

UMCCC, the NCRC and Translational Science

Mission Statement

Our research mission is the conquest of cancer through innovation and collaboration. We seek to accomplish this by creating a stimulating, collaborative research environment where M.D.'s and Ph.D.'s, medical and post-doctoral research fellows and clinicians, graduate students and undergraduates alike can come together to conceive, inspire and drive scientific innovation. Through our integrated, multi-disciplinary approach we will establish the University of Michigan as the international leader in cancer stem cell research and resulting targeted therapies.

About Dr. Wicha's Laboratory

Dr. Max S. Wicha is a pioneering force in Cancer Stem Cell (CSC) biology. According to the ISI Citation Index, Dr. Wicha is the most highly-cited investigator in the entire field of CSCs. His group was the first to identify breast CSCs. Dr. Wicha's laboratory identified a number of stem cell markers and developed in vitro and in vivo models to isolate and characterize these cells. These research models and resources have been widely adopted by other investigators. His laboratory subsequently elucidated a number of intrinsic and extrinsic pathways which regulate self-renewal and cell fate decisions in CSCs. Recently, he has focused on translating his pre-clinical research findings into the development of clinical trials designed to target breast CSCs.

Historical Context- A Record of Success

The University of Michigan Comprehensive Cancer Center (UMCCC) <http://www.cancer.med.umich.edu/about/index.shtml> was founded by Dr. Max S. Wicha in 1988 and actively facilitates innovative, collaborative oncology research throughout the University of Michigan and beyond. The UMCCC is a matrix organization with 311 members representing ten schools and institutes across the University. Eight of these ten schools are ranked in the top ten nationally. The UMCCC is currently ranked third nationally in peer-reviewed grants support from the National Cancer Institute. The strategy of the UMCCC has been to organize multidisciplinary research programs that reach across traditional department and school boundaries to promote and coordinate prevention, basic and clinical cancer research. UM cancer investigators have made numerous fundamental discoveries over the past decade. The creation of a translational research engine at the NCRC represents a unique opportunity to transform these important discoveries into clinical advancements that will significantly improve the way cancer is diagnosed and treated.

Dr. Wicha Pioneers Translational Science at the North Campus Research Complex

Cancer remains the number two cause of disease-related mortality in the United States and worldwide. Recent articles have reinforced what cancer clinicians know very well; progress in the treatment of the most common forms of cancer has been frustratingly slow, yielding only modest improvement in survival rates. In contrast, spectacular advancements have been made in basic research to characterize and understand the fundamental molecular underpinnings that drive cancer. These laboratory discoveries have the potential to completely transform our

approach to cancer, but only once basic molecular knowledge is translated into practical treatments. The molecular analysis of tumors has revealed significant variation in the pathways that drive tumor growth and metastasis. The discovery of genes linked directly to cancer and the molecular pathways these genes influence has allowed scientists to draw a more accurate road map of the nuances of cancer and its progression. Today's drug development efforts use this map to focus on targeted therapies that tackle cancer specific events with greater precision. Targeted therapy is now the dominant approach in cancer therapeutics, driving the majority of new cancer drugs being developed in both academic and commercial biotechnology. The development of targeted therapies requires collaboration of specialized investigators to:

- Identify and characterize new molecular targets
- Validate these targets in cell cultures and in animal models
- Develop new drugs to hit these targets
- Test these new drugs in clinical trials

The Cancer Stem Cell Hypothesis

There is ever increasing evidence that the development of many cancers may be driven by a subpopulation of cells termed Cancer Stem Cells (CSCs). These cells display self-renewal and boundless differentiation potential and exhibit radiation and chemotherapy resistance which may contribute to relapse and death. Significant progress in developing more effective cancer therapies may depend on the effective targeting of CSC populations. The University of Michigan is already one of the leading institutions in the world in basic cancer research and drug discovery and is world renowned for its expertise in CSC biology. Developing a translational research engine at the NCRC represents a unique opportunity to translate the most important CSC basic science discoveries into clinical advancements that will significantly improve the way cancer is diagnosed and treated.

Recent Developments

In May 2012 Dr. Wicha relocated his Experimental Breast Cancer Research Laboratories and over fifty researchers to the North Campus Research Complex (NCRC) buildings 26 and 20W and established the Translational Oncology Program (TOP). With the formation of the TOP, Dr. Wicha has engaged the interest of the best and brightest CSC researchers to the NCRC. The TOP will be directed by renowned CSC investigator, Dr. Diane Simeone, whose pancreas research is highly regarded. The TOP seeks to drive innovative cancer therapies and is uniquely qualified with numerous leading laboratories in CSC research. TOP investigators are presently exploring cancers of the breast, lung, pancreas, head and neck, colon, prostate and thyroid. By working

together and sharing the ample scientific resources of the NCRC, TOP scientists can make progress more rapidly than would be possible by working alone. It is hoped this collaborative approach will revolutionize cancer treatments by targeting and destroying the cells responsible for disease recurrence and metastasis. In Dr. Wicha's words, " In many ways, the NCRC embodies the very best of Michigan and epitomizes what sets our institution apart – our ability to focus the efforts of the top minds in diverse fields to find answers to society's greatest challenges."