Targeting Cancer

The University of Texas at El Paso

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Targeting Cancer

Having made significant investments in its research capacity, The University of Texas at El Paso is taking aim at cancer, one of the major health issues affecting our region’s bicultural population.

The focus on biomedical research is evident throughout our campus, located just north of the Rio Grande in the El Paso-Juárez metropolis of 2.4 million people on the U.S.-Mexico border.

As highlighted in this publication, much of the work is being conducted by teams in UTEP’s Border Biomedical Research Center (BBRC), which have access to state-of-the-art laboratories and equipment in our new $45 million Bioscience Research Building.

BBRC researchers are investigating promising drug therapies or vaccines for a variety of malignant diseases, including leukemia/lymphoma, and breast and prostate cancer. Since 1992, the BBRC has been supported by funding from the Research Centers in Minority Institutions Program (RCMI), administered by the National Center for Research Resources at the National Institutes of Health.

In the College of Engineering, researchers have joined the battle against cancer, thanks to recent investments in its bioengineering programs. UTEP engineers are looking for ways to improve cancer screening and diagnosis with medical imaging technologies, and are investigating improved cosmetic tissue-reconstruction methods for cancer patients.

Another critical public health problem addressed by UTEP researchers is disparities in health outcomes among Hispanics. For example, breast cancer, the No. 1 cause of cancer death among Hispanic women, is less likely to be diagnosed at the earliest stage in Hispanic women, compared to non-Hispanic white women. These issues are being addressed by the Hispanic Health Disparities Research Center, a collaboration between UTEP and the University of Texas at Houston School of Public Health.

TARGETED THERAPY

Novel drug holds potential for treatment of T and B cell leukemias and lymphomas.

A biochemistry research team led by Professor and Chair of Biological Sciences Robert Kirken, Ph.D., is testing a promising new drug for treating leukemias and lymphomas of T and B cells, white blood cells that play an important role in the immune system.

Kirken’s team has found that an enzyme primarily expressed in these immune cells, known as Jak3, plays a critical role in the uncontrolled division of cells characteristic of these types of cancers. Their drug targets Jak3, inhibiting its activity and disrupting its ability to send cell-growth signals down the biochemical pathway, but not affecting other enzymes or cell types.

In laboratory testing, the researchers have had encouraging results—the compound was successful in reducing the growth of certain human leukemia and lymphoma cell lines. In animal studies, the drug is also well tolerated and does not appear to elicit the side effects that limit many pre-clinical compounds.

Current treatment options for leukemia and lymphoma include chemotherapy and radiation therapy to kill cancer cells. But healthy cells are affected as well, leading to an array of side effects, such as anemia, fatigue, nausea, diarrhea and hair loss.

Kirken’s approach of using an enzyme inhibitor to selectively target this enzyme, which is not found in other tissues such as the stomach, heart, liver, kidney or brain, would mean that cancer patients may be able to avoid problems with the side effects associated with drug toxicity.
MICROTUBULE-G PROTEIN INTERACTIONS
Chemical pathways may be effective drug targets

Research Assistant Professor of Biological Sciences Sukla Roychowdhury, Ph.D., is investigating the mechanisms of cell division to find biochemical pathways that could become effective drug targets to control cancer cell growth and division. She is studying the chemical interactions of microtubules, protein filaments that play a key role in cell division. Microtubules participate in the organization and function of the mitotic spindle, a vehicle necessary for chromosomal segregation.

Roychowdhury is focused on determining the mechanism by which the G protein signaling cascade regulates organization and function of the mitotic spindle. Understanding these functions will help determine if the G protein pathway can be targeted for identifying new anti-mitotic drugs for cancer therapy.

FATTY ACIDS AND COLON CANCER
Researchers look for effective drug targets

A research team led by Professor of Biological Sciences Siddhartha Das, Ph.D., hopes to develop effective drug therapies for colorectal cancer by understanding the biochemical responses triggered by certain dietary fats. American diets, which are typically high in processed foods made with vegetable oils and low in fresh fish, often have an imbalance of omega 6 fatty acids, which promotes an inflammatory immune system response that leads to a variety of health problems, including colorectal cancer.

Das’ group is exploring the link between dietary fat and colorectal cancer by studying the behavior of a particular omega 6 fatty acid, arachidonic acid. The synthesis and metabolism of arachidonic acid seems to play a major role in producing inflammatory molecules responsible for uncontrolled cell growth that leads to tumors of the colon.

