Please refer to the application instructions in order to complete sections A, B, C, and D of the Biographical Sketch.

A. Personal Statement

The present review proposal application explores the anti-cancer activity of capsaicin analogs in human cancers. Our published data shows that capsaicin displays potent anti-tumor activity in human lung. Furthermore, our results also indicate that capsaicin sensitizes human SCLC cells to camptothecin-induced apoptosis. However, one of the major drawbacks of capsaicin is its unfavorable side effect profile. Capsaicin produces burning sensation, irritation in the gut and gastric mucosa. Such side effects have led to patients stopping capsaicin-based therapies. The present review proposal explores structure activity relationship (SAR) studies to identify the non-pungent capsaicin-analogs with potent anti-cancer activity. Although, such SAR studies have been done to test the analgesic activity of capsaicin-analogs, very few of these have been explored for their anti-tumor activity. I have extensive research experience in the field of novel drug discovery in lung cancer. I screened the NCI “Diversity Set” combinatorial drug library to identify novel synthetic compounds which would display anti-cancer activity in human lung cancer. Furthermore, I went on to validate the “hit compounds” in cell culture and nude mouse models. I have also close to ten years of research experience in the field of cell cycle research, signal transduction and its applications to lung cancer.


My research work was recognized by the ASPET-Astellas Award in Translational Pharmacology, 2009. In addition, Marshall University has recognized my research work by selecting me for Marshall University Distinguished Artists and Scientists Award (MU-DASA), 2009 and the Dean’s Award for Excellence.
in Basic Research, 2013. I was selected for receiving John and Francis Rucker Outstanding Graduate Faculty Award for providing outstanding mentorship to undergraduate and graduate students working in my laboratory. Since, undergraduate mentoring is a key component of the NIH-R15 application; this award will help me to effectively mentor many undergraduate and graduate students. Taken together, I believe that I have the required expertise to lead the proposed project. My collaborator Dr. Monica Valentovic will provide vital scientific and technical input to the biodistribution and bioavailability-related aspects of this project. The results obtained from the present grant foster the hope of novel combination therapies in human SCLC

B. Positions and Honors

Positions:
2000-2001 Postdoctoral Fellow, Columbia University, NY
2001-2007 Postdoctoral Fellow, Moffitt Cancer Center, Tampa, FL
2007- present Associate Professor, Department of Pharmacology, Physiology, Toxicology, Marshall University School of Medicine, Huntington, WV25755

Honors
1. Dean’s Award for Excellence in Basic Research, 2013.
2. Recipient of the John and Francis Rucker Outstanding Graduate Faculty Award, Marshall University, 2011.

Professional Memberships
1. American Association of Cancer Research
2. American Society for Pharmacology and Experimental Therapeutics (ASPET).
3. American Society of Investigative Pathology
4. Sigma-Xi Scientific Society

D. Contribution to Science

1. One of my major research interests is the biochemical mechanisms by which tobacco components like nicotine accelerate the growth of human lung cancer. Nicotine is the addictive component of cigarette smoke. During my postdoctoral fellowship, I showed for the first time that nicotine could block the apoptotic activity of gemcitabine, cisplatin and taxol in human lung cancers. Clinical studies show that patients who smoke during chemotherapy have worse outcomes than those who quit before starting chemotherapy. Our observations provided a mechanistic insight into these clinical observations. We also discovered that nicotine behaved in a manner analogous to growth-factors in human lung cancers. It amplified growth-stimulatory pathways in human lung cancer and also regulated the cell cycle machinery. We believe or findings are relevant for lung cancer patients who are exposed to nicotine via cigarettes, second hand smoke, electronic cigarettes or patches or hums to quit smoking.


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2. Our publications have revealed new knowledge on the signaling pathways by which nicotine promotes the proliferation, angiogenesis and metastasis of human lung cancers. We conjectured that disruption of the nicotine-signaling pathway should inhibit the growth of human lung cancers. Our studies were the first to show that inhibitors to the nicotine-signaling pathway attenuate angiogenesis and cause apoptosis in human lung cancers. We also extended these drug-discovery studies to tobacco-related diseases like diabetic retinopathy.


3. The field of “Nutrition and Cancer” is one of the emphasis research areas at the Marshall University School of Medicine. My laboratory studies the anti-tumor activity of capsaicin, the pungent ingredient of chili peppers. Our studies showed for the first time that capsaicin exerted potent anti-tumor activity in human SCLCs. We also found that the bioavailability of capsaicin was greater in the lung compared to the liver, blood and kidneys. Our laboratory also first identified the signaling pathway underlying the anti-cancer effect of capsaicin in human SCLCs.


E. Research Support

   A. National Institute of Health R-15 AREA grant
   PI on Grant
   Title: Capsaicin and Small Cell Lung Cancer Therapy
   Duration of Grant: 2012-2019
The above research proposal is examines the anti-tumor activity of natural and synthetic mom-pungent capsaicin-analogs.

Role: PI on Grant

A. WVU-Marshall Health Partnership grant
   Co-PI on Grant
   Title: Long-term effects of e-cigarettes on cardiac and respiratory structure and function
   Duration of Grant: 2016-2017
   Budget: $50,000

Role: Co-PI on Grant

The above research proposal examines whether nicotinic receptors in the lung contribute to lung remodeling and impair tissue functions of the lung.

F. Completed Research Support

A. Young Clinical Scientist Award Program from Flight Attendant Medical Research Institute
   PI on Grant
   Duration of Grant: 2009-2014
   Title: Nicotine/Acetylcholine Signaling in Lung Cancer
   Budget: $100,000/year

The above proposal examined whether acetylcholine and acetylcholine-related signaling proteins promote the growth of human lung cancers in both tissue culture and mouse models.

Role: PI on Grant

B. American Retina Foundation
   PI on Grant
   Duration of Grant: 2009-2010
   Title: Nicotine/Acetylcholine Signaling in ARMD
   Budget: $12,000/year

The above mentioned research grant analyzed the role of nicotinic acetylcholine receptors in aberrant angiogenesis which occurs in the eye of age-related macular degeneration (ARMD) patients, who are exposed to cigarette smoke.

Role: PI on Grant

C. ASPET-Astellas Award Program from American Society of Pharmacology and Experimental Therapeutics
   PI on Grant
   Duration of grant: 2009-2010
   Title: α7-nicotinic receptor inhibitors in small cell lung cancer therapy
   Budget: $30,000

The ASPET grant investigated the feasibility of a high throughput drug screen for identifying novel compounds relevant to the treatment of human small cell lung cancer.

Role: PI on Grant

D. Research Starter Grant from the Pharmaceutical Manufacturer’s Association of America.
   PI on Grant
   Duration of grant: 2007-2009
   Title: “α7-Nicotinic Receptor Signaling in Non-small cell Lung Cancer”.
   Budget: $30,000 a year
The above grant assessed if long term exposure to nicotine could increase the expression of nicotinic acetylcholine receptors on lung tumors, which may contribute to chemoresistance of such tumors. Role: PI on Grant