented lioposmal forms of certain peptides that attract and activate macrophages.

Macrophages are migrating monocytes that are important in the cell-mediated immune response to disease. Macrophages transport compounds having immunomodulatory properties to a disease site such as a tumor, where they mediate tumor destruction by effector cells of the immune system. Such macrophage-mediated destruction can be enhanced by localizing these cells at the tumor site.

Compounds, particularly synthetic peptides, exist that stimulate macrophage activities such as chemotaxis, aggregation, enzyme secretion, as well as other functions relating to cell motility. The ability to localize such factors in the vicinity of a tumor would enhance the macrophage-mediated destruction of the tumor.

Researchers at The University of Texas M.D. Anderson Cancer Center have developed a formualtion to administer such chemotactic peptides so that they become enriched in a locality, particularly in the lung and liver. This system improves the activation of macrophages compared to aqueous solutions of chemotactic peptides and shows reduced toxicity compared to aqueous administration of immunomodulating compounds such as tumor necrosis factor. Administration of chemotactic peptides in combination with antibiotics, or anti-inflammatory or anti-neoplastic drugs may enhance the therapeutic efficacy of treatment. Experimental results have shown the elimination of viruses and proliferating tumor cells by alveolar macrophages stimulated by this administration system. The formulation is characterized by its excellent macrophage stimulating activity and by its excellent pharmacokinetics.

The product could consist of a kit of vials containing the various components for oral, parenteral, or topical administration. Colorings, flavorings, or perfumes may be added to enhance the appeal to the patient.

Although the invention was developed as treatment modality for cancer, it is adaptable to the treatment of any disease or inflammatory response and may, in fact, be most easily and rapidly developed into a product for the treatment of topical inflammatory infections. The market for products to treat infections of the mouth and nose, for example, is estimated to be $10 million. The power and versatility of this formulation holds the potential, however, for a great variety of therapeutic products.

MDA Ref No.: 187-0490/MEB

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"B-CELL LINES IMMORTALIZED WITHOUT EBV (AND METHOD)

The potential products represented by this technology include:

1) targeted drug delivery systems, the market for which may reach an estimated $400 million to $4 billion in the United States by 1992;
2) therapeutic drugs such as anti-cancer drugs from lymphokines derived from B-cell lines, possibly obtaining a share of the estimated $1.7 billion recombinant lymphokine market;
3) reagents for diagnostic and screening kits for clinical use, possibly obtaining a share of a potential $2 billion worldwide market for cancer screening;

The University of Texas System M.D. Anderson Cancer Center has applied for a patent on a novel method of producing liposomes coated with correctly oriented immunoglobulin FAb' fragments. The efficiency of covalent FAb' binding to the liposomes is greater than 90%. The resulting immunoliposomes can be used to generate immortal human B-Cells lines *in vitro* from normal or patient donors. The immunoliposomes bind to B-cells and induce polyclonal activation. These activated B-cells can be immortalized with the use of other lymphokine factors. This immortalization process does not require Epstein-Barr Virus (EBV). Also, B-cells immortalized by the UT method are surface IgA and IgG positive, as opposed to EBV immortalized B-cells, which are surface IgM positive. Immunoliposomes will be valuable reagents to generate immortal cell lines for research. Immortal B-cell lines can potentially be used as an improved source immune B-cells for the production of monoclonal antibodies.

The relative simplicity of generating immunoliposomes, and their high binding efficiency and low toxicity, make the system a potential basis for scaled-up production of targeted drug delivery vehicles, such as for anti-cancer drugs and particularly drugs for B-cell lymphomas or neoplasias.

This technology has potential therapeutic applications. B-cell lines established from a donor can be used to generate homologous antibodies to help the donor fight a disease. Additionally, B-cell lines may be a good source of lymphokines produced by B-cells. It is possible that lymphokines produced from an immortal normal mammalian source will have better or more specific therapeutic activity, or lower toxicity, than the currently available genetically engineered lymphokines produced by bacteria.

MDA Ref No.: 117/175

The system can be used for diagnostic purposes. In familial studies, where a family member has been diagnosed as having B-cell lymphoma or B-cell neoplasia, or any other cancer, cell lines can be established from other members of the family and their risk of developing cancer in the future can be evaluated. A screening test may be developed. B-cell lines established from a donor could be subject to chromosomal analysis to determine whether or not blood from the donor is safe to use in a recipient.

MDA Ref No.: 117/175-0490
(MEB)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"ANTI-FILARIAL THERAPEUTIC"

This disclosure describes a medical breakthrough that is a potential cure for parasitic diseases caused by filarial worms in humans and domestic animals.

Nearly four hundred million people worldwide suffer from chronic parasitic infections caused by filarial worms. Such infections are a major cause of morbidity in endemic areas of Africa, Asia, the Middle East, Pacific Islands, Central and South America, Mexico, and the West Indies. These parasites are responsible for elephantiasis and river blindness. Mature female parasites can live for fifteen years or more inside the host, releasing thousands of larval worms (microfilariae) a day.

Current treatments for filarial infections are unsatisfactory. Chemotherapy is effective against microfilariae, but is not effective against adult parasites. The same is true for Ivermectin. Available chemotherapeutic agents, such as diethylcarbamazine, can induce a severe allergic response, known as the Mazzotti reaction, to the dead and dying microfilariae. The Mazzotti reaction can sometimes be fatal, or, with certain filarial species, result in permanent eye lesions and blindness. Control of mosquitos and other intermediate carriers of the parasites has not proven effective to prevent transmission of the infection.

Researchers at M.D. Anderson and at the University of South Florida have made an important discovery that is a potential cure for filarial infections. A U.S. patent application has been filed on this discovery. The patent application describes using a particular class of enzyme inhibitors to block the maturation of microfilariae and their release by an adult parasite. In doses non-toxic to the host, the adult parasite can be killed (unlike Ivermectin). The method has been shown to work *in vitro* and against transplanted infections in mice. The drug may be given intravenously, or possibly even orally, and offers a potential treatment for filariasis in humans and in animals of veterinary importance while possibly avoiding the side effects of toxicity or allergy observed with conventional chemotherapeutic agents of filarial infections.

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(MEB)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"AIDS VACCINE"

HIV (human immunodeficiency virus) has been implicated as the causative agent of AIDS (acquired immune deficiency syndrome). Although vaccines exist for many other types of viruses, none have been developed against HIV. The essential problem has been the unique properties of the virus.

The virus causes the body to produce both antibodies (made by B cells) and cells specialized for immune attack (T cells). Circulating antibodies have been shown to be ineffective in blocking virus infection and even appear to enhance the process of virus infection. These immunological properties of the virus have made it difficult to develop a vaccine.

Researchers at The University of Texas M.D. Anderson Cancer Center have developed a novel strategy to overcome these immunological roadblocks. The prototype vaccine would be composed of a mixture of synthetic peptides derived from proteins found in the virus. The unique property of such a vaccine is its ability to induce T cell immunity without inducing production of circulating antibodies that would enhance infection. Patent protection is being pursued for this technology which involves a pharmaceutical-like formulation that has no biological risk of infection.

The market for a safe AIDS vaccine is estimated to be more than $100 million in the U.S. This number is probably conservative due to a growing public awareness of the danger of the disease and a desire for protection against it.

MDA Ref No.: 060-0390
(TLR)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"BIOLOGICALLY REVERSIBLE PHOSPHATE PROTECTIVE GROUPS"

Many drugs that show excellent therapeutic activity in the test tube have proved disappointing when administered to patients because of the problem of biological incompatibility. In certain circumstances the drugs are rapidly degraded in the blood before they reach the target site. In other circumstances the drugs are not sufficiently fat-soluble to pass through the cell membrane. Chemists have long sought to overcome such problems by modifying the composition of the drugs to make them more suitable for administration to living organisms. "Masking Groups" are commonly used for this purpose. The masking groups are designed to be removed from the drugs once they reach the target site(s) so that they can perform their anticipated function.

Two promising classes of drugs that suffer from biological incompatibility problems are phosphates and phosphonates. Both types of compounds, being ionic, are usually unable to pass through cell membranes. Moreover, most phosphates are degraded rapidly in the blood. Masking groups have not been reported, so far, to overcome these limitations. Such masking groups have now been developed at the University of Texas M. D. Anderson Cancer Center. These groups allow phosphates and phosphonates to enter cells and be converted to active forms under biological conditions. The solubility of the modified compounds and their rate of activation can be controlled by judicious selection of the masking groups.

Applications of the technology include:

- Development of new anticancer, antiviral and antiparasitic drugs.
- Overcoming cell resistance to existing anticancer drugs.
- Counteracting specific metabolic deficiencies.
- Modulating vital biochemical pathways.

Patent protection has been obtained for this technology.

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(TLR)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NOVEL ANTI-TUMOR ALDOPHOSPHAMIDE ANALOGUES"

This invention relates to new anti-cancer and immunosuppressive drugs.

Cyclophosphamide has been used as an anti-tumor and immunosuppressive agent for many years. The drug is not active in its own right. It is converted in the liver to 4-hydroxycyclophosphamide, a metabolite that rapidly rearranges to aldophosphamide (ALD). ALD is highly unstable and spontaneously dissociates to phosphorodiamidic mustard (PDM), the presumed biologically active form of the drug. Because cyclophosphamide is not active unless it is metabolized in the liver, it has no therapeutic indications in certain clinical circumstances where this is not possible (see below). To overcome this limitation, ALD analogues have been developed at the University of Texas M. D. Anderson Cancer Center. These analogues are converted rapidly to ALD, and subsequently to the active metabolite PDM, by enzymes present in all tissues including cells in culture.

Potential applications of this new technology include:

- autologous bone marrow transplantation
- regional chemotherapy
- limb tumor perfusion
- in vitro tumor sensitivity testing
- development of anticancer drugs with novel mechanisms of action

The ALD analogues have already found use as bone marrow purging agents for AML (acute myelogenous leukemia) and ALL (acute lymphocytic leukemia) patients.

These compounds are chemically stable and relatively easy to prepare and formulate.

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(TLR)

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NON-CONFIDENTIAL DESCRIPTION
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"EXTREMELY POTENT ANTITUMOR ANALOGS"

The invention describes new chemical derivatives of doxorubicin up to 10,000 times more powerful than the parent compound. These new analogs are anticipated to have little or no cardiotoxicity and appear to act via a different biochemical pathway from the parent compound.

Doxorubicin is presently the ethical drug most widely sold for cancer chemotherapy throughout the world. It is, however, cardiotoxic at therapeutic doses, and resistance to the drug builds over time. The result is that higher and higher doses must be used to achieve palliation, but with increasing cardiotoxicity.

The inventors have developed and reduced to practice a method for synthesizing new doxorubicin analogs which have extreme potency in vitro. Toxicity testing with tumor cells indicates that these new analogs are up to 10,000 times more potent than doxorubicin while lacking the molecular features responsible for cardiotoxicity. Moreover, they retain their activity against tumor cell lines that are resistant to doxorubicin. Most interestingly, preliminary data indicate that the mechanism of action of the analogs is quite different from that of doxorubicin. These new analogs are stable, highly water soluble, and are activated intracellularly. The synthesis process is relatively uncomplicated, inexpensive, and yields greater than 50% analog.

If animal testing proves these new analogs to have reduced cardiotoxicity as well as extreme potency, they would be expected make a significant cut in the world market for not only doxorubicin, but for other chemotherapeutics as well. The market for all cancer chemotherapeutics is estimated to be $3 billion worldwide and $600 million in the U.S. alone. The world market in 1989 for doxorubicin was estimated at $250 million.

Patent protection on doxorubicin expired in 1988, and the patent for process protection will expire in 1991. The possibility of marketing exclusivity further enhances the attractiveness of these new analogs. Patent protection is being pursued on this technology.

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TLR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"CANCER-PREVENTING COMPOUNDS"

This disclosure describes the use of a certain class of compounds which can prevent the cellular damage caused by carcinogens.

It is widely accepted that all carcinogens (cancer-causing agents) operate by the same chemical mechanism: carcinogens are electrophilic (or become so within the cell), and these electrophiles react with nucleophilic DNA within the cell. Simply put, the DNA is damaged, and the stage is set for cancer. Scientists are now searching for ways of preventing cancer at this level, rather than responding to it once the disease has commenced.

One way of preventing electrophilic damage to DNA would be to introduce compounds which can act as intracellular scavengers. These compounds would act to "neutralize" the damaging effects of carcinogens on DNA. The requirements for an effective preventative scavenger are: 1) it must effectively block carcinogenic damage; 2) a therapeutic concentration must be possible within the cell; 3) it must be hydrophobic enough to interact with hydrophobic carcinogens; and 4) it must have minimal toxicity to the cell and organism. Although several compounds exist fitting the first three criteria, all have proven to be too toxic.

The class of compounds described here meet all these criteria. In in vitro and mouse studies, pre-administration of these compounds prevented the DNA damage associated with exposure to powerful carcinogens without toxicity or other discernable side effects.

A few of the possible areas where these compounds may find use include:

- people who are genetically predisposed to cancer
- workers in certain high-risk industries
- cancer patients who need an "antidote" for toxicity after a round of aggressive chemotherapy
- cigarette additive to help offset health risks
- vitamin supplement for the general population

Of these, chemoprevention offers the most immediate benefit for industry and public. The U.S. market for chemopreventives, largely untapped, is estimated at $300 million for 1990. As the public and industry move toward a proactive rather than a reactive position toward cancer, preventatives (both over-the-counter and prescription) will make up a larger and larger segment of the health care market. Patent protection is being pursued on this technology.

MDA Ref No.: 209/266-0390 (TLR)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"**DEFINED HIGH-CALCIUM MEDIUM FOR CULTURE OF EPITHELIAL CELLS**"

The invention is a proprietary "high-calcium," chemically-defined culture medium which makes possible the long-term culture of both human and non-human epithelial cells.

Two general types of media are presently used in cell culture: serum-supplemented and chemically defined. The former have been used for years in culturing various cell types because exact nutritional requirements were unknown; use of 10-15% animal serum or other crude extracts in a culture medium ensured that unidentified growth factors or other nutrients were present in sufficient quantity to encourage cell growth. Because of the undefined nature of any serum or extract, however, certain types of studies have been difficult or impossible.

This medium is specially formulated to support both the proliferation and differentiation of human and non-human epithelial cells without the use of undefined elements. It is particularly appropriate for culture of epidermal keratinocytes isolated from laboratory animals such as adult mice. The convenience and reproducibility of cultivation suggest this medium could enable carcinogenic, toxicologic, and biochemical studies in mouse and human model systems which have not been previously possible. Patent protection is being pursued on this technology.

Industry and academia are experiencing a gradual but definite changeover from serum-supplemented to chemically defined media. These media use no sera or other undefined elements, but rather add certain levels of hormones, growth factors, vitamins, etc. specifically tailored for the cell type under study. The use of defined media minimizes both batch-to-batch variation and potential of contamination. Moreover, defined media allow precise modulation of the cellular environment and can enhance purification of cellular products. The demand for defined media is expected to grow rapidly in the next ten years; industry analysts predict the market for defined media will increase from the present $200 million to $1.8 billion by 1999.

MDA Ref No.: 113-0390
(TLR)

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Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"**DETECTION OF CML mRNA**"

This disclosure describes a novel probe for the rapid detection of certain leukemias.

Chromosomal abnormalities are common in most forms of leukemia. 88% of chronic myelogenous leukemia (CML) patients have a chromosome abnormality known as the Philadelphia chromosome. Some patients with acute myelogenous leukemia (AML) have this abnormality as well.

These patients may benefit from diagnostic technology pioneered by researchers at The University of Texas M.D. Anderson Cancer Center. The test utilizes probes made through recombinant DNA techniques. These probes enable the detection of certain abnormal sequences in the patient's genes. The test is performed by running a quick "dot-blot" for detection of abnormal RNA. A positive result in the test indicates the patient may be suffering from a myelogenous leukemia. Probes presently commercially available for CML detect DNA translocations, and must be performed using the time-consuming "Southern" procedure.

Approximately 25,000 new cases of leukemia will be reported this year, a significant portion of which could benefit from this technology. The total market for DNA probe services is estimated to be $200 million worldwide. Patent protection has been issued for this technology, and continuations-in-part are pending.

MDA Ref No.: 024/70/108-0490
(TLR)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"NOVEL IMMUNOSUPPRESSIVE AGENT"

This disclosure describes an immunosuppressive substance produced in response to UVB light.

Artificial immunosuppression is important in preventing graft and organ rejection. Presently cyclosporin is the drug of choice to suppress the immune system into accepting foreign tissue. Cyclosporin has a number of side effects, however, and it also lowers the body's resistance to so-called opportunistic infections.

Ultraviolet light has long been known to exert an immunosuppressive effect, but the mechanism of its action has been unclear. The inventor and others have shown that it is UV-B light which suppresses rejection of foreign tissue (alloantigens). The doses of UV-B light which must be administered to achieve the effect are too high for clinical use, so the mechanism of action has been sought.

The agent has been tentatively identified, and studies are now underway to isolate the agent responsible for this immunosuppression. Preliminary data using cultured cells and mice show encouraging results.

The implications of this area of research are important in terms of clinical application. After the agent is characterized and tested, it can be used as an immunosuppressive in transplant and graft operations. This niche is presently occupied by Cyclosporin almost exclusively. The present worldwide market for Cyclosporin is in the about $1 billion, and transplantation is becoming more common. Furthermore, Cyclosporin will be losing patent protection in 1995, opening the market further for new immunosuppressives.

Patent protection is being pursued on this technology.

MDA Ref No.: 184/298/374-0390
(TLR)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NEW METHOD OF MICROENCAPSULATION FOR TARGETED DRUG DELIVERY"

This disclosure describes an improved method of synthesizing microcapsules and outlines some possible uses for the technology. Microcapsules are useful as sustained-release and specific-release drug delivery systems.

Most therapeutic drugs are administered in a single dose. The blood level of the drug increases rapidly after administration, then drops off again in rollercoaster fashion shortly after. The advent of time-release formulas (such as over-the-counter cold medicines) has solved a large part of this problem. The drug is diffused throughout the body, however, without specificity. Clinicians continue to seek not only improved methods of sustained drug delivery, but also methods for targeting drugs to particular organ systems within the body.

Such improved methods have been developed at The University of Texas M.D. Anderson Cancer Center. "Shells" ranging from 500 microns to less than 1 micron have been developed. These shells can contain solids, liquids, or gases, and are ideal for a number of applications including:

- targeted delivery of toxic substances such as chemotherapeutic agents.
- targeted delivery of imaging materials for diagnostic procedures.
- targeted delivery of dissolving agents for blood clots, cholesterol, etc.
- delivery of chemically unstable substances or emulsions.
- controllable rate of delivery for any therapeutic drug.

Varying the shell design not only controls delivery rate of the drug, but also allows cellular and organ targeting; such versatility has not been previously demonstrated.

Cis-platin, the cancer chemotherapeutic, has been successfully encapsulated, as have been a number of imaging agents for diagnostic procedures. Human phase I studies are expected to commence in 1991.