Das is studying the cross-talk (interactions) between phospholipid-hydrolyzing enzymes (i.e., phospholipase A2) and enzymes of inflammatory pathways (i.e., cyclooxygenase 2) in colonic epithelial cells, because these interactions regulate the production of prostaglandins (inflammatory agents) from dietary arachidonic acid. Das is interested in drug compounds that target the enzyme to reduce the production of inflammatory molecules.

HEAT TREATMENT
Magnetic nanoparticles hold promise for cancer therapy

Hyperthermia therapy—exposing tumors to high temperatures to kill cancer cells—holds promise as a cancer treatment, but it has its drawbacks. It generally only works well on small tumors that are easy to reach directly, for example. Larger regional tumors or metastases throughout the body are usually only weakened with hyperthermia therapy, meaning a patient may still have to undergo chemotherapy or radiotherapy.

Assistant Professor of Physics Cristian E. Botez, Ph.D., is proposing research that could lead to improved hyperthermia therapy by using magnetic fields to heat magnetic nanoparticles within a tumor. Botez is interested in developing novel magnetic nanoparticles by altering their chemical makeup to improve their rate of energy absorption. This targeted therapy holds promise for killing deep-seated tumors without affecting healthy tissue.

CANCER BIOMARKER ANALYSIS
Medical imaging technology helps diagnosis and screening

UTEP’s Medical Imaging Informatics laboratory, directed by Professor of Electrical and Computer Engineering Wei Qian, Ph.D., focuses on the collection and interpretation of data from medical imaging systems, such as X-ray, magnetic resonance imaging, computed tomography and ultrasound, to name a few.

One of the laboratory’s main focuses is improving the survival rates and quality of life of cancer patients through the use of computerized cancer biomarker analysis. This advanced technology integrates medical, cellular and molecular imaging data into a computerized system to assist physicians in detecting, diagnosing and treating cancers.

Qian is interested in using cancer biomarker analysis and the laboratory’s other research capabilities to study breast cancer in Hispanic women. According to the Centers for Disease Control, breast cancer is the No. 1 cause of cancer death in Hispanic women.
A NOVEL APPROACH
Compound may be effective in treating hormone-resistant cancers

Assistant Professor of Biological Sciences Marc Cox, Ph.D., is investigating a novel antiandrogen drug compound for the treatment of metastatic prostate cancer. Patients with this disease are usually treated with hormone therapies to lower androgen levels, a key stimulator of prostate tissue growth. These androgen-deprivation strategies may be effective in controlling disease for several years, but prostate cancers eventually develop resistance to hormone therapy, enabling tumors to progress. Patients with hormone-resistant prostate cancers have limited treatment options. Annually, approximately 29,000 deaths are attributed to prostate cancer in the United States, according to the Centers for Disease Control. Thus, there is a need for effective anti-tumor drugs for hormone-resistant cancers. Cox’s drug compound targets a novel molecular mechanism associated with the regulation of the androgen receptor. The drug compound shows promise as an effective and efficient inhibitor of the androgen receptor, with the possibility of less toxic side effects.

GROWTH FACTORS IN LEUKEMIA
Studying the role of LEDGF/p75

Assistant Professor of Biological Sciences Manuel Llano, Ph.D., is studying the role of the lens epithelium-derived growth factor (LEDGF/p75) in leukemia development. LEDGF/p75 is a cellular protein that regulates different cellular genetic programs. Disregulation of some of these programs result in the development of a type of cancer called myeloid leukemia. Disregulation occurs following the fusion of the cellular protein NUP98 to the LEDGF/p75 protein. However, the exact mechanism operating in the development of these leukemias is not known. Llano plans to investigate how the chimera NUP98/LEDGF leads to alterations in these genetic programs that end in the development of leukemia.

DIAGNOSIS VIA CELL RIGIDITY
Atomic force microscopy reveals mechanics of cells

Assistant Professor of Physics Marian Manciu, Ph.D., who has led UTEP’s efforts to establish bachelor’s and master’s programs in medical physics, is interested in developing improved diagnostic methods by studying the mechanics of cancer cells. Even at the cellular level, diseased tissue often has a different elasticity, or rigidity, compared to healthy tissue. Manciu proposes using atomic force microscopy to measure the rigidity of cells. This kind of technology, which uses nano-sized probes to “feel” surfaces, is effective for measuring and manipulating matter at a microscopic scale. Manciu believes understanding the mechanics of diseased cells could lead to significant breakthroughs in cancer screening.

