Our Department - Biochemistry and Cancer Biology

Departmental Overview
William A. Maltese, Ph.D.
Chairman, Dept of Biochemistry and Cancer Biology

The Department of Biochemistry was one of the original basic science departments established with the founding of the Medical College of Ohio. In 2006 the name was changed to the Department of Biochemistry and Cancer Biology to reflect the increasing emphasis on cancer research. The missions of the department are to advance the frontiers of medical science through high quality basic and translational research, to train the next generation of physicians and scientists, and to serve the broader scientific community through dissemination of new knowledge and participation in peer review activities. All faculty members are actively engaged in medical and/or graduate education through formal classroom teaching activities and service as research mentors or advisors for medical students, M.D./Ph.D. students, or graduate students in the Biomedical Sciences programs of the College of Medicine and Life Sciences. The department takes pride in providing a collegial and supportive environment in which students can obtain state-of-the-art training in modern biomedical research approaches while interacting closely with faculty advisors. Many former students have obtained prestigious postdoctoral fellowships and gone on to successful careers as scientists with pharmaceutical and biotechnology companies or faculty members at colleges and universities throughout the United States.

Faculty, Staff and Students of the Department of Biochemistry and Cancer Biology
The department is home to the Cancer Biology Track in the Biomedical Sciences Graduate Program. Dr. Kandace Williams, a Professor in the department, also serves as Cancer Biology Track Director and Associate Dean for Graduate Programs in the College of Medicine and Life Sciences. The research goals of the department are closely aligned with the strategic plans of the College of Medicine and Life Sciences and the University of Toledo. Federal funding for research programs within the department has averaged between 2.5 and 3 million dollars for each of the last five fiscal years. Much of the ongoing research in the department is focused on using knowledge of cancer genomics, cell biology and signaling mechanisms to identify new cancer biomarkers or therapeutic approaches. However, other areas of research excellence are well represented. These include the studies of Drs. Amir Askari and Lijun Liu on the sodium pump and cardiac hypertrophy, supported by the NHLBI’s longest-running program-project grant, the work of Dr. Maurice Manning, which has produced peptide agonists and antagonists of vasopressin and oxytocin receptors that are utilized by researchers throughout the world, and the obesity research of Dr. Cynthia Smas, which resulted in the recent discovery of a new protein that appears to play a key role in triglyceride metabolism. The department is highly supportive of interdisciplinary research, with ongoing collaborations involving faculty in UTMC’s clinical departments, the College of Pharmacy, the College of Engineering, and the College of Natural Science and Mathematics. Anyone interested in learning more about the available resources or the range of faculty research interests represented within the department can obtain additional information by visiting the department’s web site: http://www.utoledo.edu/med/depts/biochem/index.html

Department of Biochemistry and Cancer Biology: Cancer Research Highlights

Targeting Cancer Invasion and Metastasis

Kathryn M. Eisenmann, Ph.D.

More than 90% of cancer-related deaths are due to the ability of cancer cells to leave the site of the original tumor and invade surrounding tissues. Ultimately, some cancer cells enter the circulation and disseminate throughout the body in a process commonly referred to as metastasis. Dr. Kathryn Eisenmann has been studying the molecular mechanisms that promote the movement of cancer cells away from the primary tumor mass. Her lab focuses on a class of proteins termed mDia formins, which regulate the actin cytoskeleton and play an essential role in tumor cell invasion.

The problem of invasion is particularly critical in brain tumors like glioblastoma, where the ability of tumor cells to invade into healthy tissue makes them inaccessible to surgical resection or treatment of the primary tumor site with radiation or chemotherapy. Dr. Eisenmann’s group recently discovered that maintaining the formin protein in an “on” or hyperactivated state with small molecules is an effective treatment for blocking glioblastoma cell invasion. This work could lead to the development of new anti-tumor strategies for this
deadly form of cancer. In studies planned for the near future, Dr. Eisenmann will explore a similar strategy in models of ovarian and breast cancer, where invasion and metastasis can be major impediments to effective treatment.