This technology potentially taps several lucrative markets. The market for cis-platin alone is estimated at $1 billion annually worldwide, while the market for water-based contrast materials for the nuclear imaging sector is estimated at $500 million. Patent protection is being pursued on this technology.

MDA Ref No.: 90-007/0390

Microencapsulation is an attractive technology for further exploitation. The capsules produced by this method are inexpensive, simple to synthesize, and are extremely cost-effective. These factors together make for a technology with a bright future in drug delivery.

MDA Ref No.: 90-007/0390

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"**ANIMAL TUMOR MARKER ASSAY**"

This invention relates to a general tumor marker which is specific for malignancy in animals.

Tumor markers are well-established as indicators of disease diagnosis and prognosis. However, most markers are specific to a particular organ or tumor type, so that some initial diagnosis must be made in order to select appropriate tests. In challenging diagnostic situations, often cancer is not even suspected. There has been no marker identified to date which is "universal" for all types of cancers.

Animals, as well as humans, are prone to develop various types of malignancies. Researchers at The University of Texas M.D. Anderson Cancer Center have developed an assay for a tumor marker which appears to be diagnostic for a number of different malignancies in animals. The marker is present in blood plasma and other body fluids (as well in the tumors themselves), regardless of the primary tumor site or type.

This assay has obvious applications in the diagnosis of cancers in animals. More uniquely, the assay also enables the clinician to verify remission after treatment and to monitor the status of disease recurrence. No test has been previously available which allows the veterinary clinician to predict the probability of relapse following treatment. The assay has been tested most extensively to date in dogs with lymphosarcoma, with excellent results. There is also strong evidence that the marker has value for other tumor types and for other animal species, including humans.

The assay will find use as a kit both in veterinary offices wishing to conduct timely in-house testing, and at veterinary reference laboratories which contract these services to veterinary clients. Furthermore, the assay is expected to make an impact on not only the companion animal market but also the agricultural sector.

Over an estimated 100 million pet dogs and cats live in the U.S., a significant percentage of which could benefit from this technology. Additionally, cancers in cattle, swine, poultry, and horses have a large economic impact in agriculture. For example, the world market for canine and feline health products is an estimated $350 million for 1990; the same market for horses is estimated to be $130 million. Patent protection is currently being pursued for this technology.

MDA Ref No.: 136/340-0390 (TLR)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"**HUMAN TUMOR MARKER ASSAY**"

This invention relates to a general tumor marker which is specific for malignancy in humans.

Tumor markers are well-established as indicators of disease diagnosis and prognosis. However, most markers are specific to a particular organ or tumor type, so that some initial diagnosis must be made in order to select appropriate tests. In challenging diagnostic situations, often cancer may not even be suspected. There has been no marker identified to date which is "universal" for all types of cancers.

Researchers at The University of Texas M.D. Anderson Cancer Center have developed an assay for a tumor marker which appears to be diagnostic for a number of different malignancies in humans. The marker is present in blood plasma and other body fluids (as well in the tumors themselves), regardless of the primary tumor site or type.

This assay has obvious applications in the diagnosis of cancers. More uniquely, the assay also enables the clinician to verify remission after treatment and to monitor the status of disease recurrence. Few tests have been previously available which allow the clinician to predict the probability of relapse following treatment. The assay has been tested most extensively in animals with excellent results, and preliminarily in humans. There is strong evidence that the marker has value for many animal species, including humans.

The assay will most likely find use as a kit both in hospitals and clinics wishing to conduct timely in-house testing, and at reference laboratories which contract these services to primary and secondary care physicians.

Cancer screening makes up a $3 billion market worldwide. The market for tumor marker screening is estimated to be $170 million in the U.S. for 1990, with an increase in growth expected as marker screening becomes more routine. Patent protection is being pursued on this technology.

MDA Ref No.: 131-0490
(TLR)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"**NOVEL METHOD FOR SYNTHESIS OF FLUOROTAMOXIFEN**"

Breast cancer is one of the leading causes of death in women. Tamoxifen, an estrogen analogue, is currently a standard treatment for certain subsets of women with breast cancer (also ovarian, uterine and prostatic cancers). Tamoxifen exerts its therapeutic effect by high-affinity binding to estrogen receptors, thereby preventing the binding of the patient's own estrogen (which would increase tumor cell growth).

Also, radioactive tamoxifen is being used experimentally as a diagnostic. Since it binds to estrogen receptors of primary and metastatic breast cancer tumors, the radiolabelling permits PET, MRI or CT imaging. 18-Fluorine is the radioactive atom most suitable for this application, yet synthesis of 18-fluorotamoxifen is long, difficult, and inefficient.

Researchers at The University of Texas M.D. Anderson Cancer Center have developed a novel method of synthesis for fluorotamoxifen which is simple, quick, and which produces a high yield. Furthermore, the binding affinity of this novel analogue to estrogen receptor is up to 5 times greater than tamoxifen. This analogue may therefore be useful in the diagnostic imaging of tumor sites. Furthermore, the high affinity may be useful in the therapeutic setting as well, since it would more effectively compete off the patient's own estrogen.

Another advantage of this new method is that tamoxifen may be radiolabelled at a high efficiency, which enhances its imaging ability and keeps costs down. Preliminary data indicate that 18-fluorotamoxifen can be prepared at 65% yield within one hour. These factors are particularly important since 18-Fluorine must be generated on a cyclotron and is quite expensive. Finally, initial studies indicate that intermediates in the synthesis can be conjugated to cytotoxic agents or contrast agents, which has far-reaching implications in diagnosis and therapeusis.

The synthesis has been completely reduced to practice, and work with rat models has demonstrated binding affinity. Animal testing is about to commence to test uptake of the receptor/analogue complex in a tumor-bearing rat model. Patent protection is being pursued on this technology.

The present market for therapeutic uses of tamoxifen is about $115 million in the U.S. Cancer diagnostics make up a market of over $300 million in the U.S.

MDA Ref No.: 189/225/309-0490 - (TLR)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NOVEL TUMOR MARKER FOR BLADDER CANCER"

This disclosure describes a simple method for the detection of bladder cancer.

The term "bladder cancer" encompasses several diseases, which together comprise the fifth most prevalent cancer among adults in the US. Much effort has been directed into research to identify tumor-associated urine markers as diagnostic and prognostic tools. Although increases in certain immunoglobulins in the urine have been linked with bladder cancer, until now no single urinary protein marker has shown to be of use.

Researchers at The University of Texas M.D. Anderson Cancer Center have discovered a novel protein in urine which correlates with bladder carcinoma. A sensitive and specific method for detection of the protein in the urine of cancer patients is under development.

The total market for tumor marker diagnostics is estimated at $170 million in the United States for 1990. Since bladder cancer accounts for 2% of all malignancies, the expected market could be extrapolated to a market of $3.5 million annually and $5 million worldwide. Patent protection is being pursued on this technology.

MDA Ref No.: 105-0390

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NON-CONFIDENTIAL DESCRIPTION
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"PLATELET ANTIBODY ASSAY"

M.D. Anderson has developed two latex agglutination immunoassay reagents for platelet antibody screening and patient-donor crossmatch. The reagents are useful for manual and flow cytometry kits and include proprietary latex coated antigen, controls, and diluents. The reagents provide a fast test for the detection of platelet reactive antibodies. Patients who have received multiple platelet transfusions often develop antibodies. Data supports the fact that patients sensitized to platelets who are transfused with crossmatch compatible donor platelets have a better therapeutic response. Also, by using the assay blood bank and transfusion centers can make more efficient use of their platelet donor reserves.

Two uses for the reagents are immediately identified. One, a screening reagent, is useful for the detection of serum anti-platelet antibodies. Test results are obtained in ten minutes and the test requires no special equipment. The second use is in crossmatch assay of patient serum with a platelet donor or a pool of donors. This test is useful for testing single donor platelet units against patients serum found to have antibodies to platelets.

The latex reagents are prepared from individual volunteer apheresis donors. Panels of platelet donors can be created for use in screening patients' serum. The assay requires microliter quantities of patient serum and the proprietary latex reagents. A crossmatch of 32 donors against one patient can be performed in 30 minutes. The test uses an ELISA reader. The assay using these reagents have certain advantages: the assay method is semiquantitative; the testing reagents are stabile for at least 3 months; the test results are available within 30 minutes; and, there is significantly reduced non-specific interference.

The University of Texas M.D. Anderson Cancer Center is proceeding with an on-going prospective clinical study to compare patient response to platelet transfusion with crossmatched and non-crossmatched donors. To date, 40 patient samples have been tested in parallel with an immuno-peroxidase assay in a screening test and resulted in greater than 95% agreement. Donor specific reagents have been made and assayed against patient sera as crossmatch assay. Using one-hour post transfusion platelet recovery data, the assay was shown to have a greater than 90% overall predictability of transfusion outcome in the 116 transfusions in 20 patients studied.

MDA Ref No.: 067/077/0390 - (TLR)

A ready market exists for the screening and crossmatch assay. There are over 4 million platelet transfusions/year in the U.S. This test is for platelet immunized patients requiring further platelet transfusions of single donor units. The estimated market for a platelet transfusion test is $20 million. Two patent applications are on file concerning this technology.

MDA Ref No.: 067/077/0390 (TLR)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"**CHROMOSOME-SPECIFIC PAINTING**"

This description outlines a breakthrough in chromosomal analysis which can be used in cancer diagnosis, genetic screening, and basic research. DNA probes developed to date detect specific portions of genes or chromosomes. When used to visualize chromosomes under a microscope, such probes detect only a small band or a small specific structure on a chromosome. For diagnostic and research purposes, there is a need to develop probes specific for the visualization of entire human chromosomes--i.e. a probe that will specifically stain all of chromosomes 1, another that will visualize chromosome 2, etc. Scientists at The University of Texas M.D. Anderson have done just that--developed a simple visual method for "painting" each human chromosome.

This invention opens new diagnostic avenues in genetic and cancer testing since it will allow for the ready detection of chromosomal translocations. Translocations, an abnormality involving exchanges of chromosome segments, are nearly always associated with some type of human disease, usually cancer. Use of this technology could enable technicians to immediately diagnose a translocation-associated disease by visual scanning of microscope slides. At present, the detection of translocations requires time- and labor-intensive banded chromosome analysis (karyotyping) with rigorous interpretation by expert cytogeneticists.

Since translocations are especially common in hematological malignancies, this test could be used in conjunction with other known clinical tests to enable tumor classification. More importantly, the availability of an easy and convenient method for visualizing diagnosed translocations will make it practical to monitor the effectiveness of treatment during the course of the disease. Also, the methodology will now make it possible to seriously investigate the role of translocations in solid tumors. Solid tumors are much more common in the human population, the inability to adequately visualize chromosomes in the cells of solid tumors, has made it difficult to determine their chromosomal bases.

Women undergoing amniocentesis or chorionic villus sampling could benefit from this test because of its ability to detect chromosomal abnormalities associated with birth defects. Women at risk (increasing in the population as young professionals are delaying childbearing until later years) will be able to have their pregnancies monitored not only for translocation abnormalities, but also for common chromosome "count" abnormalities (such as Down Syndrome). These probes will be uniquely useful in such analyses. The probes could be packaged in kit form for use in cytogenetic reference labs, cancer centers and hospitals, and universities. Patent protection is being sought for this technology.

MDA Ref No.: 206-0890(TLR)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"**DEVICE FOR FINE-NEEDLE ASPIRATION**"

Fine needle aspiration (FNA) is becoming increasing used as a minimally invasive method of tissue biopsy. The clinician inserts a needle into a suspected mass in the patient either by palpation or through radiologic guidance (under local anesthetic) and withdraws a tissue sample into a syringe. The sample contains cells which may then be subjected to standard diagnostic techniques including cytology, immunohistochemistry, and flow cytometry.

The procedure has been used successfully in the detection/diagnosis of breast, ovarian, lung, lymph node, kidney, adrenal, pancreatic, liver, and other cancers. Clinicians performing the procedure include pathologists, oncologists, radiologists, gynecologists, urologists, endocrinologists, and even general practitioners. The procedure is reimbursable, simple, and well-tolerated by the patient. Used since 1930, an increasing number of institutions have turned to FNA as a cost-effective method of obtaining diagnostic tissue, especially in this day of escalating medical costs. At The University of Texas M.D. Anderson (MDA) alone, use of the technique has increased from 1200 procedures in 1985 to over 4000 in 1989.

The procedure is performed using a variety of device combinations. Most commonly, a needle (usually 20-25 gauge) and syringe are used, sometimes in conjunction with a manual holder or "gun". Several problems have resulted from this manual procedure. 1) Often the clinician must make multiple passes (with multiple setups) in the patient in order collect sufficient material to analyze. This is costly in terms of clinician and technician time. 2) Obtaining tissue for additional prognostic studies (e.g. DNA content, steroid receptors, etc.) is frequently difficult with available techniques. 3) The clinician's attention is often diverted to control of the instrument rather than to the delicate task of locating the mass.

A renowned pathologist at The University of Texas M.D. Anderson Cancer Center (MDA) has conceived a device which could solve these problems. Consistency and adequacy of sample are ensured, with calibrated evacuation for ease in slide preparation. Unlike present devices, the shape of this device places the clinician's hand near the needle for best control and sensitivity. With the features of this instrument, an estimated 50% in total processing time for the procedure could be saved, depending on the laboratory setup. Patients will probably tolerate the procedure better with other design improvements.

MDA Ref No.: 196-0890 (TLR)

A patent search indicates that no other such device is under protection in the United States. Further, the frequency of the procedure and the variety of clinicians utilizing it translate to an attractive market for such a convenient device. MDA is presently seeking a corporate partner to collaborate on the final design of the device. The partner would potentially be given exclusive manufacturing, selling and distribution rights.

MDA Ref No.: 196-0890 (TLR)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"**TREATMENT FOR ORAL MUCOSITIS**"

This disclosure describes a drug and its use to treat oral mucositis and other mucosal lesions.

One common side effect of cancer chemotherapy or radiotherapy is the production of irritation and/or lesions in the mucous membrane of the mouth, or mucositis. Severity ranges from discomfort while eating to mucosal toxicity. Toxicity is often sufficient to warrant the administration of less than the optimal dosage of chemotherapy or radiotherapy. Even in less severe cases, oral irritation may necessitate the patient being fed by nasogastric tube to maintain body weight, and nasogastric tubes are associated with a high rate of morbidity themselves.

Researchers at The University of Texas M.D. Anderson Cancer Center have formulated and are using a drug for the treatment of oral mucositis. The drug has been found to reduce the severity and pain of oral ulcers induced by cancer therapeutics. Furthermore, tests in humans show that the drug itself is well tolerated, with few side effects and virtually no toxicity.

The drug may also find use in the treatment of other disease which result in the formation of oral ulcers, such as canker sores, erosive lichen planus, and herpes simplex. Further, such maladies as bedsores, pemphigus, and proctitis may also be remedied.

Nearly one million Americans will be diagnosed with some form of cancer this year. The majority of these patients will undergo either radiotherapy or chemotherapy or both. Millions more continue to undergo therapies as long-term disease management. Presently, no such product is available commercially, and the U.S. market is estimated at $10-40 million per year. Patent protection is being pursued on this technology.

MDA Ref No.: 030-0990
(TLR)

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NON-CONFIDENTIAL DESCRIPTION
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"**HUMAN CHROMOSOME TRANSFER**"

This description outlines an efficient and simple method to produce and isolate essentially pure populations of single human chromosomes.

Scientists have long studied chromosomes, either indirectly through classical genetics, or directly through molecular biology techniques developed in the last 20 or so years. Present studies, such as mapping the human genome, would be simplified if scientists had an efficient way to isolate and study large quantities of single specific human chromosomes.

In presently known procedures, chromosomes are fused individually with a recipient cell, usually rodent, through a process known as microcell-mediated transfer. Cell hybrids can be formed in this fashion, each containing hamster or mouse chromosomes and a few or one human chromosome. In some cases, chemical procedures enable the selection of hybrid cells containing only the desired human chromosome. These hybrids, however, are usually unstable in culture, tending the lose the human chromosome after a few cell division unless they are maintained in chemical selection medium. All microcell hybrids containing unwanted chromosomes must be eliminated by the selection process.

This invention solves several of these problems by subsequently enabling the packaging of the desired human chromosome separately from the rodent chromosomes. By using a proprietary chemical method, the desired human chromosome can be packaged singly into a microcell with a micronucleus under conditions where no rodent chromosomes can be packaged. These microcells can easily be purified and are "viable" for a few hours in the sense that they have many of the characteristics of normal whole cells, such as DNA-associated proteins, an energy source, etc. The human chromosome may then be inserted into any recipient cell by cell fusion. Further, the entire process is simple, inexpensive, and efficient.

The invention can be used to aid in mapping human, mouse, or other genomes of interest. Furthermore, this method has potential long-term application in gene therapy. Using this approach, a specific normal human chromosome could be added to a cell containing a defective gene.

Patent protection is being sought for this technology.
MDA Ref No.: 151-0990

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
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"**SYNTHETIC EGF PEPTIDES**"

Description
This description outlines the only known biologically active EGF peptides that have been synthesized which may have use in wound healing and cancer treatment.

Epidermal Growth Factor (EGF) is a naturally-occurring peptide hormone in all mammals which stimulates growth of certain cells and promotes wound healing. The cell membrane receptor for EGF (EGF-R) is related to viral oncogeny, v-erb B, and is overexpressed in many human tumors, including brain, bladder, breast, and squamous cell carcinoma of the head, neck and lung. Thus the activation of EGF-R by EGF or TGF- (another molecule that binds to EGF-R), is an important regulatory event in stimulating the division of normal cells and malignant cells.

Researchers at The University of Texas M.D. Anderson Cancer Center have identified an active portion of the EGF by synthesizing peptides which acts as a competitve inhibitor to TGF- , binds to the EGF-R and induces some of the biologic effects of EGF. It is possible to utilize these peptides alone and/or to bind them to toxins, antibodies, or DNA material for therapeutic pruposes. Internal administration of these peptides coupled to an appropriate delivery system could target internal wound healing or cancer therapy in tumors that overexpress the EGF-R.

Market:
The worldwide market for post-operative use of EGF as a healing aid is estimated at $1 billion. The anti-cancer market is smaller, but still significant at an estimated $100 million in the U.S.

Patents: One US patent has issued and two others are pending.

Availability: Available for exclusive license

MDA Ref. No.: 159/365/419-0195(FSR)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"CULTURE SYSTEM FOR 3-D EPITHELIAL CELL GROWTH"

This summary describes a Three Dimensional Matrix Associated Culture System (MACS) which utilizes a NASA-designed Rotating Wall Vessel (RWV). MACS allows for the co-culture of different cells to recreate a three-dimensional structure and permits study of tumor cell differentiation.

MACS provides optimal conditions for in vitro growth and cultivation of tissues. Cell interaction which will induce morphological changes similar to tumor tissue growth in nude mice is possible. A three-dimensional tissue may be created in an **in vitro** system that has the characteristics of tissue grown **in vivo**.