IDENTIFYING CANCER BIOMARKERS
Mass spectrometry may identify drug targets, improve screening

Improved methods to diagnose and treat a wide variety of cancers are on the horizon, thanks to mass spectrometry technology, which is being used by Associate Professor of Biological Sciences Igor Almeida, Ph.D., to identify biomarkers on tumor cells. Mass spectrometry helps scientists identify molecules by measuring their precise molecular mass and determining their makeup. Almeida is using the technology to analyze B-cell lymphoma samples to look for novel lipids, carbohydrates, and proteins, some of which could be effective targets for therapeutic drugs and as biomarkers for diagnosis or prognosis. Mass spectrometry also is being used to develop better screening tools for other types of cancer. For example, researchers are using the technology on urine samples to identify certain proteins that can reveal the existence of prostate cancer in a patient. And others are using the technology to find breast-cancer biomarkers in saliva, which could lead to a simple saliva-based test to detect breast cancer.
PURSUING A BREAST CANCER VACCINE
Understanding T cell anti-tumor responses

Professor of Biological Sciences June Kan-Mitchell, Ph.D., and her laboratory are working towards developing vaccines to treat breast cancers, based on understanding how the human immune system recognizes breast cancer cells. They have developed a new method to educate naïve T cells in the test tube to recognize tumor cells, which will lead to defining in chemical terms what the human immune system recognizes.

This approach will be used to measure and understand anti-tumor T cell responses, which are normally not particularly effective in patients. More importantly, it will allow Kan-Mitchell and her team to design artificial vaccines that may prove more effective.

BIOPRINTING NEW TISSUE
Cutting-edge technology could be used in breast reconstruction

Assistant Professor of Mechanical Engineering Tao Xu, Ph.D., is leading research at UTEP in bioprinting, the use of inkjet printing technology to engineer tissue. As the name suggests, printing cartridges are loaded with cells rather than ink, and layers of cells are sprayed down on a surface to create living tissue.

Xu is interested in applying this technology to help breast cancer patients who require reconstruction after a mastectomy. A major challenge in this procedure is the reconstruction of the nipple. Current reconstructive techniques have the drawbacks of scarring, skin graft rejection or unsatisfactory cosmetic results.

Xu believes bioprinting can produce a better result. He proposes applying differentiated stem cells on bioabsorbable scaffolds to reconstruct a nipple that will have less risk of rejection and ultimately a longer lasting cosmetic result.

Xu also is interested in the use of electronic therapies to kill cancer cells. Xu’s lab seeks to bioengineer micro-sized photovoltaic devices that can be introduced into a tumor to kill cancer cells by generating an electric current. These devices will be triggered by using a deep penetrating, near-infrared light.

ARSENIC EXPOSURE AND CANCER
Understanding toxicology at the cellular level

Instructor of Biological Sciences Horacio Gonzalez, Ph.D., is interested in studying arsenic exposure’s link to cancer development at the cellular level.

To understand the molecular disturbances that lead to cell malignancy, Gonzalez is turning to epigenetics, the study of changes in gene expression caused by factors other than changes in the DNA sequence. These mechanisms include alterations of the complex regulatory network of signals and molecules that affect the behavior of genes.

Gonzalez proposes studying microRNAs—small sequences of ribonucleic acid that regulate gene expression—in cells exposed to arsenic. Some microRNAs have been shown to be aberrantly expressed in a variety of tumors and in the blood of cancer patients. He hypothesizes that arsenic will alter microRNAs in malignant-ly transformed cells, and studies of this will help lead to a better understanding of the cause-and-effect relationship of epigenetic changes and cancer.
INCREASING HISPANIC PARTICIPATION
Programs boost minority representation in education and research.

Radiation Oncology
Since 2006, UTEP has been putting more Hispanics in the cancer treatment and research career pipeline through an innovative program led by Assistant Professor of Physics Marian Manciu, Ph.D. The “Increasing Minority Representation in Radiation Oncology Physics” program is a collaboration between UTEP and The University of Texas Health Science Center (UTHSC) at San Antonio. Funded by a $500,000 National Institutes of Health grant, the program offers a bachelor’s degree in physics with a concentration in medical physics. The main objective of the project is to create a permanent pipeline of talented Hispanic students extending from El Paso high schools to a M.S. in medical physics at UTEP and ending with the Ph.D. program offered by the UTHSC at San Antonio Radiation Oncology Department.

Addressing Health Disparities
The Hispanic Health Disparities Research Center, founded in 2003, is a collaborative effort between UTEP and The University of Texas at Houston School of Public Health – El Paso Regional Campus. Researchers are continually adding to the body of knowledge of Hispanic health issues, and are investigating strategies to improve the well-being of Hispanics, particularly those who live along the border.