(Figure) Human glioblastoma cells (yellow) invade through a slice of normal rat brain while maintaining contact with blood vessels (red). Cell nuclei are stained blue.

Relationship Between Chromatin Remodeling and Melanoma Progression

Ivana de la Serna, Ph.D.

Metastatic melanoma is an aggressive disease that has a median survival rate of 6-9 months. Vemurafenib is a newly developed drug that causes melanoma tumor regression and increases patient survival. However, patients become resistant to the drug within a year of treatment. Studies in Dr. de la Serna’s laboratory have determined that vemurafenib alters the expression and function of a protein complex called SWI/SNF. SWI/SNF normally regulates gene expression by modifying the way that the genetic material, DNA, is compacted to form the three dimensional structure of chromatin. The change in SWI/SNF function caused by vemurafenib may alter the expression of genes that contribute to the process by which melanoma cells become resistant to this drug. Further definition of the effects of vemurafenib on the SWI/SNF complex could uncover new treatment options that might be utilized to prevent melanoma cells from becoming resistant to this valuable anti-cancer agent.

Discovery of New Anti-Cancer Drugs that Induce a Novel for of Cell Death

William A. Maltese, Ph.D. and Jean H. Overmeyer, Ph.D.

Treatment of cancers with radiation and conventional chemotherapeutic drugs typically kills cancer cells by damaging their DNA and inducing a cell death pathway known as apoptosis. However, many cancers reoccur after such treatments because subpopulations of tumor cells evade apoptosis and develop drug resistance.
RKIP is a Master Regulator of Metastasis

Examples of cancers that are prone to develop resistance to apoptosis include glioblastoma, melanoma, breast carcinoma and lung carcinoma. Dr. Maltese and his colleague, Dr. Overmeyer, have discovered a new cell death pathway termed ‘methuosis’, which can be activated in cancer cells that are resistant to classical apoptosis-inducing drugs. This form of cell death is independent of DNA damage, and instead occurs because the tumor cells engulf extracellular fluid and eventually explode. In collaboration with Dr. Paul Erhardt and investigators in the Center for Drug Design and Development, new compounds are being developed which can be used to induce methuosis in cancer cells. Several of these drugs are being tested in preclinical models to assess their anti-tumor efficacy, optimal mode of delivery and potential toxicity to normal cells.

Targeting Cancer Invasion and Metastasis

Kam C. Yeung, Ph.D.

The prognosis for patients with metastatic prostate or breast cancer remains poor. Dr. Yeung’s laboratory studies molecular signaling pathways that regulate the metastatic potential of cancer cells. Years ago he was the first to identify a unique protein termed RKIP. This protein has been proven to be a suppressor of metastasis in prostate and breast cancer. Loss of the gene for RKIP is a valuable biomarker that correlates with cancer progression. In addition to RKIP, many other genes that contribute to metastasis have been identified. In an exciting development, Dr. Yeung’s recent studies have established that RKIP functions as a “master regulator” that can control the expression of a wide array of other genes required for cancer metastasis. As a key control point, RKIP therefore represents an emerging novel therapeutic target for patients afflicted with metastatic breast or prostate cancer.

New Investigator

Vivek Nagaraja M.D.
Assistant Professor, Division of Rheumatology
Department of Internal Medicine

I am extremely happy to join the distinguished group of physicians and researchers at the University of
Toledo Medical Center. I would like to start with providing a brief background about my professional education. I completed medical school at the M.S.Ramaiah Medical College in Bangalore, India. This was followed by a two-year stint in the United Kingdom where I did transitional year training in both medical and surgical specialties. I later completed a residency in Internal Medicine at the University of Arizona. Encouraged by the experience in caring for the elderly in UK, I completed a fellowship in Geriatric Medicine at the University of Arizona. Subsequently, I moved to Ann Arbor for 2-year fellowship training in Rheumatology at the University of Michigan, which I completed in July 2014. I am board certified in Internal Medicine and Geriatric Medicine.