The RWV rotates cells around the horizontal axis and combines cell growth with microcarrier beads to simulate microgravity. The RWV encourages three dimensional cell growth because of the very low shear stress.

The MACS has multiple value to the researcher and/or manufacturer of cell products. It permits the growth of cell cultures at very high concentration (about 1×10^7 cells/ml in 240-500 ml). It facilitates the identification of specific growth factors in neoplastic and normal tissues. Because of the ability to co-culture different types of cells, it allows the study of cell interactions that induce differentiation.

The technology encompasses three disclosures from MDA and four patent applications and one disclosure from NASA/Johnson Space Center.

148-0990

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"ANTI-SENSE THERAPEUTIC FOR LEUKEMIA"

This description outlines a potential treatment for chronic myelogenous leukemia (CML). CML is a relatively uncommon form of cancer which affects primarily middle-aged and older people. About 8000 new cases per year are reported in the U.S. Treatment options include radiation and/or chemotherapies and are often successful but result in numerous undesirable side effects.

CML incidence is linked with a chromosomal translocation of human chromosomes 9 and 22, resulting in the so-called Philadelphia chromosome. This translocation places two oncogenes, known as *abl* and *bcr*, into physical proximity. The expression of the protein products from this junction correlates with the disease state.

Antisense therapeutics represent one of the latest advances in disease treatment. The cause of many diseases is the cellular production of abnormal proteins. These proteins are coded for by DNA and reproduced as messenger RNA (mRNA) in the cell. Antisense therapeutics are "mirror images" of the faulty mRNA and bind to them, thus preventing their translation into protein. Unlike conventional therapeutics, antisense therapies are specific for the diseased cells and theoretically have little or no effects upon normal cells.

Researchers at M.D. Anderson Cancer Center have developed a potential treatment for CML using antisense technology. An antisense oligonucleotide, specific for a portion of the *bcr/abl* mRNA product, has been synthesized. Administration of this oligonucleotide to cell lines with the Philadelphia chromosome resulted in a dramatic decline in their growth rates in a dose-dependent manner. Most importantly, this inhibition has been shown to be specific for cells with Philadelphia chromosome.

Clinically, this discovery will be applied toward the *in vitro* (and *in vivo*) treatment of leukemic bone marrow cells. Aspirated bone marrow will be treated *in vitro* with the oligonucleotide, while nuclease-resistant antisense nucleotides will be used systemically for the treatment of CML. Normal cells would remain unaffected while diseased ones would be killed or severely inhibited. Since the cells can be treated with microgram quantities of oligonucleotide, at least for *in vitro* use, the cost of treatment is expected to be quite low. Patent protection is being pursued for this technology.

215/1190

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Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"A METHOD FOR IDENTIFYING PATIENTS SENSITIVE TO INTERFERON ALPHA"

Interferon alpha is used in the treatment of leukemias and other diseases. However, only a certain portion of the population is sensitive to this treatment. With chronic myelogenous leukemia (CML), for example, only about 15% of patients go into complete remission while the remaining 85% ultimately relapse and must be put on less effective forms of treatment. On average, patients waste three months of treatment time at a cost of $100 million annually on CML alone.

A method is now available for determining which patients will benefit from interferon alpha treatment. Researchers at M.D. Anderson have developed a blood test and a packaged kit for use in CML treatment that determines when interferon will be effective. The technique is based on the discovery that certain proteins are implicated in the activation of interferon inducible genes. This finding provides the basis for various assays to identify cancer patients having cancers sensitive to treatment with interferon alpha. The test is rapid and easy to interpret.

Patent protection is being pursued for this technology.

252 - 1/93
(MLC)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"IL-2 ANALOGUES WITH LOWER TOXICITY"

The invention relates to analogues of human Interleukin-2 (IL-2) that might have lower toxicity.

Human IL-2 is a potent immunoregulatory cytokine capable of promoting T cell proliferation and modulating the functions of NK cells, activated B cells, and lymphokine-activated killer cells (LAKs). Although IL-2 has proven useful in the treatment of some cancers (e.g. renal carcinoma), its toxicity is such that only about 10% of the optimal dosage can be tolerated in humans. This toxicity appears to be due to induction of secondary lymphokines such as Tumor Necrosis Factor (TNF), Interleukin-1s (IL-1), and Interferon-gamma.

Researchers at M.D. Anderson Cancer Center have discovered that mutant IL-2 activates LAK cells with greatly diminished activation of TNF or IL-1 production. Such analogues could theoretically acheive therapeutic effect without toxicity.

The worldwide market for IL-2 in 1991 was about $125 million. If these new analogues prove efficacious, their market could be even greater due to increased dosages and more widespread usage. Patent protection is being sought for this invention.

279/0992 TLR

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"AN EXTRACHROMOSOMAL CLONING AND EXPRESSION VECTOR"

Researchers at M.D. Anderson are developing a mammalian cloning and/or expression vector whose episomal maintenance and replication is controlled by non-viral regulatory DNA sequences. This invention is being developed as an alternative to cosmid vectors to accommodate DNA regions > 40 kpb and as an alternative to YAK vectors by permitting normal expression and transcript processing of mammalian genes. It will enable the cloning of large regions of mammalian DNA for amplification or for the controlled maintenance of a low copy number for regulated expression of cloned segments.

Features of the vector will include:

* stable, autonomous replication as an autosomal unit
* marker/selection for episome persistence and amplification
* accommodates complete genes with regulatory sequences
* efficient introduction and recovery from host cells

This vector has obvious application in the biosynthesis of human proteins that have biomedical utility; the estimated U.S. market for existing vectors is $50 million.

This vector could accommodate medically important genes for introduction into and complementation of genetic deficiencies; the total U.S. market for gene therapy is projected at $1.3 billion by the year 2000, with the market for cancer and viral treatments alone at $750 million.

In the short term, the vector has potential for several research applications, including the analysis of the factors influencing the persistence, expression and replication of extrachromosomal DNA molecules.

Patent protection is being sought for this technology.

102-0591
(TLR)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"DIRECT DRIVE DEFIBRINATION UNIT"

Fibrin is an insoluble protein which is the main constituent of blood clots. Whole blood for certain medical, research and clinical laboratory applications is often treated to remove fibrin. Specific uses for defibrinated blood include isolation of hemoglobin for use in blood substitutes, isolation of clotting factors for treatment of hemophiliacs, production of blood agar plates, and isolation of T lymphocytes using the Rosette assay. The U.S. market for blood is expected to be at $374 million by 1995, while the market for blood substitutes is estimated to grow to $35 million.

The current technology for defibrination is an indirect-drive system which causes a fibrin-containing clot to form around a magnetic stir bar. There are multiple problems with this method: 1) excess technician time is required; 2) stir bars frequently jump out of magnetic fields, causing quality control problems that require entire batches to be rejected; and 3) due to high numbers of reject batches, more blood must be drawn to ensure sufficient end product. All of these problems translate to higher cost to the end user of the blood product.

Researchers at the University of Texas System M.D. Anderson Cancer Center have developed a device which defibrinates blood using a direct drive system. The advantages of the system are as follows:

* stirring is ensured at a constant rate since no magnetic stir bar is used
* risk of contamination is greatly decreased since the operation takes place in a closed, sterile system
* red blood cell concentration is increased
* product rejection by producer or consumer is decreased
* excess blood does not need to be drawn in anticipation of batch rejections
* technician time can be reduced up to 50%

These advantages together result in significant cost savings through decreased labor and improved product quality and consistency. The device, which is in use at the Cancer Center, has already resulted in several thousands of dollars in savings even though a relatively small volume of blood is routinely processed. Patent protection is being pursued both domestically and abroad for this technology.

123-0990 - LBW

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"PROBE FOR 5Q DELETION"

This invention is a laboratory reagent and method to detect a deletion in the human chromosome 5q31, which may be diagnostic of AML, myelodysplasias and other hematologic diseases. Currently, 5q deletions are detected through traditional cytogenetic analysis. The clinical utility of the probe has been demonstrated in five M.D. Anderson patients and is the subject of a U.S. Patent Application filed by The University of Texas M.D. Anderson Cancer Center.

M.D. Anderson estimates the market for leukemia probes to be about $12.5 million annually.

The invention consists of a probe for the detection of the 5q31 deletion by Fluorescent In Situ Hybridization (FISH). Other probes for 5q deletions are described in the literature, but the present invention pin-points the critical area of deletion far more exquisitely than previously described probes. While presently not widely practiced in the clinic, FISH will certainly become indispensable to reference labs in the future.

235-0192
MEB

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NON-CONFIDENTIAL DESCRIPTION
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"DIAGNOSTIC METHODS USING PCR DNA AMPLIFICATION"

This is a group of inventions describing methods to detect with great sensitivity altered genetic material for the diagnosis of disease, including leukemia, sickle cell anemia, thalassemia, and diabetes.

Each method exploits some particular characteristic of defective DNA in a disease and uses the Polymerase Chain Reaction (PCR) to detect the characteristic defect of the particular disease. For example, the point mutation responsible for sickle cell anemia, or the bcr/abl chromosome translocation associated with leukemia, may be detected with great sensitivity by these methods. Additionally, residual leukemia cells which survive anticancer therapies can be detected to evaluate whether any further course of treatment is necessary.

Patent applications are pending or have been issued to The University of Texas System which disclose not only specific primer sequences for each method, but which also teach the methods utilized for diagnosis. These patents or applications are available to be licensed from The University of Texas M.D. Anderson Cancer Center.

072/076/120-0192
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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"A LIGHTWEIGHT MODULAR RADIOTHERAPY TREATMENT CHAIR"

Radiation therapy is a widely applied method for cancer treatment. Traditionally, most cancer patients receive radiation treatments while lying recumbent on a specially designed treatment table. However, certain patients benefit more from receiving radiation in a seated position. For example, patients who need to have head and neck, or check cavity malignancies irradiated without exposing the shoulders and lungs are best treated in the seated position. The force of gravity along the vertical axis of the body allows for more precise targeting of radiation treatments to the tumor and not to the surrounding tissue. A chair also provides the best treatment for patients with severe curvature of the spine, or excess salivation; lymphoma patients with large breasts who require mantle irradiation; or head and neck patients with a short neck.

Existing treatment chairs do not adapt well to the needs of modern radiotherapy clinics. Treatment technologists frequently must alternate between the use of chairs and tables to accommodate different patients. They also need to alternate use of a chair between a simulator and different treatment machines. Existing chairs are bulky and difficult to adapt to these varying situations.

Researchers at M.D. Anderson have developed a radiotherapy chair that improves upon existing models in that it is modular and lightweight. It is thus easy to assemble and adapt to a variety of simulators and treatment machines. The design permits treatment of different body regions while the patient remains in the same seated position and it improves on field matching between treatment episodes. The chair permits isocentric treatment.

The M.D. Anderson treatment chair could be used in any radiotherapy clinic. There are approximately 1200 such clinics in the U.S. and only a small proportion of these use a chair at the present time. New clinics adopting the chair would account for a $500,000 yearly market. As the benefits of irradiating patients in the seated position become known to radiotherapy professionals, the demand for such a versatile and easy to use chair in established clinics should increase also. A patent has been issued for this chair.

219
(LBW)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"NEW MASK FOR OXYGEN SUPPLEMENTATION DURING FIBEROPTIC BRONCHOSCOPY AND TRANSESOPHAGEAL ECHOCARDIOGRAPHY"

The flexible fiberoptic bronchoscope has revolutionized pulmonary medicine. Of all innovative techniques that have been introduced in recent years for the diagnosis of pulmonary disease, none has had greater impact than fiberoptic bronchoscopy. Over 196,000 bronchoscopies are performed each year in the United States. The U.S. market for respiratory supplies is projected to be about $380 million by 1993, with an annual growth rate of 4%. Masks for use in bronchoscopies could account for as much as $2 million of this market.

During a bronchoscopic procedure, physicians require that patients maintain a blood oxygen saturation of 90%. Because patients frequently have co-existing underlying lung disease, an adequate level of saturation cannot be maintained unless oxygen is supplied via a mask. Existing masks, however, are not designed to accommodate the use of a bronchoscope.

Pulmonary professionals at M.D. Anderson have designed a new mask that greatly improves the ability to maintain adequate oxygen saturation during bronchoscopy. This mask allows insertion of the bronchoscope without interrupting oxygen flow, while minimizing the escape of supplemented oxygen. It also allows the introduction of a suction catheter and maximizes work area under the mask. Doctors who have tested the mask have been very satisfied with its performance.

Further studies have shown that this new mask is also very useful for transesophageal echocardiography, a procedure that provides a more detailed acoustic window to the heart and mediastinum than standard transthoracic echocardiographic images.

227
(LBW)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"NASOGASTRIC TUBE
WITH CONTINUOUS TEMPERATURE MONITORING DEVICE"

The market for electromedical devices such as patient monitoring devices is projected to be worth $1,685 million by 1993, with an annual growth rate of 7%.

Continuous monitoring of core body temperature is a valuable component of the maintenance of the intensive care patient. This measurement is usually achieved by means of a thermistor that is inserted into the esophagus of the patient and left in place for an extended period. For patients who require the insertion of a naso-gastric tube, the addition of a thermistor increases the discomfort of having so many tubes down their throats.

Nursing professionals at M.D. Anderson have designed a nasogastric tube that also has continuous temperature monitoring capability. This device should greatly simplify temperature monitoring and contribute to patient comfort.

91-019

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NON-CONFIDENTIAL DESCRIPTION
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"RECONSTITUTION NEEDLES"

Technicians in hospital pharmacies reconstitute hundreds of vials of drugs each day. As the fluid is added to each vial, excess pressure must be vented to the outside air or else the drug will spray the technician when the needle is withdrawn. There are vented needles available on the market, such as that made by Kendall-McGraw, but these are difficult to insert into the rubber stopper sealing each vial. Alternatively, pharmacy technicians will insert a separate filter needle to vent excess pressure, along with a standard 18GA needle.

Pharmacy technicians at M.D. Anderson have designed a novel reconstitution needle that is easier to use than the available vented needles and is less wasteful than simply using two needles. With this new design, the number of needle manipulations the technician has to perform is reduced, saving technician time and reducing the risk of accidental needle sticks. Additionally, because this reconstitution needle prevents any aerosol from escaping from the vial, it is ideal for use with cytotoxic drugs or other agents which may be hazardous to the healthcare worker.

An estimated 2,000 million needles are used each year in the U.S. by healthcare workers. At M.D. Anderson'n in-patient pharmacy, 55 thousand vented needles are used each year in preparing chemotherapy vials. Additional vented needles are used in M.D. Anderson's clinics and for non-chemotherapy uses. A safe and easy-to use vented needle such as this should be very useful in smaller, community hospitals as well as in larger medical centers.

237-92
KTL

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"MULTI-ELECTRODE ARRAY SWITCHING DEVICE"

Prior to performing a craniotomy, a neurosurgeon must map the areas of the brain that control motor function, so that these areas can be spared during the surgery. The present method of brain mapping requires that a neurophysiology technologist sequentially plug and un-plug electrodes into an electromyography evoked potential machine. This procedure is both tedious and time-consuming.

Inventors at M.D. Anderson have developed a switching device which automatically switches electrical currents to the desired electrode, allowing for quick, easy referential montage selection, eliminating the need to plug and un-plug so many wires. They have built and tested a prototype, which is already saving the Neuro-Oncology Department an estimated $30,000 per year in physician and anesthesiologist time.

The worldwide market for neurodiagnostic equipment is estimated to be $400 million. While a device such as this might represent the lower-cost end of the equipment spectrum, its cost-saving ability could potentially add great value to the higher-end evoked potential machines.

ID91-033

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NOVEL SHAKER-BATH FOR COST-CONSCIOUS LABORATORIES"

Waterbaths are a standard piece of equipment in virtually all biological laboratories. They are used for everything from thawing frozen specimens to running temperature-controlled experiments. *Shaking* water baths are required for experiments where cell suspensions or chemical formulations need to be mixed while being maintained at constant temperature.

Existing shaking waterbaths are priced from $2,300 to $2,600. Many laboratories can not afford this expense. Inventors at M.D. Anderson have invented a device that can convert virtually any medium to large-sized waterbath into a shaking waterbath. The device can even allow a bath to be used for dual purposes simultaneously. For example, one could use the shaking portion for DNA work and use the stationary part for protein gel work.

Another application for this device would be in the electronics industry, for cleaning circuit boards. The method entails gently shaking newly manufactured boards in a solvent bath.

This device could be priced as low as $600 to $1000. At this price, any cost-conscious lab would be eager to buy one. A prototype has been built and tested in M.D. Anderson laboratories. Patent protection is being pursued on this invention.

91-017

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"PERCUTANEOUS DRAINAGE SYSTEM"

This product is a one piece drainage system (the "Hohn System") for patients recovering from surgery. The market for this product could be as many as 100,000 devices per year. The product is an entirely closed-system device that may be manufactured from-off-the shelf sterile components. A working prototype of the Hohn System has been developed and used in four (4) patients with excellent clinical results. The prototype has also met with enthusiastic physician acceptance at M.D. Anderson. The simplicity of the System allows the patient to perform the fluid drainage him or her self, and more importantly, reduces the risk of infection and secondary contamination.

When recovering from surgery, fluid collects under the skin of many patients. For example, this is a common problem after surgery for breast cancer and melanoma. The fluid must be removed from under the patient's skin to promote proper healing of the surgery. The Hohn System marks a significant advance over the current methods of performing this task.

The most commonly employed technique for collecting uninfected fluid is repeated needle aspiration until no more fluid is drawn into the syringe. This method can be cumbersome, messy and painful for the patient, particularly where large collections are required. If there is a large volume or if there is infection, a tube may be required for effective drainage.
Fluids which cannot be drained by needle or tube aspiration (due to infection or other reasons) are most commonly managed by lancing the overlying skin and allowing the fluid to drain into bulky dressings applied over the skin opening. The disadvantages of this so-called open drainage are numerous: 1) the patient has to change dressing whenever it gets wet; 2) soilage of bedding and clothes always occurs; 3) if infection is present there is a risk of the drainage contaminating other patients and personnel; and 4) if infection is not initially present secondary infection of the cavity may occur through the drainage site. The Hohn System largely eliminates all of these difficulties.

The Hohn System is an entirely closed system so there is no leakage of fluid to soil the patient or cause contamination or infection. It is capable of draining large and small volumes whether or not infection is present.

M.D. Anderson intends to pursue patent protection on the Hohn System.

255/0992

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"A TOMOGRAPHIC POSITRON CAMERA WITH ADJUSTABLE DIAMETER"

Description:
This invention relates to a high resolution and low cost Positron Emission Camera (PET) that is excellent for imaging tumors in localized areas such as breast cancer, brain tumors, lymph nodes metastasis and others.