In regard to cancer health disparities, researchers have proposed a study of the willingness of Mexican-origin and Puerto Rico-origin Hispanics to participate in cancer screening studies. It is hoped the results of the in-depth, multi-city study will improve recruitment of Hispanics into biomedical studies, which in turn will increase the amount of health data on this population.

Assistant Professor of Nursing Diane Monsivais, Ph.D., is interested in learning more about cancer pain management in Hispanic populations. She has proposed a focus group study to gather information regarding cultural attitudes and beliefs about pain management, including the use of medications and non-pharmacologic interventions.

Assistant Professor of Nursing Gloria Lopez-McKee, Ph.D., hopes to translate and culturally adapt three instruments which will be used to gather data about factors which impact mammography screening among low-income, low-literacy Hispanic women. These instruments include the following: Champion Mammography Self-Efficacy Scale, McCance Breast Cancer Knowledge Test, and Champion Revised Susceptibility, Benefits and Barriers Scale for Mammography Screening. The Spanish language versions of these instruments are being compared to the original English versions with respect to their psychometric equivalence.
Core Facilities

Targeting Cancer

BORDER BIOMEDICAL RESEARCH CENTER CORE FACILITIES

Cancer researchers have access to state-of-the-art laboratories and equipment in UTEP’s Border Biomedical Research Center (BBRC), housed primarily in the new, five-story, 100,000-square-foot Bioscience Research Building in the heart of campus. The Border Biomedical Research Center was established in 1992 and is supported by the Research Centers in Minority Institutions Program (RCMI), administered by the National Center for Research Resources at the National Institutes of Health. The center offers six core facilities for researchers: research.utep.edu/bbrc

Analytical Cytology
The Analytical Cytology Facility provides researchers with assistance in the design of protocols and preparation of specimens for various types of microscopy, including electron, Zeiss Pascal confocal, and Zeiss Axioskop epifluorescence with video-enhanced imaging capabilities. Leica ultramicrotomes and freeze-substitution equipment, a Pelco microwave fixation oven and standard darkroom facilities support cell image collections.

Cell Culture and High Throughput Screening
The Cell Culture and High Throughput Screening (HTS) Facility provides support to researchers by culturing and manipulating mammalian, bacterial and insect cell lines. This facility contains nine Class II Biosafety cabinets as well as 12 CO2 incubation chambers placed within six self-contained culture suites. The core repository contains more than 250 different cell lines. In addition, the facility includes cell sorting and HTS equipment that will facilitate cell analysis and characterization as well as provide compound/drug screening assay development.

Biomolecule Characterization
The Biomolecule Characterization Facility provides research groups with equipment for separation and characterization of biomolecules, and the synthesis and amplification of nucleic acids. Equipment available in the facility includes liminometer, fluorometer, electrophoresis systems, documentation equipment, UV/VIS spectrophotometers, molecular imagers, qualitative and quantitative thermal recyclers, low-and high-pressure liquid chromatography systems, capillary electrophoresis, gamma and beta scintillation counters, preparative centrifuges, ultracentrifuges, flow cytometer and an electrospray ionization mass spectrometer coupled to a nanoHPLC system for performing proteomic analysis.
Statistical Consulting

The Statistical Consulting Laboratory provides statistical and computing support to researchers. Statistical support is provided through seminars, experiment design, statistical analysis of data and interpretation of results. Computing support is provided in software and hardware selection and maintenance, spreadsheet design and database management.

DNA Analysis

The DNA Analysis Facility supplies researchers with all of their nucleic acid analysis needs. This includes cycle sequencing of DNA on an ABI capillary system, with data output in several formats. Molecular genotyping of IR dye labeled fragments is also performed on glass slides, which include two-color hybridizations and microarray analysis. Other tools available to researchers include thermocyclers for gradient PCR and qRT-PCR, storage PhosphorImager, UV/VIS and fluorescence spectrophotometers, SpeedVac concentrator and a digital gel documentation system.

Bioinformatics Computing

The Bioinformatics Computing Laboratory offers computing support ranging from mathematical modeling to software usage, DNA sequencing, and microarray analysis, including both the computational and experimental components in biomedical research. Services include developing databases and software for genomics and proteomics data analysis, biomolecular sequence analysis and structure prediction, and glycosylation site prediction. Web-based computing tools are available for O-glycosylation prediction, RNA secondary structure studies and searching, formatting and visualization of pseudoknots.

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To learn more about a project or to discuss potential research collaborations, please contact the key investigator directly.
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