I started my research focus in health services during the Geriatrics training; in setting up a home based primary care program to the dual-eligible (Medicare and Medicaid eligible beneficiaries) patient population. Over the past year, I shifted focus to research on patient reported outcomes (PRO). PRO refers to any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else. In other words, it is the voice of the patients about their health. Questionnaires or survey tools used to collect this information in a standardized way is referred to as PRO measurement (PROM). Although this concept is not new to the practice of medicine, there has been a renewed research interest in the past few years in this area due to the changing phase of our healthcare. The National Institute of Health appropriately identified the need to further research in this area and developed the PROMIS® (Patient Reported Outcomes Measurement Information System), a system of highly reliable, precise measures of patient–reported health status for physical, mental, and social well–being (http://www.nihpromis.org). PROMIS® tools measure what patients are able to do and how they feel by asking questions.

At the University of Michigan, I started the PRO research by evaluating the validity a new PRO tool (PROMIS-GI) to assess the burden of a rare rheumatic disease called Systemic Sclerosis when it affects the gastrointestinal tract of patients. We found this instrument to be valid and published the work (http://www.ncbi.nlm.nih.gov/pubmed/24692332). This work got me interested further in the concept of PROM.

Most of the rheumatic diseases are a result of immune system disorders. They can affect different organ systems and can be quite disabling (like in rheumatoid arthritis or lupus). Usually, no single test or investigation is helpful to provide an idea about the status of disease activity in patients with rheumatic diseases. A lot depends on the clinical evaluation by a rheumatologist. In these situations, a standardized way of collecting information from the patient about their self-reported health will certainly help the clinician to supplement decision-making on further management of the disease. Also, many symptoms or conditions like fatigue, sleep impairment, pain, physical function etc cannot be measured or quantified with any form of testing. PROMIS® has well validated measures to better assess these conditions using a smart survey, which is both time effective and somewhat individualized to the person taking the survey (previous response determines the next questions posed).

Using the PROMIS® measures, I started a study looking into surveying patients coming to the out-patient rheumatology clinic at University of Michigan. Interested patients took an online survey (either in the clinic or at home) on a desktop or personal device like a tablet. The survey focused on different aspects of health (14 domains in total). This research is currently ongoing and 543 participants have completed the survey. I am starting the groundwork to implement this project at the University of Toledo. The report of this survey is generated as a heat map (Figure 1) and the individual scores are compared to the Unites States general population. I would like to develop an average score for the different domains in patients coming to rheumatology clinic. The vision is to have patients complete a similar survey prior to their clinic visit and enable clinicians (and patients) to compare the scores with the general population and rheumatology patient population.
Beyond the division of Rheumatology, this survey can be customized to different specialties of Internal Medicine. For example, domains like fatigue or depression can be measured across patients coming to different sub-specialty clinics (like heart failure, COPD, HIV, rheumatoid arthritis patients). Data on these domains using the PROMIS® tools, helps to compare these domains in different disease populations using a common scale of measurement. The results can be used to appropriately allocate resources and improve physician – patient communication.

**The Newly enrolling clinical trials**

An Open-Label, Multicenter, Phase 4 Study to Demonstrate the Prognostic Usefulness of AdreView™ Scintigraphy for identifying Subjects with Heart Failure who will Experience Death during 60 Months Follow-up.
Dr. Goodenday - Medicine

A Randomized, Double Blind, Cross-Over Trial Comparing the Safety and Efficacy of Insulin Degludec and Insulin Glargine, With or Without OADs in Subjects with Type 2 Diabetes
Dr. Hejeebu – Medicine

A Randomized, Double Blind, Cross-Over Trial Comparing the Safety and Efficacy of Insulin Degludec and Insulin Glargine, Both with Insulin Aspart as Mealtime Insulin in Subjects with Type 1 Diabetes
Dr. Hejeebu – Medicine

Noninvasive Blood Glucose Monitoring Method Based on Imaging of the Eye
Dr. Kleerekopper - Medicine

---

**Contact Us**

Health Science Campus • Center for Creative Education Bldg.
2920 Transverse Drive, Floor 3 • Toledo, OH 43614