Equipped with radially translating detector segments and a rotation motion to tailor detector rings to the size of the object, the camera is able to image both large (whole body) and small objects (brain, breast and limb) with high detection sensitivity. Compared to conventional cameras, the new camera has several appealing features:

Significantly higher resolution for small objects. Because each detector ring segment can be translated radially, the complete detectors are closer to the object, and thus provides high detection efficiency. As no rotation of detector rings is needed, fast dynamic imaging (mostly for brain imaging) can be achieved without imaging errors.

High level of resolution and quality uniformity for larger objects. Like the conventional cameras, a rotation of detector rings is required to image large objects. However, the new PET only requires a 45^0 rotation as opposed to 180^0 for standard cameras. The much less rotation level gives the new camera a higher level of uniformity and less imaging errors.

Most importantly, the cost of producing a new PET is significantly lower than that of a standard one. It is estimated that the price of a new PET will be less than $1 million, while a standard camera is currently sold at $2.7 million. Further saving could be realized if the camera is used with a new detector design invented by the same inventor.

Market:
This invention has broad applications in both research and clinical areas. Besides tumor imaging and diagnosis, the technology can also be used in treatment response monitoring, imaging tumor estrogen receptor density, quantitative imaging of tumor glycolysis rate, tumor protein synthesis rates and DNA synthesis rates. Presently, there are about 100-120 PET cameras installed in regional cyclotron centers. Lowering production cost is believed to be the major driving force for the future growth of this market. Great commercial value is expected for this technology which promises higher quality and lower cost.

Patent: Three U.S. patents have been issued; one is pending.
Availability: Available for exclusive or non-exclusive license.
MDA Ref. No.: 236/264/401/462 (KQ/0795)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"ANTI-MICROBIAL COATING FOR IMPLANTABLE DEVICES"

Implantable devices are being used increasingly in the management and care of patients. Some of the more common implantable devices are intravenous catheters, vascular shunts, artificial heart valves and bone and joint protheses. Unfortunately, these implantable devices often suffer infectious complications that are expensive to manage and can require removal of device.

Physicians at M.D. Anderson Center and the Baylor College of Medicine in Houston, Texas have discovered a combination of antimicrobial agents that is highly effective in preventing infection by these microorganisms. The researchers have demonstrated, in animal experiments, that implantable devices coated with this combination show significantly lower rates of microbial infection than devices coated with alternative antimicrobial agents.

The total worldwide market for intravenous catheters is presently about $170 million. The U.S. market for artificial heart valves is presently about $170 million and is expected to exceed $250 million by 1994. Last year the joint and bone prosthesis segment of the orthopedic implants market posted U.S. sales of approximately $1.4 billion. Devices such as these that are equipped with anti-microbial coatings should capture a large share of their respective markets.

232-0392
(JSC)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"ASSAY PROCEDURE FOR DETECTING UV-SENSITIVITY AND SUSCEPTIBILITY TO SKIN CANCER"

It is believed that the response to environmental carcinogens varies among individuals depending upon their genetically determined DNA repair capabilities. Furthermore, evidence suggest that tissues and organs directly exposed to the environment are most affected by genetic sensitivity to mutagens.

In ultraviolet light (UVL) induced DNA damage, the first step of repair requires excision repair to cleave off the damaged segment. The hereditary disease xeroderma pigmentosum (XP) is known to be highly deficient in excision repair. Individuals with this genetic defect develop various skin cancers, including melanoma, in childhood.

The XP syndrome probably represent the extreme end of a continuum of UV sensitivity. Individuals with moderately deficient or slightly deficient DNA repair systems are probably more liable to acquire skin malignancies than those with an efficient set of repair enzymes when both are exposed to a similar amount of sun light.

A researcher at The University of Texas M. D. Anderson Cancer Center (MDA) has developed, to our knowledge, the first practical in vitro assay method to estimate UV sensitivity of individuals who might be more liable to develop skin malignancies following excessive sun exposure. The assay requires a sample of peripheral blood to be cultivated in vitro in a conventional blood culture medium. The cultured blood is then exposed to a chemical mutagen that mimics the genotoxic effects of UV light. After exposure to the chemical mutagen, the individual's chromosomes are examined for mutations or breaks.

Results indicated that samples from persons with XP had the highest sensitivity to the chemical mutagen, i.e., greatest number of chromatid breaks, followed by persons with known melanoma. Normal control individuals experienced a statistically significant lower number of chromatid breaks, i.e., were able to repair the mimicked UV damage. Skin cancer is the most common type of cancer and its incidence has increased dramatically in recent years. There were an estimated 32,000 new cases of skin cancer (melanoma only) reported in the U.S. last year. Concerns about ozone depletion and increased UV exposure have heightened individual awareness of the risk of developing skin cancer.

The worldwide market for cancer screening is approximately $2 billion with UV-induced cancer screening accounting for about $600 million of this market. A simple blood test for sensitivity to UV exposure should capture a significant portion of this market.

262-0492 JSC

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"NOVEL SOLUTION FOR THE PREVENTION OF THROMBOTIC AND INFECTIOUS COMPLICATIONS OF VASCULAR CATHETERS AND OTHER MEDICAL DEVICES"

Indwelling medical devices, including vascular catheters, have become essential in the management of hospitalized or chronically ill patients. Unfortunately, vascular catheters have become the major source of hospital acquired sepsis. Hence, the benefit derived from indwelling medical devices such as vascular catheters is often upset by infectious complications. Thrombotic occlusion of the lumen of central venous catheters is another complication that will often lead to the removal of catheters. This is why the current standard care of catheters includes flushing the lumen of central venous catheters with heparin. However, heparin has no antimicrobial activity, and infections, as well as thrombotic occlusion, continue to occur frequently despite the prophylactic use of heparin flushes. Knowledge of the pathogenesis and microbiology of central venous catheter-related infections is essential in order to provide effective prevention for this problem.

A researcher at The University of Texas M.D. Anderson Cancer Center (MDA), in collaboration with a scientist at Bowman Gray School of Medicine, Wake Forest University, have developed a novel solution that prevents thrombotic and infectious complications of vascular catheters and other medical devices. The unique solution has been show to have the following properties:

1. Antistaphylococcal and antifungal (anti-Candida) activity against free-floating as well as adherent organisms embedded in biofilm.

2. Prevents and alters/dissolves the fibrous glycocalyx biofilm layer.

3. Anticoagulant that prevents thrombotic occlusion of the catheter lumen as well as thrombin formation which is the substrate for catheter infection.

4. This agent can be given intraluminally without a toxicity concern to humans.

5. It kills adherent staphylococci and Candida and is not the same agent a clinician would use therapeutically (such as Vancomycin, Ampho B, or Azoles).

275-92 (JSC)

There are at least two applications for this novel solution:

1. This solution could be used to flush central venous catheters daily instead of a daily flushing with 100IU/ml of heparin. This combination will represent a major improvement over the standard practice of flushing CVC with heparin q daily.

2. The combination could be used to coat catheter surfaces and other medical devices. The solution will prevent the formation of fibrin sheath and fibrous glycocalyx and will kill microorganisms. The solution has been shown to significantly reduce glycocalyx formation compared to heparin and control.

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A patent application is being filed on this new invention.

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"TUMOR MARKER FOR SQUAMOUS CELL CARCINOMA"

Researchers at M.D. Anderson Cancer Center (Houston, TX) and the National Institute of Environmental Health Sciences (Research Triangle Park, NC) have identified a secreted protein which may serve as a tumor marker for squamous cell carcinomas. Expression of the marker correlates with differentiation of squamous epithelium. In healthy individuals, the epithelium of the upper aerodigestive tract is usually non-keratinizing. However, many premalignant lesions and carcinoma undergo aberrant squamous cell differentiation. Eighty percent of head and neck cancers and 90% of non-small-cell lung cancers are squamous cell carcinomas. Some other cancers such as breast, bladder, prostate, cervical, uterine, ovarian, and non-basal cell melanoma may also be squamous cell carcinomas.

The annual United States incidence of new cases of non-small-cell lung cancer is estimated at 128,000, and that of head and neck cancers at more than 60,000. Also it is estimated that each year there are 175,000 new incidences of cancer of the breast, 50,000 of the bladder, 122,000 of the prostate, 20,000 of the ovary, and 46,000 of the uterus and cervix in the U.S.

The new protein marker, whose molecular weight is around 16kDa, is usually not detectable in the serum of healthy individuals, but patients with squamous cell carcinomas may exhibit elevated levels of the protein marker in their serum and other body fluids.

Other potential markers for squamous cell carcinoma have been identified, and include transglutaminase type I, cholesterol sulfotransferase, keratin K-1, involucrin, loricrin, and filaggrin. However, these markers are all located intracellularly, and are of limited clinical usefulness because they cannot be detected in body fluids. TA-4, the only presently known squamous cell marker found in blood, is associated only with ovarian cancer, and was detected in only 50% of patients. Thus, a marker with more widespread clinical applications has long been sought.

The 1990 U.S. market for tumor marker in vitro diagnostic tests was $85 million; this market is expected to grow by 11% annually, reaching a projected value of $145 million by 1995. The U.S. market for tumor marker tests specific for lung, breast, prostate, ovarian, and uterine cancers was $78 million in 1990, representing 88% of the total market for tumor marker in vitro diagnostic tests. Patent protection is being sought for this technology.

247-92 JMR

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"ASSAY FOR THE QUANTIFICATION OF DRUG-INDUCED DNA-TOPOISOMERASE COMPLEXES FROM PATIENTS WITH MALIGNANT DISEASES"

A road block to the development of more effective cancer chemotherapy is the difficulty of identifying and characterizing exploitable differences between normal and cancerous cells.

Topoisomerases, which are enzymes that alter the three-dimensional structure of cellular DNA, are the targets of a number of anticancer drugs. The magnitude of the effect of a drug treatment on topoisomerase biochemistry often predicts the magnitude of that drug treatment's cytolytic effects. Quantification of the effect of a topoisomerase-directed agent on the topoisomerases from malignant cells of an individual patient will likely predict the response of that patient's disease to a specific drug treatment. To date, no reliable method has been developed to assay drug-induced, topoisomerase-DNA complex formation in clinical specimens.

Researchers at The University of Texas M.D. Anderson Cancer Center have developed a novel method to quantify the magnitude of drug induced DNA-topoisomerase effects in samples from patients with malignant diseases. This new assay method, for which patent protection is being applied for, will allow the study of the pharmacodynamics of topoisomerase-directed drug action in patients while receiving these drugs. Intermediate end-points of success or failure of a given cycle of chemotherapy can be evaluated for their prognostic significance using this novel assay. It is envisioned that the assay would be in the form of a kit which would include filters, buffers, and a labeled probe.

92-027 5/92

JSC

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"NOVEL BONE AND PROSTATE-DERIVED PROTEIN FACTORS AFFECTING PROSTATE CANCER GROWTH DIFFERENTIATION AND METASTASIS"

Over the past ten years prostate cancer has emerged as an extremely prevalent disease. An estimated 122,000 new cases of prostate cancer were reported in the U.S. last year. It is the second most common cancer in men, after skin cancer, and the second leading cause of cancer deaths in men. Approximately one out of every eleven men in the U.S. will develop prostate cancer.

Prostate cancer appears to spread selectively to the bone. More than 50% of the patients with prostate cancer, at the time of diagnosis, already have advanced diseases as evidence by bone metastasis. Therefore, bone is the primary sight of prostate cancer metastasis and one of the keys to controlling the spread of the disease.

Researchers at The University of Texas M.D. Anderson Cancer Center have discovered novel bone marrow proteins which are believed to be important for normal prostate and prostate cancer cell growth in vitro and in vivo. These researchers have developed monoclonal and polyclonal antibodies which react specifically to prostate and bone-derived growth factors (patent application submitted). The antibodies can be used as diagnostic, prognostic or therapeutic agents and may be clinically valuable in predicting the responses of patients to standard and novel clinical protocols for the chemotherapeutic intervention of the advanced stages of prostate cancer.

272-0492

JSC

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"TOXIN-RESISTANT TRANSGENIC ANIMALS"

The invention is a novel use of existing cloned genes which can be applied to produce genetically engineered livestock which are resistant to many plant toxins.

Animals which eat plants as their main source of nutrition are continually exposed to the variety of toxins which plants naturally produce. These toxins vary in structure and strength; effects on livestock range from muscle tremors to death. Livestock producers in America estimate that $250-300M per year is lost due to sickness, birth defects, and death caused collectively by these toxins.

In the last few years, research efforts have focused on a small family of genes which code for resistance to many of the above toxins. The novelty of this invention lies in the use of one of these genes to produce an animal resistant to many plant toxins. Through genetic engineering techniques, the gene will be placed into the sperm or egg of a plant-eating animal, such as a cow or sheep, and the fertilized egg will be transplanted into a host mother. As the fetus develops, the gene will be expressed only in the gut lining because of special (patent pending) engineering. After birth, most plant toxins that are absorbed by the animal's gut will be detoxified. Thus, these animals will live longer and healthier, and birth defects in their offspring will be fewer. As a potential added benefit, humans consuming the beef and/or milk will be exposed to lower levels of these toxins. Patent protection is being pursued on this technology.

90-012
0390

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"OXYGEN FLOWMETER AND TUBING CONNECTOR DEVICE"

Oxygen supply is critical in many medical and surgical situations. Oxygen is provided to the patient by means of tubings connected to an oxygen supply.

Patients often have to be transported from one facility to another (for example, from the operating room to the intensive care unit); this often necessitates the use of mobile oxygen supply units. To meet patient needs, supply systems using different diameters of oxygen tubing are used. This requires a variety of connectors. In addition, oxygen delivery systems used in some settings (i.e. PAR) may not readily interface with oxygen sources for short term transport. This requires a change in the delivery system resulting in a very short term use of the alternative system which is not cost effective.

A researcher at M.D. Anderson has designed a connector, not commercially available, that will allow different size tubes to fit to it. Thus, when using different delivery systems, the connector on the oxygen flowmeter need not be changed. This saves time, and minimizes any interruption of oxygen flow to the patient.

ID:91-037

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"NASOGASTRIC TUBE ANCHOR"

Nasogastric intubation of patients is one of the more common procedures done in medical treatment. (For example, nasogastric tubes are inserted through the nostrils to the stomach for aspiration of stomach contents). These tubes are usually in place for extended periods.

The current means of securing the nasogastric tube to the patient include suturing, use of adhesive tape, or use of headbands. However, several problems have been noted. Normal movement of the patient sometimes causes nasal septal ulcers and/or necrosis because of excessive tube movement while the tube is in direct contact with an inner portion of the nose. Headband assemblies are more complicated and time consuming to use. Both the adhesive tape and headband assemblies are easily removed by a belligerent patient, and prolonged use of adhesive tape can cause skin irritation.

A surgeon at M.D. Anderson has designed a simple innovative method to place a bridle around the nasal septum. Such a bridle can be secured to a nasogastric tube so that the inadvertent removal or intentional removal of such a tube by the patient is almost impossible.

The market is large; around 421,000 intubations of the gastro-intestinal and respiratory tracts are needed a year in the U.S. alone. A patent is being sought for this invention.

MDA Ref. No. 207-0592/KL

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"MODIFIED STAPHYLOCOCCAL TOXIN GENE CASSETTE FOR GENE THERAPY"

The invention is a retroviral vector to target a modified Staphylococcal enterotoxin alpha (MSEA) gene to solid tumors such as cancers of the brain, breast, prostate, and liver. The technology has particular potential for the treatment of brain tumors, of which there are an estimated 16,000 new incidences annually in the U.S., the majority of which do not respond to current treatments.

A major problem associated with the use of bacterial toxin genes as cancer therapeutics is the persistence of low basal levels of toxin gene transcription, or "promoter leakiness", which causes unwanted toxin expression and cytotoxic effects in non-tumor cells. Researchers at M.D. Anderson Cancer Center have constructed a retroviral vector designed to overcome this problem.

The retroviral vector contains an MSEA gene, coding for a modified form of the toxin, which forms pores in human tumor cell membranes and causes cell death. The vector is designed to overcome the problem of non-specific cytotoxicity. First, the retrovirus attaches to receptors common to all cell surfaces, but present in increased amounts on actively proliferating cells, thus ensuring preferential uptake by tumor cells. Second, the gene construct is designed so that intracellular expression is induced by an externally controlled promoter.

"Switching on" MSEA toxin gene transcription causes intracellular expression of a modified form of the toxin, resulting in slow tumor cell killing without toxic effects from rapid build up of cell necrosis products. In addition, MSEA toxin can potentially increase tumor cell susceptibility to chemotherapy because pore formation may overcome multi-drug resistance. The modified toxin also has the potential to achieve an anti-tumor immune response by the presentation of "superantigen complexes" on tumor cell surfaces.

Gene therapy based on this technology can be used in the treatment of cancers and viral infections. When injected into solid tumors, gene therapy can potentially achieve more specific targeting, fewer side effects, and increased tumor toxicity compared to conventional chemotherapy. The potential U.S. market for gene therapy (cancer and viral applications) is estimated to reach $750 million by the year 2000.

292-0692 - JMR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"BINARY TOXIN GENE TECHNOLOGY FOR GENE THERAPY"

The invention is a combination of two retroviral vectors for targeting a Diphtheria toxin A (DTA) gene to solid tumors such as cancers of the breast, prostate, liver, and pancreas. The technology has particular potential for the treatment of brain tumors, of which there are an estimated 16,000 new incidences annually in the U.S., the majority of which do not respond to current treatments.

A major problem associated with the use of bacterial toxin genes for gene therapy is the persistence of low basal levels of toxin gene transcription or "promoter leakiness", which causes unwanted gene expression and cytotoxicity in non-tumor cells. Researchers at M.D. Anderson Cancer Center have developed a binary vector strategy to overcome this problem.
The researchers use a combination of two retroviral vectors to ensure stringent regulation of intracellular DTA expression. This binary toxin strategy consists of one vector containing an "interrupted" DTA gene, which can be transcribed and expressed only after excision and recombination by the product of the second vector. Intracellular expression of the activated recombined gene is induced by the conditional expression of a separate gene regulated by an externally controlled promoter.

When injected into solid tumors, the retroviruses attach to receptors common to all cell surfaces, but present in increased amounts on actively proliferating cells, thus ensuring preferential uptake by tumor cells. Hierarchical control over toxin gene expression is achieved by making DTA transcription dependent on the conditional expression of a separate gene.

Gene therapy based on this technology can be injected into solid tumors, potentially achieving more specific targeting, fewer side effects, and increased tumor toxicity compared to conventional chemotherapy. The projected U.S. market for gene therapy (cancer and viral applications) is estimated to reach $750 million by the year 2000.

291-0692

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"RETROVIRAL VECTOR FOR ANTISENSE K-RAS EXPRESSION"

The invention is a retroviral construct that can express antisense RNA to a specific oncogene. The retrovirus can efficiently transduce human tumor cells and is constructed to express high levels of the antisense RNA in the cancer cell. Expression of antisense RNA directed against specific oncogenes can alter characteristics of the malignant phenotype including cell proliferation and tumorigenicity (1). The antisense K-*ras* RNA specifically eliminates production of the mutant gene product p21 protein.

Antisense RNA producing constructs could be potential agents for prevention and therapy of cancer. Oncogene mutations have been identified in both premalignant and malignant lesions in solid tumors (2-5). If these constructs could be efficiently delivered to premalignant or malignant cells they could alter the characteristics of those cells to prevent or reverse malignancy. Although recent studies indicate that cancer cells have multiple genetic abnormalities, data from, our laboratory and others indicates that reversal of a single genetic lesion can reverse the characteristics of the malignant phenotype (6,7). Thus, it may be necessary to target only one or two genetic lesions to have a profound effect on the cancer cell.

Unfortunately, efficient delivery systems for antisense have not been previously available. This invention provides a vector that can deliver the constructs to a high percentage of tumor cells. It is envisioned that this will function as a regional therapy for premalignancy or as adjuvant therapy for patients with resected early stage lung cancer who are at risk for local recurrence. Recent experiments indicate that human lung cancer cells in a nude mouse model will take up the retrovirus. Injection of retroviral supernatants inhibits the growth of human tumors implanted subcutaneously in a nude mouse model.

This invention incorporates several novel features which contribute to its efficiency of transduction, specificity and efficacy. The vector achieves high levels of antisense expression in human cancer cells of epithelial origin.

Recent experiments have shown that the efficacy of these constructs is greater than would be expected by the known efficiency of transduction. For example, transduction efficiency for one cycle of infection is 30%. Yet this results in an 83% reduction in cell proliferation. Thus, these constructs may have a very significant therapeutic effect even though 100% transduction efficiency is not achieved. These agents are effective in curing human lung cancer in mice when administered in the same way they would be to patients. Institutional approval has been received from M.D. Anderson to begin clinical trials.
92-038 7/92 - JSC

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"RETROVIRAL VECTOR FOR p53 EXPRESSION"

The invention is a retroviral construct that can express a normal tumor suppressor gene. The retrovirus can efficiently transduce human tumor cells and is constructed to express high levels of the *p*53 tumor suppressor gene in the cancer cell. Expression of *p*53 can alter characteristics of the malignant phenotype including cell proliferation and tumorigenicity (1). The normal *p*53 gene product specifically replaces the function of mutant or deleted *p*53.

Retroviruses expressing normal tumor suppressor genes could be potential agents for prevention and therapy of cancer. Mutations in tumor suppressor genes have been identified in both premalignant and malignant lesions of solid tumors (1-4). If these constructs could be efficiently delivered to premalignant or malignant cells they could alter the characteristics of those cells to prevent or reverse malignancy. Although recent studies indicate that cancer cells have multiple genetic abnormalities, data from our laboratory and others indicates that reversal of a single genetic lesion can reverse the characteristics of the malignant phenotype (5,6). Thus, it may be necessary to target only one or two genetic lesions to have a profound effect on the cancer cell.

Unfortunately, efficient delivery systems for gene constructs have not been previously available. This invention provides a vector that can deliver the constructs to a high percentage of tumor cells. It is envisioned that this will function as a regional therapy for premalignancy or as adjuvant therapy for patients with resected early stage lung cancer who are at risk for local recurrence. Recent experiments indicate that human lung cancer cells in a nude mouse model will take up the retrovirus. Injection of retroviral supernatants inhibits the growth of human tumors implanted subcutaneously in a nude mouse model.

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295-7/92 - JSC

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"SUNSCREEN ADJUNCT FOR PREVENTING UV RADIATION INDUCED IMMUNOSUPPRESSION"

The invention is a method for preventing UV radiation-induced immunosuppression by topical application of a specific, liposomally encapsulated, DNA repair enzyme to sunlight exposed skin.

Exposure to UV radiation causes damage to DNA in epidermal cells through the formation of pyrimidine dimers. The resulting DNA damage is associated with the occurrence of skin cancer in areas of repeated sun exposure. A researcher at M.D. Anderson Cancer Center has shown in animal studies that UV irradiation also causes suppression of the cellular or T lymphocyte-mediated arm of the immune system. Immunosuppression is thought to be associated with cytokine release from epidermal cells as a consequence of UV-induced DNA damage.

The researcher has shown that UV induced immunosuppression of contact and delayed hypersensitivity responses can be prevented by topical application of an enzyme that specifically excises and repairs pyrimidine dimers in UV-damaged DNA. Liposomal encapsulation of the enzyme ensures that it is localized to the epidermis, and increases its effective delivery to epidermal cells. Recent studies from other laboratories have demonstrated that UV radiation has similar immunosuppressive effects in humans. Use of this liposmal enzyme preparation as a sunscreen adjunct will provide protection against UV induced DNA damage, as well as more directly preventing the resultant immunosuppression.

Latent viral infections such as Varicella and Herpes zoster (shingles, chicken pox), Epstein-Barr virus (mononucleosis), and Cytomegalovirus are thought to be activated by immunosuppression. UV irradiation has been shown to activate Herpes simplex (fever blisters), and certain autoimmune diseases, such as lupus. Organ transplant recipients are susceptible to human papilloma virus infection, or warts, on UV exposed skin. UV radiation has been shown to activate HIV expression in human cells in culture, and in the skin of transgenic mice in vivo, and HIV infected individuals often suffer from skin lesions in UV exposed areas.

There are 150,000 organ transplant recipients worldwide, and 500,000 lupus patients in the U.S. alone. Worldwide incidence of HIV infection is estimated at 9-11 million in 1992, and projected to reach 30-40 million by 2000. Increasing public awareness of the effects of rising UV radiation levels associated with atmospheric ozone depletion presents a worldwide marketing opportunity.

MDA Ref. No: 299-92-JMR

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NON-CONFIDENTIAL DISCLOSURE
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"A NEW METHOD OF MICROENCAPSULATION FOR TARGETED DRUG DELIVERY"

Description

This disclosure describes an improved method of synthesizing microcapsules and outlines several uses for the technology.

Microcapsules are useful as sustained-release and specific-release drug delivery systems. Most therapeutic drugs are administered in a single dose. The blood level of the drug increases rapidly after administration, then drops off again in rollercoaster fashion shortly after. The advent of time-release formulas (such as over-the-counter cold medicines) has solved a large part of this problem. The drug is diffused throughout the body, however, without specificity. Clinicians continue to seek not only improved methods of sustained drug delivery, but also methods for targeting drugs to particular organ systems within the body.

Such improved methods have been developed at The University of Texas M.D. Anderson Cancer Center. "Shells" ranging from 500 microns to less than 1 micron have been developed. These shells can contain solids, liquids, or gases, and are ideal for a number of applications including:

* targeted delivery of toxic substances such as chemotherapeutic agents.
* targeted delivery of imaging materials for diagnostic procedures.
* targeted delivery of dissolving agents for blood clots, cholesterol, etc.
* delivery of chemically unstable substances or emulsions.
* controllable rate of delivery for any therapeutic drug.

Varying the shell design not only controls delivery rate of the drug, but also allows cellular and organ targeting; such versatility has not been previously demonstrated.

Cis-platin, the cancer chemotherapeutic, has been successfully encapsulated, as have been a number of imaging agents for diagnostic procedures. Animal studies are about to commence to test safety, efficacy, and toxicity of microencapsulation.

Market

This technology potentially taps several lucrative markets. The market for cis-platin alone is estimated at $1 billion annually worldwide, while the market for water-based contrast materials for the nuclear imaging sector is estimated at $500 million.

Patent Protection: One issued patent, two pending
Availability: Available for exclusive license
MDA Ref. No.: 178/243/283-0390

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NON-CONFIDENTIAL DISCLOSURE
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"ELECTRICALLY IONIZED CATHETER PREVENTING INFECTIONS"

This present invention relates to novel bacterial barrier for clinical catheters and indwelling devices.

Intrusive medical devices such as central venous catheters (CVCs), urinary catheters and endotracheal catheters may introduce infection into hospitalized patients when used since the devices are subject to microbial colonization. The most common source for catheter colonization is the patient's skin, whereby organisms migrate from the skin along the intercutaneous catheter segment and ultimately enter the bloodstream and can create serious infections. Protection against infection is particularly desirable at or around the catheter insertion point to limit entrance of organisms into the intercutaneous tunnel.

Researchers at M.D. Anderson have designed, built and tested an indwelling device for helping prevent bacterial infection associated with catheterization procedures. The assembly features an inexpensive, easily employed catheter assembly which has proven effective in tests for fighting infections and colonization associated with catheterization. The catheter assembly comprises a catheter tube having a distal end for intercutaneous insertion into a patient's bloodstream. A central exterior portion of the catheter tube is surrounded by parallel helical conductive elements which are connected to a power source capable of creating an open circuit and inducing ionophoretic activity in the surrounding area.

Animal data supports the efficacy of the new device. A patent has been issued on this technology.

MDA Ref. No.: 231/1292 (JSC)

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NON-CONFIDENTIAL DISCLOSURE
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"METHOD FOR THE DETECTION OF BCR-ABL AND ABNORMAL ABL PROTEINS IN LEUKEMIA PATIENTS"

More than 95% of patients with chronic myelogenous Leukemia (CML) possess the Philadelphia chromosome (PH^1). The abnormal chromosome present in leukemia cells originates from a reciprocal translocation between chromosomes 9 and 22. The fused genes generate a hybrid mRNA with a continuous open reading that encodes for the BCR-ABL protein. Current techniques for early detection of Ph^1 positive cells and methods to clinically follow therapeutic progress have been limited. A need exists for an assay that can detect and quantitate Ph^1 positive leukemic cell proteins.

Research scientists at the University of California in collaboration with M.D. Anderson Cancer Center have developed a Western blotting assay system that provides a method of early detection of abnormal Ph^1 positive cells and BCR-ABL gene products. These qualitative tests can be used by the oncologist to determine the tumor burden and to closely monitor the leukemic state as the patient progresses through accelerated and blast crises stages of the disease.

The Regents of the University of California own rights to this invention and are seeking a licensee(s) to bring the technology into commercial use as a diagnostic kit. If your company would like to explore this invention further, we will provide detailed information for your evaluation under the cover of a Secrecy Agreement.

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"GEODESIC PRIMADOME"

Holding facilities for non-human primates and other animals are in use by zoos, veterinary centers, and research facilities. The design of these holding facilities is important for the well-being of the animals; where necessary, the animal's natural habitat is simulated.

Researchers at M.D. Anderson have designed a modified geodesic dome to house non-human primates such as chimpanzees. The design incorporates a wire mesh into the structure, thus allowing the chimpanzees to exercise. The dome provides sufficient space, is light-weight and movable yet strong, and is aesthetic. The construction of the dome does not require much material and labor. Another advantage is that the size and structural strength of the dome can be altered to suit the primate's activity.

The modified geodesic dome can be used for zoos and any other facility that houses animals, and can also be adapted for use as a prison exercise yard. The potential market for the geodesic primadomes, as used for animals only, is approximately $2.5 million in the United States.

261-0592
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
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“A NOVEL FACTOR TO INDUCE MONOCYTE CYTOTOXICITY”

The invention is a novel peptide which acts as a biological response modifier to induce monocyte antitumor cytotoxicity, and is more potent than interferon-gamma.

Immune protection is provided by a dual system of cellular and humoral defenses against foreign invaders. The cellular arm of the immune response is directed against invading foreign tissue, cancer cells, intracellular viruses, and parasites, and is mediated by T- lymphocytes. Phagocytic cells in the blood, such as monocytes, macrophages, and polymorphonuclear leukocytes, bind and ingest, or lyse foreign substances, often prior to the humoral or antibody response. T-lymphocytes have been found to release soluble factors, such as interferon-gamma, which stimulate monocyte antitumor cytotoxicity.

A researcher at M.D. Anderson Cancer Center has characterized, cloned, and sequenced a novel factor produced by a T-cell hybridoma cell line which stimulates monocyte antitumor cytotoxicity. This factor exhibits different physical and chemical properties from those of interferon-gamma and other reported monocyte activating factors, and is more potent than interferon-gamma. Both the isolated molecule, a 29 kDa protein, and a synthetic peptide have stimulated monocyte antitumor activity in vitro against a number of human tumor cell lines.

A synthetic peptide which induces monocyte cytotoxicity is now at the pre-clinical stage of development. Clinical applications of this molecule are in the treatment of both solid and hematological tumors. Treatment could include traditional infusion therapy, as well as adoptive immunotherapy and gene therapy, where a patient's monocytes could be harvested, expanded or transfected ex vivo, and reinfused. Diagnostic applications include development of an assay to quantitate factor blood levels for monitoring therapy and as a T-cell malignancy marker.

An estimate of the potential market for this factor can be derived by comparison with that for an analogous product such as interferon. The U.S. market for interferons used in cancer therapy was almost $60 million in 1992, an increase of 30% from 1991 figures. The worldwide market for interferons as cancer therapeutics was $200 million in 1992, and is projected to reach $500 million by the year 2000.

The technology is the subject of two issued and four pending patents.

93-UTHSC170
JMR

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NON-CONFIDENTIAL DESCRIPTION
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"NOVEL METHOD FOR SELECTIVE CELL DESTRUCTION BY ELECTRICAL SIGNALS"

This invention is a method for selectively destroying specific subsets of cells within a mixed cell population.

In a recent discovery, researchers at M.D. Anderson Cancer Center and the University of Wales demonstrated that selected populations of human cells can be induced to burst when exposed to electrical signals which are specific to, and dependent on, the biophysical properties of each cell type. Factors determining the electrical signals at which bursting occurs are cell size and electrical properties, which in turn are determined by age, viability, differentiation state, and stage within the cell cycle. Thus a subset, such as cancerous cells, within a mixed cell population can be selectively destroyed without harming other cell types.

While this technology is at an early development stage, potential clinical applications cover a broad spectrum of hematological malignancies and other conditions. Leukemic cells could be purged from autologous bone marrow, and T lymphocytes could be destroyed in allogeneic bone marrow to prevent graft versus host disease. Another application is in the apheresis of peripheral blood, such as leucocyte cytoreduction for leukemia and lymphoma, and cytoreduction of platelets in thrombocytopenia. By using monoclonal antibodies to target specific cells, the T cells involved in autoimmune diseases, such as rheumatoid arthritis and lupus, could be selectively destroyed.

This technology could be incorporated into a continuous flow treatment system with computerized image processing, cell separation and cell destruction capabilities. Miniaturized, micro-processor controlled electrode arrays, and an appropriate software package would allow detection, separation, and destruction of specific types of cells under known conditions. A continuous flow treatment system such as this will have an operating speed up to one thousand times faster than a flow cytometer, and be faster and simpler than current cell destruction using physical separation methods such as absorbent columns or centrifugation.

The therapeutic market for arthritic diseases in the U.S. is expected to be $2 billion in 1992, with the autoimmune patient population growing at 15% annually. Colony stimulating factors will allow a significant increase in the number of bone marrow transplants, the current market for which is $10-20 million.

Patent protection is being sought on this technology.
313-1192 JMR

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Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"WATER PHANTOM DEPTH MEASUREMENT DEVICE"

The water phantom is commonly used to calibrate the output of radiotherapy machines, measure depth-dose and other beam parameters. Quite often a cylindrical probe is placed at a desired water depth inside the water phantom tank.

The measurement of the depth of the probe in the water is usually done by using a regular ruler. However, surface tension causes a "water-rise" at the ruler-water interface; this often leads to erroneous depth readings.

A physicist at M.D. Anderson has developed a device to accurately measure the depth of the probe in the water. The device uses tiny pointers for reading water dept in such a way that avoids the problem of "water-rise." Besides, unlike rulers, the device rests freely on the probe, thus allowing a "hands-free" operation. The device is small, light, and simple to use.

This device can be useful to every facility that has radiotherapy equipment and water phantoms, especially output calibration of radiotherapy machines which is done as frequently as once every week.

92-12/0393
TDC

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER SYSTEM

"PARENTERAL ADMINISTRATION FORMULATION OF BUSULFAN"

The invention is a method for dissolving busulfan in a liquid vehicle, allowing intravenous administration of a stable formulation at a known dosage level. This will result in expanded use of high dose busulfan chemotherapy in bone marrow transplant conditioning regimens, with equal or improved efficacy to existing regimens using oral administration.

Busulfan is an alkylating agent which has been used extensively for conventional chemotherapy of hematologic malignancies and myeloproliferative diseases. However, bone marrow and lung toxicity have proved to be dose-limiting. Autologous or allogeneic bone marrow transplant, preceded by high dose cyclophosphamide therapy combined with total body irradiation, is an effective treatment for leukemia and lymphoma. High dose combination chemotherapy using busulfan, most commonly in combination with cyclophosphamide, overcomes some of the problems associated with total body irradiation for conditioning of bone marrow transplant patients. Total body irradiation is excessively toxic to the lungs, cannot be used on patients who have already received radiation therapy, and precludes the opportunity for a second transplant.

However, oral busulfan has several serious effects in the liver and lungs, and can lead to fatal liver failure. Severe nausea and vomiting leads to loss of some or all of the administered dose. Intestinal absorption is erratic and is influenced by the patient's nutritional state, concurrent administration of other drugs, time of last meal, and by individual biological variability. Thus, oral administration has an inherent, and unpredictable, safety problem. Potential overdosing can lead to fatal liver and lung toxicity while underdosing may lead to recurrent or persistent malignancy after bone marrow transplant.

An intravenous formulation allowing stable and precisely defined busulfan dosages will be of great benefit to the clinician.

Projected U.S. figures for annual bone marrow transplants show that by the year 2000 there will be 25,000 transplant procedures for leukemia, lymphoma, and other malignancies. An estimation of 15,000 transplants for leukemia and lymphoma in the U.S., and at least double this number world wide, represents a potential market of $30 million annually for busulfan used in high dose chemotherapy for transplant conditioning. The use of colony stimulating factors to improve marrow engraftment, and the development of stem cell transplants derived from peripheral blood can be expected to expand this market significantly.
342-0593 JMR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NOVEL ANTHRACYCLINE ANALOGS"

Description
The anthracycline antibiotic Doxorubicin (DOX) is an effective anti-cancer agent that has been widely used against a variety of human malignancies. Unfortunately, its anti-tumor activity is also associated with adverse systemic effects and the development of drug resistance that decrease its chemotherapeutic efficacy. These limitations have spawned efforts to develop DOX analogs with greater tumor cytotoxicity and less susceptibility to drug resistance.

Researchers at M.D Anderson have synthesized two novel anthracycline analogs with modified basicity which have unusually high activity against a variety of multidrug resistant (MDR) cell lines. When tested in *in vitro* cytotoxicity assays, these analogs have very significant activity against murine and human cell lines which are known to be sensitive and resistant to doxorubicin, doxorubicin analog AD198 and vinblastine. These results suggest that the altered basicity of the analogs play a role in circumventing drug induced resistance and therefore have potential as anti-cancer agents with increased effectiveness.

Market
The current market for anthracycline anticancer drugs is in excess of $300M, with an expected annual growth rate of 9%. Thus, there appears to be substantial commercial opportunities for novel anthracycline analogs with improved clinical performance. Patent protection is currently being pursued for these analogs.

Patents
A U.S. patent has been filed.

Availability: For exclusive license

MDA Ref. No.: UTSC:337

337/0793/FSR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M. D. ANDERSON CANCER CENTER

"NUTRITIONAL COMPOSITIONS WITH ANTIPROLIFERATIVE AND CHOLESTEROL LOWERING EFFECTS"

Elevated cholesterol, particularly low density lipoprotein (LDL), is a major risk factor for atherogenesis and coronary heart disease. It is thought that high levels of serum cholesterol contribute to the formation of plaques within the walls of arteries, resulting in narrowing and eventual life threatening blockages. Consequently, maintaining the recommended level of serum cholesterol has been a major health concern for the general population.

Although prescription drugs to lower cholesterol are available, these are generally reserved for patients who have extremely elevated levels of cholesterol since there is a risk of side effects. Healthy individuals whose cholesterol levels are only nominally elevated, generally rely on the modification of their diet to reduce and maintain serum cholesterol to recommended levels. For many people, this approach is difficult and often not successful.

Scientists at M.D. Anderson have developed a natural product technology that has been shown in rats to reduce serum cholesterol levels by as much as 29% when given as a dietary supplement in low and high fat diets. Moreover, LDL, (the so called bad cholesterol), was lowered by as much as 43% without appreciably altering the high density lipoprotein (HDL) component. The compound that is responsible for these results, occurs naturally in many fruits and vegetables and appears to be nontoxic to rats at the concentrations tested. Furthermore, the reduction in cholesterol is achieved in a manner which is different than that observed with prescription drugs. These drugs appear to reduce lipoprotein levels in association with a stimulation of cell proliferation. In fact, many well known cholesterol lowering drugs have been reported in the literature to be carcinogenic in different animal models. In contrast, the natural compound identified by M.D. Anderson scientists has been shown to possess antiproliferative properties characterized by its antitumor activity in animal studies.

According to the American Heart Association, over 150 million Americans have total cholesterol levels above 200 mg/dl, which is considered "high" or borderline high. Thus, this novel cholesterol lowering technology has substantial market potential as a presumably over-the-counter dietary supplement that could be supplied as a food additive or as a health drink. We are presently seeking patent protection for this exciting technology.
173-1293 TDC

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NON-CONFIDENTIAL DISCLOSURE
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NOVEL STEM CELL INHIBITING PROTEIN"

Cytokines secreted by accessory cells have been reported to regulate proliferation and differentiation of bone marrow stem and progenitor cells *in vitro* and *in vivo*. These include the Interferons, Tumor Necrosis Factor, and a family of chemoattracting cytokines, or Chemokines, characterized by Macrophage Inflammatory Protein-1 alpha (MIP-1 alpha). Functionally, chemokines stimulate cell chemotaxis, but each chemokine exerts its effects on a particular subset of cells. Chemokines which suppress hemopoietic stem and progenitor cell proliferation include MIP-1 alpha, Interleukin-8 (IL-8), and Platelet Factor 4 (PF4).

Researchers at M.D. Anderson Cancer Center, Indiana University School of Medicine, and Memorial Sloan Kettering Medical Center have isolated, purified, and characterized a chemokine which causes dose-dependent and reversible suppression of human hemopoietic progenitor cells *in vitro*, and which is expected to be less toxic than IL-8. A biologically active version of the 9.9 KDa protein has been cloned and expressed in baculovirus expressing cells and in E. coli.

Neutropenia associated with myelosuppression remains the leading dose-limiting toxicity of systemic cancer chemotherapy. The recent introduction of recombinant hemopoietic growth factors (HGFs) has already had a major impact on the management of patients receiving cancer chemotherapy. However, there is evidence that use of HGFs may cause bone marrow stem cell depletion, since stem cells which have been induced to cycle and proliferate will be killed by repetitive high dose chemotherapy. This novel chemokine could be used in conjunction with HGFs to suppress stem cell growth and thus prevent bone marrow cytotoxicity.

Clinical applications of this molecule will be in its use as a stem cell protective agent to allow the administration of increased doses of chemotherapy or radiotherapy without increased bone marrow toxicity. American Cancer Society statistics estimate an incidence of 1,170,000 cases of cancer in the U.S. for 1993, approximately half of which will receive chemotherapy and/or radiotherapy. The potential market for this compound can be compared with that for Ethyol, which has been estimated at $400 million annually.

Patent protection is being pursued for this technology.

360/1293

KVF

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THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER
NON-CONFIDENTIAL DESCRIPTION

"MPM-2 ANTIBODY"

General Description:
MPM-2 is a murine monoclonal antibody (IgG) which was raised against mitotic HeLa cell lysates in 1983 at M.D. Anderson Cancer Center. The antibody preferentially recognizes mitotic cells in all species tested (eg. human, mouse, mosquito, physorum, annelid etc.) It decorates both the soluble and structural fraction of mitotic cells. The antibody has been used in the laboratory, both at M.D. Anderson and other institutions, for immunoprecipitation, western blottting and immunocytochemistry on cytospins and paraffin block preparations, and in flow cytometry. In fact, M.D. Anderson has sent almost 200 antibody aliquots to researchers in more than 100 laboratories in the United States and throughout the world, and the number of new requests is increasing rapidly.

Epitope Description:
MPM-2 appears to recognize the mitotic-specific phosphorylation of a large number (50) of phosphoproteins. Phosphatase treatment of samples eliminates their MPM-2 reactivity. The phosphoproteins recognized by MPM-2 are thought to play important roles during mitosis. While most MPM-2 antigens remain to be identified, three known antigens include microtubule-associated protein-4 (MAP-4), topoisomerase II , and the mitosis regulatory protein cdc25. Although the phosphokinases which create the phosphoepitope are not well described, one identified kinase is MAP kinase.

Major Current Uses for MPM-2:
1. MPM-2 can be used to decorate mitotic cells in paraffin blocks and can be used to measure mitotic frequencies in tumor specimens. Since MPM-2 does not recognize apoptotic bodies, use of the antibody overcomes problems associated with morphologic determinations of mitotic frequencies, and the signal generated is easily quantifiable by automated image analysis sytems. we therefore anticipate significant antibody demand from clinical pathologists.

2. MPM-2 can be used in conjunction with flow cytometry, and allows easy differentiation of cells in G_2 phase from those in mitosis. This distinction is not currently possible on the basis od DNA content alone. Thus the antibody would be useful for flow cytometry applications.

3. The phosphoproteins recognized by MPM-2 appear to play important roles in cell cycle control as well as in functional aspects of cell division. Thus the antibody will be extremely useful for researchers trying to dissect out these cellular functions.

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JMR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NOVEL PROSTATE SPECIFIC ANTIGEN MARKER"

Clinical Significance

The PSA test has become an important factor in the diagnosis and clinical management of prostate cancer. The test is widely used, along with the digital rectal examination and diagnostic ultrasonography, to permit an early diagnosis of prostate cancer in "high-risk" men. After radical prostatectomy, a fall in the serum PSA concentration to an undetectable level gives assurance of curative therapy; while measurable PSA concentrations which remain after surgery signals the presence of extra-capsular disease and the need for additional therapy. Serial PSA monitoring of patients after curative therapy can identify patients who develop recurrent disease, in many cases, long before clinical symptoms indicate recurrence.

Current Needs and Potential Problems

The clinical accuracy of the PSA test is related to the specificity and sensitivity of the test procedure, and this is primarily controlled by the antisera used in the assay. Since PSA is a member of the kallikrein family of serine proteases, there is question about the specificity of current antisera for PSA. We have recently demonstrated for the first time that all currently available test methods use monoclonal and polyclonal antisera that will cross react with HgK-1 (human glandular kallikrein). Thus, if HgK-1 is present in the circulation, it will be measured as PSA. Since HgK-1 and PSA are under similar gene control mechanisms, it is highly likely that HgK-1 is overexpressed, and when so, there is every reason to believe that it is also present in the circulation at elevated concentrations.

Even at low concentrations, the HgK-1 protein or other kallikreins might be responsible for "background" PSA values which limit the test sensitivity and detection limit for the PSA test.

A recent advance in the preparation of site-directed antibodies has permitted investigators at MD Anderon Cancer Center to prepare highly specific antibodies to PSA which do not cross react with proteins homologous to PSA. This new antibody will make it possible to answer the following questions:

1. Are PSA-related proteins present in the circulation?
2. Do these cross-reactive proteins result in false-positive test results for PSA?
3. Are these cross-reactive substances responsible for background noise, which limits the PSA detection limit?

Future of PSA

The clinical utility of PSA is clearly related to these specificity and sensitivity issues of the PSA antisera. Laboratory and clinical studies to assess the significance of the new MD Anderson antisera are now being planned and will be initiated in the near future. If our hypothesis is correct and this new MD Anderson antiserum resolves cross-reaction interferences, it will result in the next generation of PSA test methods. Currently the PSA test generates a lucrative market of over $145M, which is expected to grow to $290M by the year 2000.

Patent Protection: Patent pending.
388:FSR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"DIAGNOSTIC IMAGING LASER DEVICE"

Description

Breast cancer is the most common malignant neoplasm and the leading cause of deaths in women in the U.S. Presently mammography and ultrasonography are the two most frequently used methods of detection. Mammography is currently the standard means of detecting nonpalpable breast cancers, but it uses hazardous ionizing radiation and the imaging of radiographically dense breasts is difficult. Ultrasound does not allow detection of significant numbers of nonpalpable cancers which are not visible on mammograms of good quality. Although MRI (magnetic resonance imaging) is superior to mammography in differentiating solid from cystic lesions, it is very expensive, has inferior spatial resolution, and cannot image microcalcifications which are often the sole indicators of breast cancer.

Researchers here at M.D. Anderson have developed a unique diagnostic device that will be able to locate tumors based on the differences in elasticity and optical properties between the tumors and the surrounding tissues. The technology utilizes the continuous-wave ultrasound to modulate the laser light passing through the focal spot of the ultrasound wave. By scanning the ultrasound focal point with the laser light acrossing the tissue, the device takes advantages of ultrasound's high penetration and laser's high quality of contrast. In addition to its high reliability in diagnostic imaging, the technique is of low cost (up to 50% cost saving of current mammography) and free of the hazards of ionizing radiation. It will allow for easier detection of tumors in dense breasts of young women that sometimes go undetected with mammography. Looking ahead, our scientific team at M.D. Anderson has the expertise and experience to carry this novel technology forward. The inventors were just awareded a reaserch grant from NIH, valued at over half a million dollars.

Early detection is the best means of improving the cure rate in breast cancers. In addition to being used as an inexpensive breast cancer screening and detection method, this non-invasive device could possibly find use in prostate cancer detection and in other areas of medical imaging. It is expected that the technology would have the potential that CT had in the 1970s or MR in the 1980s.

Patent A US. patent is pending

Availbility Avaible for exclusive license

MDA ID # **94-20 (UTSC:460)** (KQ/1195)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

“NEW USE FOR BREQUINAR SODIUM”

Researchers at the University of Texas M.D. Anderson Cancer Center have discovered a new use for brequinar sodium (DUP 785) while investigating its anti-tumor effects on patients at the hospital. Using a mouse model, we have demonstrated the reversal of serum levels of a compound known to increase to dangerously high levels during the course of certain cancers. The total number of patients suffering from this secondary disease is estimated to be over 90,000 annually. Furthermore, brequinar sodium needs to be investigated for efficacy and safety in chronic sufferers which can treat an additional market of over 75 to 200 million people, or $1billion worldwide. If you are interested in obtaining more information on this technology, please contact M.D. Anderson's Office of Technology Development.

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"RAPID SCREEN TEST FOR METASTATIC MELANOMA"

This year over 500,000 new cases of skin cancer (squamous cell carcinoma, basal cell carcinoma, and melanoma) will be detected and one out of 500,000 moles will become malignant. Of those cases of skin cancer, over 29,500 will be diagnosed as malignant melanoma in the United States and over 80,000 will be diagnosed in Europe. Experts predict that 1 to 2 percent of the US population may develop melanoma if the current rates continue to increase.

Scientists at M.D. Anderson have developed a novel single step DNA PCR screening assay for the direct determination of the presence of an HLA class II allele using whole blood that appears to define a subpopulation of melanoma patients destined to develop metastatic disease. Having already statistically proven its significance in determining melanoma, further studies showed the same gene was associated with the risk of recurrence in melanoma patients presenting with localized disease.

Standard molecular oligotyping for determination of HLA class II alleles is very labor intensive, requiring extraction of genomic DNA, dot-blotting of PCR-amplified DNA products, and allele-specific hybridization of dot-blots with radiolabeled oligonucleotide probes. Therefore, our scientists have developed a non-radioactive method using unique primers and conditions, and whole blood to allow for the rapid determination of this particular allele. The advantages of developing a quick, inexpensive and accurate test will make it the procedure of choice for screening melanoma patients and others with this allele.

Using this genomic marker, dermatologists and medical oncologists will be able to identify those melanoma patients more likely to progress and therefore benefit from adjuvant therapy. if you are interested in obtaining more information about this technology, please contact the University of Texas M.D. Anderson Cancer Center's Office of Technology Development.

442/0195/FSR

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"ANTIMICROBIAL COATING OF ORTHOPEDIC DEVICES"

The U.S. is the largest geographic market for orthopedic products, representing almost 50% of the estimated 1994 worldwide sales of $4,057 million. Western Europe accounts for about 32% of the market, Japan 10% and the rest of the world 8%.

Over 4.4 million people in the U.S. have at least one internal fixation device and over 1.3 million people have an artificial joint. About 120,000 hip protheses are implanted every year in the U.S. On average, about 1-5 % of these orthopedic implants usually become infected. Most organisms that cause infection of these orthopedic devices are inoculated at the time of surgery or shortly thereafter, although the infection may not clinically manifest itself for months. The use of antibiotic-impregnated cement at the time of insertion of orthopedic implant is not feasible for some patients, including those who already have an infected implant in place, and may be associated with defects in the host defense system.

Scientists here at M.D. Anderson Cancer Center, in collaboration with others at Baylor College of Medicine, have developed a new method of coating orthopedic devices and other medical implants with a combination of antimicrobial agents. Neither of the antibiotics used are considered as front line therapeutic agents, therefore, the impact of bacterial resistance, if it ever develops, is extremely small. Other medical implants coated with this antibiotic combination have been shown to be very safe. The patients who have been enrolled in a randomized clinical trial to evaluate the efficacy of antibiotic-coated central venous catheters versus uncoated catheters have demonstrated no adverse side effects. Orthopedic devices coated with this combination of antibiotics would replace the use of antibiotic-impregnated cement. It can also be used in patients who already have an infected orthopedic prosthesis ; in such patients, a one-step replacement surgery can be as successful as the traditional two-step replacement surgery, and can induce tremendous cost saving.

446/0195

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NON-CONFIDENTIAL DESCRIPTION
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"APPLICATIONS OF STABLE RADIOLABELED LIPOSOMES"

Liposomes will play an important role in the development of diagnostic imaging as carriers of various contrast agents, and paramagnetic elements. Their diagnostic use as carriers of radiopharmaceuticals is more advanced in nuclear medicine than in other branches of diagnostic imaging, and their future use as therapeutics is very promising. These 99m-Technetium labeled liposomes were found to be excellent radiopharmaceuticals for diagnostic imaging purposes. Results show that they are also nontoxic to human white blood cells. The incorporation of various molecules into these very stable liposomes can be developed for active targeting techniques by using membrane determinants for in vivo targeting of blood cells, and in vivo targeting of tissues and organs. Nonspecificity is a drawback shared by all other currently used infection imaging agents, such as Ga citrate, radiolabeled white blood cells and radiolabeled immunoglobulins.

These radiolabeled liposomes fulfil many important characteristics required for a useful radiopharmaceutical. First of all, they are very easy to prepare and demonstrate excellent in vivo stability. The incorporation of additional compounds into the membranes protects the 99m-Technetium from interacting with plasma and blood cells, therefore delaying vesicle opsonization. The fluidity of these vesicles along with their hydrophilic protective coat results in delayed uptake by the reticuloendothelial system. Also, the liposomes are very inexpensive and non-toxic. Furthermore, such liposomes can easily be lyophilized and stored in a kit form for instant easy preparation. The kit preparation would require only the addition of a radiotracer, then mixing and dispensing for a specific dosage injection.

The diagnostic nuclear medical imaging market is increasing by about a twenty percent annual growth rate. Worldwide revenues were over $1 billion in 1994 and are expected to be over $3 billion by 1998. Innovative products in this area have the potential of being very successful and profitable.

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"RADIOLABELING OF WHITE BLOOD CELLS USING LIPOSOMES"

This procedure is a new, simple, and safe method for selectively radiolabeling white blood cells in whole blood. It is based on the phagocytosis of 99m-Technetium labeled liposomes, which can be very useful for diagnostic imaging of infections and inflammations. The method is simple and does not require cell separations and washings that could harm the cells and eventually affect the results and reliability of the diagnostic imaging. Also, the currently used methods for white blood cell labeling based on phagocytosis of radiolabeled particles have drawbacks that are related to difficulties in preparing the particles with definite physicochemical characteristics, and other difficulties related to the separation of the non-phagocytosed particles from the labeled cells. With liposome technology, it is possible to prepare liposomes of any size and charge in order to actively target different cell types. In addition, this technology has a very high labeling efficiency and there is no elution of the radiolabel from the cells. Nontoxic substances are used and the normal cell functions are preserved.

Because of the increasing demand for new radiopharmaceutical products and better imaging agents, the market is expected to grow rather rapidly in the next few years. Worldwide, the market is expected to grow to more than $1 billion, and will be driven by disease-specific radiopharmaceuticals. Products that are able to bind to specific receptors and make definite diagnoses for tumors and other infections will be in the forefront of the technology.

455/0295

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NON-CONFIDENTIAL DESCRIPTION
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"MACROPHAGE TARGETING AND POTENTIATION OF THE THERAPEUTIC EFFICACY OF ANTIMYCOBACTERIAL AGENTS"

Description:

Opportunistic infections are the major cause of morbidity and mortality in immunosuppressed individuals, particularly patients with cancer and acquired immune deficiency syndrome (AIDS). Infection due to *Mycobacterium avium-intracellular complex* (MAC) is the most frequent and fatal complication in AIDS patients. MAC is an intracellular pathogen that is resistant to many of the standard antituberculous drugs. This resistance, in many cases, is attributed to low permeability of the drugs to the intracellular sites, lessor retention inside the cells or degradation before the drugs reach their tissue targets. In addition, the difficulty in achieving high concentrations of these agents in appropriate sites where the infection resides, may contribute to the pathogens resistance.

The research and studies being done here at M. D. Anderson Cancer Center are focused on the enhancement of the therapeutic efficacy of antimycobacterial agents by targeting to macrophages and/or by using them in combination with immunomodulators or macrophage activators. Macrophages are the major host cells in mycobacterial infections; they also constitute the major natural defense against mycobacteria, and other fungal and bacterial diseases. Host defense against intracellular parasites is primarily a function of macrophages activated by cellular immune mechanisms. It is well recognized that liposome-encapsulated drugs are delivered efficiently to circulating monocytes, which accumulate them in the liver, spleen, lungs, skin and other tissues. This makes liposomes an attractive means to deliver drugs to macrophage-associated and disseminated forms of infections. Using liposomes overcomes many of the problems described above, in addition to allowing parenteral administration of poorly soluble and toxic drugs. Moreover, the problems of stability and absorption in the gastrointestinal tract can be avoided while enhancing the uptake by macrophages and tissues where infection resides.

The antimicrobials selected, particularly clofazimine, showed very good activity against MAC, can easily be encapsulated into liposomes, and their antibacterial activity is maintained or increased after liposome encapsulation. In addition, they are also very stable. The lipid composition used has been shown to be non-toxic and is also being used in clinical studies without any toxic effects. These drugs also showed high activity against *Mycobacterium tuberculosis*, including some of the most drug resistant strains. Also, significant reduction in infection has been achieved using this drug in a macrophage *in vitro* model and a mouse *in vivo* model.

Mycobacterial infections are on the increase, and this trend should continue with the recent upsurge of tuberculosis infections in immunosuppressed as well as normal healthy individuals. This rise in the U.S. is largely attributed to the AIDS epidemic, and will continue due to the lack of an effective cure for AIDS, as well as mycobacterial diseases. This marketplace is very significant and will continue to become more important. From an estimated market value of $807.5 million in 1993, treatments for HIV, AIDS and related infections are expected to reach a market value of over $1.4 billion by 2000.

Availability: exclusive license

Patent(s): US. Patent application pending

Ref: 007GA

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
Web Page: www.mdanderson.org/~otd/

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"MAPPING OF ADENOVIRUS 5 E1A FUNCTIONAL DOMAIN REPONSIBLE FOR SUPPRESSION OF NEU TRANSFORMATION VIA TRANSCRIPTIONAL REPRESSION OF NEU"

Overexpression and amplification of oncogenes or proto-oncogene with increased tyrosine kinase activity has been clinically implicated in the genesis of human malignancies. The Neu, also known as c-erbB-2, HER-2 or NGL, was found to be overexpressed in many human cancers, including breast and ovarian cancers.

The previous studies have shown that adenovirus 5 E1A protein can suppress neu oncogene expression and suppress the tumorgenicity and metastatic potential mediated by neu. The nature E1A proteins consist of several domains. They are the N-terminal nonconserved domain-CRI, the nonconserved spacer between CR1 and CR2, the CR2 domain, the CR3 domain and nuclear localization domain.

By cotransfecting several sets of adenovirus 5 E1A constructs with Neu promotor-CAT plasmid into NIH3T3 cell, the investigators at M.D. Anderson Cancer Center successfully localized the functional domain responsible for tumor suppression. This mini-E1A provides a new reagent for treatment of cancer. Since the deleted region is known to be associated with transformation by inactivation of tumor suppressor gene RB or transactivation of several virus gene such as E1B, the mini-E1A may avoid any potential side effects caused by these regions and therefore make it a better neu suppressor.

It is anticipated that the technology has broad applications in gene therapy, primarily in breast cancer and ovarian cancer. In addition, the mini E1A can also be sold as a protein product for ex vivo sensitization of cancer cell to chemotherapy during bone marrow purging.

MDA 96-26; UTSC: 503
KQ(09/96)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"METHOD FOR THE LONG TERM GROWTH OF SELF-RENEWING PLURIPOTENT HEMATOPOIETIC STEM CELLS"

Description:
Researchers at the University of Texas M.D. Anderson Cancer Center have for the first time identified the unique culture conditions to support the continuous proliferation of undifferentiated pluripotent hematopoietic stem cell clones in short and long term culture. These clones have been shown to maintain their undifferentiated phenotype, genotype and functional characteristics of PHSC's for a period greater than six months. The long-term cultured PHSC clones are also able to reconstitute the hematopietic system of irradiated mice for a long time and can generate all blood cell types.

Despite the fact that several research groups have tested cytokines in various combinations for their capacity to support proliferation of PHSC in mice and man, in all cases proliferation was associated with differentiation usually along the myeloid/erthroid lineages. Our researchers tested many cytokine combinations and discovered a unique combination of known and a novel cytokine that allows for the long term growth of PHSC cell lines and clones from fetal liver and bone marrow cells of mice.

The establishment of culture conditions that allow for the long-term proliferation, expansion and cloning of undifferentiated PHSC is a breakthrough in the field of science with wide repercussions in the field of cancer therapy and clinical research. It would revolutionize the field of bone marrow transplant, therapy of malignant and non-cancerous blood cell diseases, and (somatic) gene therapy. It would also offer a unique opportunity to specifically stimulate or inhibit PHSC differentiation, and permit the identification of compounds, genes, or cell surface antigens that affect the growth or differentiation of PHSC. Identification of genes involved in self-renewal and differentiation would facilitate marked imrprovements in gene therapy of leukemic or otherwise hematopoietically comprimised patients.

Market:
The market potential for products based on this technology is enormous. The market for blood products is estimated at $2.2 billion; BMT in the U.S. is expected to increase to over $125 million annually; the anemia products market is estimated at $1.5 billion; over 170,000 cancer patients metastasize to the bone marrow and could benefit from stem cell rescue; and the market for using this technology in somatic gene therapy and clinical research can easily exceed $100 million.

Patent Status: Patents pending
Availability: Available for exclusive license
UTSC: **448/456/481**FSR/2/95

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"MONOCLONAL ANTIBODIES AGAINST PROTEIN TYROSINE KINASES KNOWN AS csk"

Description:

Researchers at M.D. Anderson have invented monoclonal antibodies to the protein tyrosine kinase, csk, initially found in neural tissue. Csk regulates the activity of membrane associated nonreceptor protein tyrosine kinases belonging to the src gene family. Five of the antibody clones

developed in M.D. Anderson's laboratory are able to recognize native and denatured $p50^{csk}$, unlike another antibody on the market distributed by Transduction Laboratories which only recognizes the denatured $p50^{csk}$ protein.

Market:

Because our clones can recognize the native and denatured $p50^{csk}$, they have a broader research application and thus can be added to the armamentarium of research tools for protein tyrosine kinase research.

Patent Status: No patent filed

Availability: Available for exclusive license

MDA Ref. No.: UTSC: 412

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"FLUORESCENCE IN SITU HYBRIDIZATION AS A MEASURE OF TRANSFECTION EFFICIENCY"

Description:
This technology describes the use of fluorescence in situ hybridization (FISH) to measure the transfection efficiency of a transient expression vector in lymphoblastoid cells. The currently accepted method for measuring transfection efficiency is based on cotransfection of another vector encoding reporter genes whose expression facilitates in situ visualization of the cells. In this method it is assumed that the transfection rate and the expression efficiency are the same for both the target and the reporting plasmids, and this may not be true. Both methods were compared, and it was concluded that the FISH method is a highly sensitive and specific measure of the transfection efficiency of a transient expression vector. Unlike current assays that are dependent upon expression of the transfected gene, this assay can detect transfection independently of expression.

Market:
This FISH method is useful for evaluating laboratory assays in which the quantitative aspects of transfection are important. It is very specific, and results in no false positives. It also reveals the physical location of transfected plasmids and thus provides accurate information for evaluating the efficiency of a transfection method. This method also helps assess the success of a transfection experiment quickly, because it can be performed immediately after transfection rather than at least 24 hours later when the transfected gene is expressed. It could lead to products such as pre-labeled probes using either the vectors or the reporter genes.

Availability:
Available for exclusive or non-exclusive license

MDA Ref. No.: UTSC: 452

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"A COLORMETRIC METHOD FOR ANTIFUNGAL SUSCEPTABILITY TESTING OF CANDIDA SPECIES"

Description

Inventors at University of Texas M.D. Anderson Cancer Center have developed a new method for antifungal susceptibility testing of *Candida* species. Using a unique combination of ingredients, they have been able to determine the minimal inhibitory concentration (MIC) of *Candida* species. Endpoint determination has been one of the most challenging areas in antifungal susceptability testing. The "trailing effect" caused by growth at azole concentrations much higher than the MIC has resulted in readings that suggest resistance or increased MIC values for known susceptable strains. Our method provides clearcut endpoints for MIC. Unlike other methods endorsed by the National Committee for Clinical Laboratory Standards (NCCLS), this method provides clear endpoints for MIC, is easier to use, more practical, more cost effective, and provides faster results.

Studies are underway to apply this method to a variety of other organisms.

Market

The incidence of antifungal infections has been increasing steadily over the years. The current 1993 market for antifungal compounds to treat fungal infections was $200M in the US and $500-600M worldwide. Eighty to ninety percent of AIDS patients and thirty to forty percent of all leukemia and lymphoma patients develop fungal infections. In 1994 there were 250,000 cases WW, 1/3 from Western Europe and 1/3 from the US.

Investigators at M.D. Anderson have developed a new method for testing the susceptiblity of candida and are looking for industrial interets to market their novel kit.

Availability:

Available for patent and exclusive license

MDA Ref. No.: UTSC: 002GA (ID95-46)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"A NOVEL PROSTATE CANCER ASSOCIATED ANTIGEN THAT IS A TARGET FOR PROSTATE CANCER DIAGNOSIS, PROGNOSIS, AND IMMUNOTHERAPY"

Description:

For years, tumor immunologists have been trying to identify specific target antigens displayed by cancer cells in the use of immunotherapy, that is, to apply these tumor antigens that can be recognizable by cytotoxic lymphocytes such as cytolytic T lymphocytes (CTL) to boost patient's own immune system.

The inventors at M. D. Anderson Cancer Center have recently discovered a novel prostate cancer associated antigen, which may represents a significant advancement in prostate cancer immunotherapy. The coding gene of the antigen was isolated from an *in vitro* model, where a series of cell sublines with different progress stages were generated from parent Prostate specific antigen (PSA) secreting cell line LNCaP. A method has been developed to screen differentially expressed mRNA expression in different cell lines. The antigen expression was found to exhibit 10 fold increased in the metastatic-staged subline. The sequence of antigen gene shows 40-45% homology to GAGE sequences, a new family of tumor specific genes coding for an antigen recognized by autologous cytolytic T-lymphocytes in human melanoma. Further studies show the antigen is expressed on the cell surface and is associated with HLA-Cw6.

The antigen has great potential in immunotherapy of prostate cancer and may serve as a prostate cancer progression marker. Potential applications in the treatment of prostate cancer include: 1) portion of the antigen could be used as an immune adjuvant to elicit the patient's immune system (especially CTLs) against prostate cancer; 2) cytokines such as GM-CSF, along with immunization with portions of the antigen to promote the effectiveness of the therapy; 3) used as a potential marker in prostate cancer progression diagnosis.

Market:

As the most common form of cancer in U.S. men, prostate cancer affects one-third of men over 50. Although surgery, especially prostatectomy, is and will still be the major mean of treatment, an effective immunotherapy will be able to well position itself and grab a significant market share. The potential market could be well over $100 million.

Availability: Available for exclusive or non-exclusive license.

MDA Ref. No.: 95-62 (KQ/0895)

NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"THE SM22*A* GENE CONTROL REGION AS A SMOOTH MUSCLE CELL-SPECIFIC REGULATORY CASSETTE FOR GENE THERAPY OF CARDIOVASCULAR DISEASES"

Description
Smooth muscle cells (SMCs) are important for the functions of the circulatory, respiratory and digestive systems. Alterations in SMC proliferation and differentiation are associated with a variety of vascular diseases including atherosclerosis, restenosis and hypertension. Although various gene therapy approaches have been investigated, where genes were transferred by adenoviral or liposome-mediated vectors into the vessel wall, none of them could assure gene

transfer specificity. Foreign DNAs were inserted into both smooth muscle cells and other vascular cells.

As an important step toward developing therapeutic strategies for treatment of human vascular diseases, the inventors at M.D, Anderson have successfully identified and characterized the control region of *sm22a* gene *of* SMC *in vivo*. A 5' flanking region has been identified to be sufficient to direct the expression of a lacZ reporter in only vascular SMCs of the mouse. No expression was ever observed in respiratory, gastrointestinal or genitourinary SMCs. This control region represents the only SMC-specific DNA sequence identified to date. Moreover, it is the only SMC marker that is not down-regulated during the course of vascular occlusive disease. Therefore, its potential use in treatment of various SMC-associated vascular diseases by SMC-specific gene delivery is enormous.

Market

Cardiovascular diseases is the leading cause of death in North America. A large part of this mortality is attributed to the damage caused by blood clots. Angioplasty is popular and useful in compressing plaques inside of blood vessels. However, 30% of angioplasty patients suffer restenosis within six months following surgery. In many circumstances, restenosis take place even after coronary bypass grafts. In the U.S. alone, the current anti-restenosis market is $500 million. Additionally, the technology is of important use in a number of other vascular diseases as well.

Availability: Available for exclusive license

MDA Ref. No.: 95-59 (KQ/0895)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"A NOVEL METHOD OF INHIBITION OF METASTASIS"

Description:
Metastasis is responsible for the majority of cancer-related deaths. For many types of cancers, the five-year survival rates for metastatic patients are only 2-10% of that of the patients with localized tumors, Although metastasis is known as a multifaceted process requiring cells to change their adhesive and migratory properties, little has been achieved in terms of understanding the underlying mechanism of metastatic invasion and therefore identifying possible inhibition methods.

The inventor at M.D. Anderson has recently conceived and developed a novel method that is able to effectively inhibit metastasis *in vivo*. The method is based on a cell surface enzyme whose expression is believed to be positively correlated with metastatic invasion. By binding to its ligand (specific oligosaccharides) on adjacent cells, this enzyme participates and mediates the metastasis processes. By introducing competitive oligosaccharide substrates that mimic the enzyme-binding site in the basal lamina, the inventor successfully demonstrated *in vivo* that those oligosaccharide substrates have significant inhibitory effects on metastases.

Advantages in applying above technology include:

No toxicity. The oligosaccharides naturally occur in human tissue and thus exhibit no sign of toxicity.

Easy to produce. No dramatic efforts are needed for synthesizing such substrates.

Since the major cause of death from cancer is due to metastases, any effective inhibitory method would be very useful in battling against cancers. Potential market for the technology is projected to be significant.

Availability: Available for exclusive or non-exclusive license.

MDA Ref. No.: 463 (KQ/0895)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"MODIFIED TURBIDIMETRIC MICROBROTH METHOD OF ANTIFUNGAL SUSCEPTIBILITY FOR FLUCONAZOLE, AMPHOTERICIN B AND FLUCYTOSINE (5FC) AGAINST DIFFERENT SPECIES OF YEASTS"

In an attempt to achieve standardization of antifungal susceptibility test, the National Committee on Clinical Laboratory Standards (NCCLS) created a subcommittee in 1966 to supervise and coordinate all recommendations toward this goal. To date, no standard is yet available.

As a potential standardized testing method, the invention adopted the reference method of the National Committee for Clinical Laboratory Standards for Yeasts (M27-P), and further modified and optimized the protocol.

The potential product applications includes in vitro determinations of MICs for yeasts both for research and clinical purposes. It can be used to monitor drug efficacy both in the clinical and experimental standpoint. it can be used to distinguish between drug failure due to resistance versus drug toxicity or medical limitaitons such as neutropenia, catheter related or site of infection. It can be used for determination of drug activity spectrum for existing and newer antifungals. It can provide data for in vivo and in vitro correlations both in clinical and laboratory settings. It can also be used to monitor efficacy of prophylactic regimens in cases of break-through infections. Provide a guide for therapeutics including continuance of empiric choices.

Availability: Exclusive or non-exclusive license

MDA Ref No: 95-58 (KQ0496)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"SHUNTED CLOSED LOOP SYSTEM"

Description:
This device is a shunted closed loop system that can be incorporated into a single or multiple lumen catheter design. A silastic sheath runs the entire length of the catheter which will have in-flow (A) and out-flow (B) injection ports. The externalized loop will allow for the introduction of antimicrobial/anticoagulant preparations along the entire length of the catheter, with diffusion from compartments A and B into the lumen and external surfaces.

Vascular catheters are inserted in more than 20 million patients in hospitals each year, and catheter-related septicemia represents the most life-threatening complication of vascular catheters. This new device will allow for the replenishment of the antimicrobial/anticoagulant agents along the path of the catheter as frequently as needed in order to maintain the potency and efficacy of the preparation. It will also allow for very prolonged and safe use of indwelling catheters, thereby eliminating the infectious and thrombotic complications that presently result from the use of long-term catheters.

Market:
The world catheter market is expected to grow 9% per year to reach $3,700 million by 1998, with the central venous category growing from $374 million in 1994 to $537 million by 1998. The predicted U.S. market in 1996 for central venous catheters will be about $272 million.

Availability: Available for exclusive license

MDA Ref. No.: 384-0696(KVF)

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NEW AGENTS FOR THE PREVENTION AND TREATMENT OF FUNGAL INFECTIONS"

Description:
Fungi are the major cause of infection-related mortality in patients with hematologic malignancy and in patients undergoing bone marrow transplantations. In addition, fungi utilize certain substances not only for their growth, but also as fungal virulence factors. Recent laboratory studies have demonstrated that a non-antimicrobial inhibitor of these substances (currently produced by Abbott and other companies as a generic product) has significant inhibitory growth activity against several pathogenic species of fungi, predominantly the species causing invasive sinopulmonary fungal infections in cancer patients. This agent showed additive to synergistic activity when combined with amphotericin B in inhibiting the growth of these pathogens. At higher concentrations, the combination was sufficient to cause total inhibition of all the pathogens tested.

Because many of these pathogens are inhaled and colonize the sinuses, which ultimately causes fulminant sinopulmonary pneumonia, products such as nasal drops, nasal inhalers, and nasal sprays could be ultimately manufactured to include this combination of the agent and a antimicrobial. In addition, the products could be mixed and given intravenously, or could be used in broncheoalveolar lavage of patients with pulmonary aspergillosis.

Market:
The antifungal market is tremendous, and several factors are influencing the need for new antifungal agents. In spite of its long years of usage, no resistance has developed to amphotericin B which is considered the antifungal drug of choice. Its toxicity has prompted others to look for different methods of delivery and/or different agents. Despite this side effect, it is still an important therapeutic option, and the worldwide market is forecasted to reach nearly $ 1 billion by 1998, with the lipid and liposomal versions accounting for a significant portion of that total.

Availability: Available for exclusive license

MDA Ref No.: UTSC:495 (ID96-29) 0696/KVF

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NON-CONFIDENTIAL DESCRIPTION
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"NEW AGENTS FOR THE PREVENTION AND TREATMENT OF HIV INFECTIONS"

Description:
The transcription process in viral replication requires certain essential substances. Binding of these substances will inhibit the replication of viruses. This binding agent can be attached to CD_4 monoclonal antibodies, and can, therefore, target cells that have CD_4 receptors and are usually infected with HIV. This agent has been shown to inhibit HIV from causing synthesis and destroying CD_4 positive cells. This agent is safe and can be given intravenously.

In addition, human mycoplasmas can act as cofactors accelerating the progression of HIV infection. They can induce vigorous replication of HIV through activation of CD_4-positive T-lymphocytes. Several antibiotics are highly active against mycoplasma, and these antibiotics in combination with this binding agent can inhibit the mycoplasma cofactor responsible for HIV activation.

Market:
The incidence of HIV is on the rise, and by the year 2000 the worldwide incidence is estimated to be between 30 and 40 million people. Any agent that can curb such a tremendous increase will have a tremendous impact on the market.

Availability: Available for exclusive or non-exclusive license

Patentability: Application in process

MDA Ref. No.: UTSC:496 (ID96-30) 0696/KVF

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"PEA3, A TUMOR SUPPRESSOR FOR HER-2/NEU-OVEREXPRESSING CANCERS"

Description:

A number of previous studies have suggested overexpression of the HER-2/neu oncogene correlates to poor prognosis and poor survival in breast cancer and ovarian cancer patients. It appears that over-expression of HER-2/neu induces tumor metastatic potential and drug resistance of tumor cells. Any novel agent suppressing HER-2/neu overexpression will likely to be an effective therapeutic in treating breast and ovarian cancer patients.

PEA 3 (Polyomavirus Enhancer Activator 3) has been known as a transcriptional factor which normally activate gene expression. The researchers at MDA discovered, however, PEA3 down regulates HER-2/neu expression through transcriptional repression. The studies found:
1) PEA3 binds directly to HER-2/neu promotor. The binding site has been identified.
2) In a HER-2/neu overexpressing ovarian cancer cell line, PEA represses HER-2/neu promoter activity in a dose-dependent manner.
3) PEA represses the transforming activity of the activated genomic rat neu.
4) In an orthotopic ovarian cancer mouse model, liposome-mediated PEA3 significantly improves mouse survival rate and survival time.

Having demonstrated its suppression over HER-2/neu overexpression, the researchers at MDA are currently completing the animal studies, followed by toxicity studies in preparation of filing an IND.

Market
The potential therapeutic applications of PEA-3 address a large medical market. As the leading cause of death among women, breast cancer presents a patient population of more then 720,000 in the U.S., with 180,000 new cases per year. The prevalence of ovarian cancer is more than 70,000 in the U.S., with annual new cases and death of more than 27,000 and 15,000 respectively.

Availability: Available for exclusive or non-exclusive license

MDA Ref. No.: UTSC:500 (ID96-40) 1296/KVF

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"A NOVEL TUMOR SUPPRESSOR GENE IN OVARIAN AND BREAST CARCINOMAS WHICH INDUCES P21"

Description:

Using Differential Display Polymerase Reaction (DDPCR), the scientists at M.D. Anderson Cancer Center have isolated and cloned a novel gene named NOEY2. NOEY2 has been localized to chromosome 1p31 where loss of heterozygosity has been observed in approximately 40% of breast and ovarian cancers. In our studies, the gene was strongly expressed in all eight normal ovarian surface epithelia (OSE) cells, but was lost in 11 of 12 ovarian cancer cell lines and 9 of 9 primary ovarian cancer cell specimens purified from patient ascites. Transection of NOEY2 greatly inhibited the proliferation of both breast and ovarian cancer cell lines that lacked endogenous NOEY2 expression. Further studies showed growth suppression was associated with down regulation of the cyclin D1 promoter activity and induction of p21. Taken together, the data strongly support the possibility that NOEY2 is a novel tumor suppressor gene. To date, cDNA and genomic sequences have been identified. Murine mAbs against NOEY2-GST fusion protein have been generated. In further our understanding of NOEY2, the scientists are working on mutational and methylation analysis.

Conceptually, NOEY2 may be delivered via viral or non-viral vectors into tumor cells in the treatment of a larger portion of breast and ovarian cancer patients. In addition, expression of NOEY2 may have significant diagnostic and prognostic applications in breast and ovarian cancer.

Patent Status: A patent application pending

Availability: Exclusive or non-exclusive license

MDA IDR 97:31

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"WATER SOLUBLE RALOXIFENE ANALOGS"

Description

Raloxifene, a pure anti-estrogen, has been used in the treatment of post-menopausal patients with estrogen receptor positive ER(+) breast cancer and osteoporosis. A response rate of 50%-60% was obtained, as compared to a 30% response rate with tamoxifen therapy. In addition, tamoxifen has agonist and antagonist estrogen activity, and long term use in some cases have reported to cause endometrial cancer. If the detection and measurement of ER(+) tumors can be non-invasively detected by a radiolabeled raloxifene, then such a ligand may predict the response of raloxifene therapy for ER(+) tumors.

Because raloxifene is not very soluble in water, a ligand has been synthesized that is more hydrophilic. This conjugate can be chelated with technetium or indium for SPECT evaluation of ER(+) lesions. By attaching the conjugate raloxifene to a water-soluble polymer that can be used as a drug carrier, it can be sustained released through the intravenous injection route. This offers the advantage of reducing systemic toxicity. Because the raloxifene conjugate can be chelated with other inorganic metals, it has the potential application in the detection of ER(+) lesions by MRI. The labeled raloxifene conjugate may non-invasively identify ER(+) recurrences without resorting to surgical procedures. Because it is more hydrophilic than raloxifene, it has less uptake in the liver and lung, which may interfere with the interpretation of breast cancer lesion since breast lesions are in the vicinity of the liver. In addition to the treatment of cancer, the raloxifene conjugate can be used as a preventing agent.

Athymic nude mice have been inoculated with human breast cancer cells and tested.

Market

Cancer treatment represents one of the most active areas of worldwide research. The combined market for breast and ovarian cancers is huge. The U.S. ovarian cancer therapeutics market reached $233M in 1995, and is expected to total $438M by 2002. The breast cancer market is well over $1 billion**.**

MDA Ref. No. IDR98-02/KVF/0398

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"SELF-EXPANDING Y-SHAPE STENT"

Description

This bifurcated stent consists of a common body and two legs that are made as a whole of one coherent element. The radially expandable and flexible tubular bodies of the stent are made of nitinol wires and utilizes nitinol's superelastic properties. The design makes it possible to use the stent in several vascular and non-vascular territories where bifurcated anatomical structures are present. The range of possible vascular applications extends from aorto-iliac bifurcation through superior vena cava junction to inferior vena cava junction. The stent would be ideal to maintain the lumen of the aorto-iliac bifurcation, for the treatment of abdominal aortic aneurysm, and for the treatment of tracheo-bronchial obstructions. This bifurcated stent can also be used in hilar biliary stenoses, and for malignant stenoses, it can be equipped with a special covering of polyurethane or silicon, or with an anticancer coating.

The stent design makes it possible to change the angles between the crossing wires, thereby creating a tighter mesh and/or a tapering shape, and resulting in a controlled expansile force. The expansile force of the stent can be increased to the point that a virtually incompressible stent can be created. In vitro studies suggest that the same size nitinol stent with a similar mesh tightness as the Wallstent could exert much more resistance to outer compression. The angle between the main body and the legs can be adjusted to accommodate the anatomy. Because of the flexibility of the stent, the angle between the legs, which is selected according to the average sizes of the given anatomical structure, can be used in the majority of the cases. Similarly, the cross-section of the main body can also be changed from a round to a somewhat elliptical shape if necessary, as in a tracheo-bronchial application. For better fixation of the stent, the crown of the commom body can be flared, and its length, as well as that of the legs, can be varied.

Market

Despite increasing worldwide competition, the stent market continues to be technology driven, as new devices allow cardiologists to customize treatment for different kinds of lesions. The market for coronary stents has grown from a mid-sized, hardly astonishing business ($220 million in worldwide sales in 1994) to one that is now over $1 billion in worldwide revenues.

MDA Ref. No. IDR98-22/KVF/0398
IDR98-21
IDR98-20

For more information, please contact: Office of Technology Development, 1020 Holcombe Blvd, Suite 1405, Houston, Tx, 77030. Phone: (713) 792-7598 Fax: (713) 794-1356
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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"NITINOL BASKET OCCLUSION DEVICE"

Description

The most widely used permanent vascular occlusion device is the Gianturco stainless steel coil. Other effective occlusion techniques, such as balloons, have been abandoned because of safety concerns. This basket occluder can cause quicker vessel occlusion. The arrangement of the coil turns largely follows the circumference of the vessel, and as a result, the central part of the lumen remains less covered by the coil. These basket occluders might extend the scope of the indication for the coil embolization, thereby making it possible to use in veins and non-tapered vascular territories where the possibility of migration is high. High-flow vascular lesions including arterio-venous malformations and fistulas could be one of the possible applications of the nitinol-core coils both in lesions of the extremities and lungs.

One of the advantages of the vascular occluding device is that it achieves a better coverage of the given segment of the vessel than the stainless steel coil does. Therefore, the mechanical blocking of the blockage of the blood stream along with the thrombosis induced by the entrapped blood within the basket leads to quicker vascular occlusion. The strength of the nitinol wires with thermal memory and superelasticity significantly facilitates the self-anchoring of the occluder and greatly reduces the possibility of migration. The occluder can be repositioned offering a prompt correction of misplacement. The guide wire compatible version of the design makes the deployment of the occluder safer and more controllable. In addition to causing a prompt and relaible ureteral occlusion, there is no need for injecting other embolic agents to complete the obstruction. This type of occluder can also be used for vascular occlusion.

Market

MDA Ref. No. IDR98-26/KVF/0398

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"SELF ANCHORING COILS FOR VASCULAR OCCLUSION"

Description

The most widely used permanent vascular occluding device is the Gianturco stainless-steel coil. Such devices known as macrocoils have been widely used for vessel occlusions throughout the body. One disadvanatge of the embolic coils is that they tend to migrate if they are used in veins or in a non-tapered vascular structure. High-flow vascular lesions including arteriovenous malformations and fistulas increase the possibility of coil dislodgement even further. A new anchoring coil has proved effective in making coil embolization safer, especially in a high-flow arterial model.

This coil anchoring system is attached to stainless steel Gianturco macrocoils and tested in a short-term and long-term pilot study with use in a high-flow arterial model. The anchor remained partially compressed when placed in a vessel with a smaller diameter than the unconstrained device. Consequently, the anchor leaned against the vessel at multiple points, resulting in a stable position. Use of the anchoring system makes it possible to achieve precise, reliable delivery of the attached occluding coil. Deployment of the anchor is accomplished in two stages. With use of this delivery technique, precise deployment of the anchor can be achieved. Optimal positioning and arrangement of the coil prevents migration. The anchoring coil would not only be able to extend the use of coils to lesions with large diameters, but it would increase the safety of this type of vessel occlusion. This anchoring system makes coil embolization safer by virtually eliminating the risk of migration. The anchor itself does not require a larger delivery system for coil placement and the presence of the anchor within the lumen of the catheter does not restrict catheter manipulation.

Embolization with the use of the anchoring coil may also play a significant role in the nonsurgical management of patients with systemic-to-pulmonary collateral vessels and shunts, as well as in the embolization of coronary artery fistulas. This occluder could also be used for transcatheter therapies performed on the venous side, including embolization of varicoceles and aberrant vessels.

Market

Patentability

Patent pending

MDA Ref. No. IDR97-14/KVF/0398 (stainless steel)
IDR97-20/KVF/0398 (nitinol)

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"SELF-EXPANDING FLEX-STENT"

Description

This is a nitinol, self-expanding version of the Gianturco-Roubin balloon-expandingFlex-stent which is used for coronary stenting. The stent's basic structure and configuration is the same as the original stainless steel balloon-expandable design. Because this new design is made of nitinol, it has become self-expanding, and consequently there is no need to use a balloon-catheter delivery system to deploy the stent. The basic stent structure makes it possible to produce a tapered stent by changing the diameter progressively from one end of the stent to the other. This self-expanding stent shows no recoil, therefore can be used in vessels having a small diameter. The construction of the self-expanding stent enables achievement of a tighter wire mesh and a higher expansile force which can be utilized in the stenting of larger vessels. In addition to its great flexibility and no tendency for longitudinal shortening, this stent restores patency with a minimum amount of metal. Because there is no need to use a balloon catheter for delivery, there is no additional trauma to the vessel wall and no temporary vessel occlusion associated with balloon assisted delivery. This stent can be coated, thereby effectively reducing intimal hyperplasia.

Market

The coronary stent market is growing exponentially. The cardiovascular stent market in the U.S., Europe and Japan is expected to reach $2 billion in annual sales be the year 2001. Coronary stents were used in over 25% of all percutaneous transluminal coronary angioplasty (PTCA) procedures in 1995 and it is projected that the number will increase to over 50% of all PTCA procedures by the year 2000. In 1996, an estimated 460,000 stents were used in coronary interventional procedures worldwide. An estimated 28% annual growth rate in unit sales over the next five years will result in almost 1.6 million coronary stents used worldwide by the year 2001.

Patentability

MDA Ref. No.: IDR98-43/KVF/0598

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NON-CONFIDENTIAL DESCRIPTION
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"CHELATORS IN COMBINATION WITH BIOCIDES"

Description

The emergence of multi-drug resistant bacteria and fungi related to the excessive use of antibiotics and other antimicrobials has been a great concern from the medical perspective. Studies have shown that chelators, when added to antibiotics and antimicrobials, improve the activity against multi-drug resistant microbial organisms through synergistic mechanisms. Other studies have shown that chelators alone can inhibit and suppress the growth of several multi-drug resistant bacteria. The chelators help certain antimicrobials to overcome the intrinsic resistance of organisms. They result in the dissolution of the biofilm layer, hence exposing the organisms to the synergistic activity of the combination of antibiotics and/or antifungals with chelators.

From the industrial perspective, all oil and gas pipelines, in addition to others carrying water and/or other chemicals, become contaminated with bacterial and fungal microorganisms. These organisms form a biofilm on the surface of the pipes, and the organisms embedded in the biofilm environment become well protected against the activity of biocides, antiseptics, and other antibiotics. The bacteria and fungi in the biofilm lead to corrosion of pipes which has a tremendous impact on the chemical, gas, oil, nuclear, and water industries. The method of treatment of these gas, oil, and water pipelines is by flushing these pipes with biocides such as chlorine or antimicrobial agents such as gentamicin. It has been shown that the addition of chelators to biocides and antimicrobial agents causes the biofilm layers to disintegrate and dissolve. This improves the activity of biocides against the embedded bacteria.

Market

Companies spend tremendous amounts on water treatment chemicals alone to fight corrosion and fouling caused by microbial organisms embedded on biofilm attached to the surfaces of pipelines. Likewise, biofilm in pipelines have always been an issue for the oil and gas industry.

Patentability

Patent pending

MDA Ref. No.: UTSC:541/KVF/0898

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NON-CONFIDENTIAL DESCRIPTION
THE UNIVERSITY OF TEXAS SYSTEM
M.D. ANDERSON CANCER CENTER

"CYTOTOXIC T LYMPHOCYTES BASED CANCER THERAPIES AND VACCINES"

Description

The immune system can be efficiently stimulated and targeted to specific antigens expressed exclusively or preferentially by experimental cancers. Previously, only HER2/neu has been shown to be the source of naturally occurring, MHC-restricted cytotoxic T lymphocyte (CTL)-recognized peptides in epithelial tumors. However, the investigators demonstrate that the human high affinity folate binding protein (FBP) is a source of antigenic peptides recognized not only in ovarian cancer but also in breast cancer. Both immunodominant E39 and E41 epitopes are shown to be presented by HLA-A2 in these cancers. These peptides are efficient at amplifying the response of tumor-associated lymphocyte (TAL) populations producing enhanced proliferation and peptide-specific IFN-γ release. Furthermore, on a per cell basis TAL stimulated with the FBP peptides exhibit enhanced cytotoxicity not only aginast peptide-loaded targets but also against FBP-expressing epithelial tumors of different histologies. The broad distribution of FBP among >90% of ovarian and endometrial carcinomas, as well as 20-50% of breast, lung, colorectal, and renal cell carcinomas, along with pronounced differential expression in malignant tissues compared to the extremely limited expression in normal epithelium, suggests the exciting potential of a widely applicable FBP-based vaccine in epithelial cancers.

MDA Ref. No. IDR98-40/KQ/0898

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NON-CONFIDENTIAL DESCRIPTION
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"DEVELOPMENT OF AN ADENOVIRUS VECTOR WITH TETRACYCLINE-REGULATABLE HUMAN TNF-α GENE EXPRESSION"

Description:

Inventors have modified the original multiple-plasmid tetracycline repressor/operator-based mammalian gene expression system. The modification warrants lower constitutive expression of the tetracycline-responsive transactivator (tTA), resulting in a system with no squelching effect on host cells. The novel system is contained within a single plasmid and is readily convertible to tetracycline-responsive adenoviral and other viral vectors. By using this type of viral vectors for tumor- or organ-specific gene delivery, it would be possible to turn off the therapeutic gene expression before the adenovirus vectors or adenovirally transduced effector cells reach the tumor deposits. The advantages of regulatable gene delivery are at least twofold: 1) greatly reduce the systemic toxicity of high-dose therapeutic gene products during the period when the vectors or genetically modified effector cells have been administered to patients but the majority of them are still in the blood circulation; 2) minimize the impact of therapeutic gene expression on the survival, specificity or distribution (homing pattern) of the effector cells *in vivo*. Therefore, the new adenovirus vectors with transcriptionally regulatable therapeutic gene expression may offer unique opportunities for systemic gene therapy of human cancers. In addition, this regulatable vector system facilitates production of various recombinant adenoviruses with insertional gene expression that are highly cytotoxic or cytostatic to the 293 adenovirus producer cells. A prostate cancer gene therapy clinical trail using this type of novel vectors is now undertaken at the University of Texas M. D. Anderson Cancer Center.

Patentability

US and PCT patents pending

MDA Ref. No. 507/KQ/1098

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NON-CONFIDENTIAL DESCRIPTION
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M.D. ANDERSON CANCER CENTER

"THE FIRST MOUSE MODEL FOR OSTEOPOROSIS THAT IS INDUCIBLE AND REVERSIBLE"

Description:
Bone remodeling is characterized by osteoclastic resorption of pre-existing bone followed by formation of new bone by osteoblasts. To define the role of bone formation in the control of bone resorption in vivo, investigators generated an inducible osteoblast ablation mouse model. This model strikingly mimics characteristics of osteoporosis as it has reduced amount of bone mass and density. More importantly, it is not only inducible through administering a drug which kills bone forming cells-osteoblast, but also reversible if a compound is given to arrest the function of the bone-resorpting osteoclast.

It has great utilites for both scientific research and pharmaceutical development. It serves as a great model to study the genetic mechanism of osteoporosis and relevant genes that may be closely associated with the disease. In addition, it is a great animal model to screen and test anti-osteoclast drug candidates.

Availability:
Non-exclusive license

MDA Ref. No. IDR98-23/1198/KQ

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