How do chemotactic cytokines regulate breast cancer metastasis? Role of the CXCL12-CXCR4-LASP1 axis.

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Assistant Professor
Dept. of Biochemistry and Cancer Biology

I joined the Department of Biochemistry and Cancer Biology in February, 2016. I came from Vanderbilt University after working under and collaborating with Dr. Ann Richmond, a renowned chemokine expert. My research is centered on cancer cell biology and mainly focuses on chemokine receptor signaling, tumor cell migration, local invasion and metastasis mediated by chemokine receptors CXCR2 and CXCR4 in breast cancer. Metastasis in breast cancer has a higher mortality than the primary breast cancer itself. Inhibition of CXCR4 signaling in metastatic, triple-negative MDA-MB-231 breast cancer cells reduced breast cancer metastases to the lung and lymph nodes in vivo. Tumors frequently overexpress chemokines and their receptors, and this has been correlated with shortened relapse-free survival. High levels of CXCR4 expression in both estrogen receptor (ER)-negative and ER-positive patients predicted poorer survival, and the CXCL12–CXCR4 axis facilitates breast cancer progression and metastasis. Interestingly, epidermal growth factor (EGF) receptor and human EGF receptor 2 (HER2) present in breast cancer cells can transactivate CXCR4.

Expression of a constitutively active mutant of CXCR4 in a luminal MCF7 breast cancer cell line resulted in impaired receptor desensitization, enhanced motility, epithelial-to-mesenchymal transition (EMT), enhanced estrogen-independent growth, and metastasis in vivo. Previously, I demonstrated that the adaptor protein LIM and SH3 protein 1 (LASP-1) directly interacts with CXC chemokine receptors, CXCR1, CXCR2, CXCR3 and CXCR4 that play a key role in the tumor microenvironment facilitating breast cancer progression and metastasis. Recently, I discovered that activation of CXCR4, EGF receptor and HER2 in a TNBC cell line can trigger nuclear translocation of LASP-1. I found that nuclear LASP-1 binds to several epigenetic regulators including a direct binding to the EMT transcription factor Snail1. Reportedly, nuclear LASP-1 inversely correlated with the overall survival. Currently, I am specifically studying the link between CXCL12-CXCR4-LASP1 axis and the epigenetic regulators and also the translational repression machinery. The resultant altered pro-tumorigenic and pro-metastatic proteome may facilitate breast cancer progression and metastasis. I look forward to collaborating with UT campus scientists in any area (preferably cancer
research) where chemokine receptors are involved.

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**New Clinical Research Staff**

Laura Elliott  
Clinical Research Quality Spec

I moved to Toledo in 1979. It was on December 10th, 1979 that I first started working in the old hospital for anyone that might remember that place down the street!! On December 15th, 1979, “MCO” officially opened its new doors and I worked that day welcoming patients to the then 3rd floor Medical Coronary Care Building. I spent the next 10 years working the 11-7 shift as well as part time shift Supervisor. In June of 1989, I became the 2nd RN to work in the Electrophysiology Lab with Dr. Blair Grubb. “MCO” was the only hospital in all of NWO that had an EP lab at that time. I stayed in this field for 11 years. In March of 2000, I first entered the world of Cardiovascular Research as a coordinator for 3 years before becoming the Director of the Heart Station and supervisor of the CV research staff. In March of 2006, I was fortunate enough to work alongside Holly once again and was a Project Manager for 11 countries outside the US for the NIH CORAL TRIAL. I obtained my CCRC, and CCRA during that time. In 2009, I was “asked” to come back to the Hospital side and became the Administrative Director of the Cardiovascular Service line. I held this position until I retired after 35 ½ years in August 2015. I then had the privilege and good fortune of being hired part time as a QA Specialist with the JCCTR! I have been married 38 years, have 3 grown children and 6 of the most fabulous Grandbabies ever!! (in my opinion of course).

Veronica Fasciana, JD  
Contract Specialist

I joined the JCCTR team on February 1st to work predominantly on Clinical Trial Agreements negotiations. It has been a great learning experience familiarizing myself with the trade practices, rules, and regulations relevant to Clinical Trials. I am a 2014 graduate of The University of Toledo College of Law. I worked in the office of Law Admissions for over a year. I valued working for UT so much that I decided to pursue a career within the University where my legal training could be more exploited. Therefore, I am very happy with the opportunity to work as Contract Specialist at the JCCTR.

I cherish family time. I have been married for almost 9 years. My husband, Nicholas, is originally from Cleveland area. All my family lives in northern Mexico, where I was born and raised. We visit my family every Christmas and once during spring or summer at the very least. Nick and I had Lucas, our son, when I was about to start Law School and he was half way through his MBA. Nick and I enjoy getting Lucas involved in as many activities as possible. Lucas swims since he was 6 months old, has played soccer several seasons, tee ball last spring and summer, and takes ice skating lessons. Lucas is going to start Kindergarten this fall at Sylvan Elementary. Nick and I do CrossFit almost every day. I am also a Sunday school teacher at Christ the King Roman Catholic Church. We love being active.

Pamela St. John  
Budget Specialist

I joined the JCCTR Team in December 2015 as an Account Clerk 1 (Budget Specialist). I have several years of accounting and budget experience and was a member of the State Employees Retirement System before joining the JCCTR. My previous position was HR Manager, processing payroll and benefits.

Some of my duties consist of monitoring/reviewing patient claims, creating budget summaries and contracts, entering studies into Study Manager, summarizing monthly budgets, monthly reports and reconciliation related to clinical trials. Anything that Danielle thinks I can handle! This is a great group to
work with and I feel very privileged to be a part.

I am married to Ray; we have three daughters and two sons. We enjoy spending time with our grandchildren with two more on the way in June and September respectively! I love hosting Family Sunday Funday Dinners! In my spare time I enjoy boating, camping and riding our Harley with Ray and our friends.

Clinical Research Snippets

Anand B. Mutgi, MD
Sadik A. Khuder, PhD

Hypertension affects one in three American adults and remains a major risk factor for heart disease and strokes. Early intervention to modify the risk factors may reduce the occurrence of hypertension and associated morbidity and mortality. This month we review a large retrospective cohort study that examined the effect of body mass index (BMI) and physical fitness on the occurrence of hypertension.

Authors of this paper conducted a retrospective cohort study that included 1,547,189 Swedish men aged 18 years who underwent examination as part of military recruitment between January 1969 and December 1997. They were followed up until December 2012. At the initial contact, these men underwent measurement of aerobic capacity, muscle strength, and BMI as part of their examination. Due to the nature of healthcare in Sweden, they were able to capture the occurrence of hypertension in this population. A total of 6 percent developed hypertension over this period with median onset around 50 years of age. After controlling for other variables including family history, elevated BMI was associated with an average 2.5-fold risk for hypertension. This risk increased with increasing BMI. Not surprisingly, lower aerobic capacity was associated with an average of 1.5-fold greater risk for hypertension however muscle strength had little effect on hypertension risk after controlling for BMI and aerobic capacity. A combination of low aerobic capacity and high BMI was associated with 3.5-fold risk in the risk of hypertension.

This study was limited by one time measurement only at the beginning and did not evaluate lifetime changes in BMI and aerobic capacity of this cohort. The study was also limited to men and may not be generalizable to women.

We feel that this was a well-designed retrospective cohort study which showed long-term effects of BMI and aerobic capacity on the occurrence of hypertension with BMI having a major impact. Lifestyle interventions at an early age to reduce obesity and improve aerobic capacity will have a significant impact on the occurrence of hypertension and reduce the related morbidity and mortality.

New Clinical Trials

M12-815: A Phase 3 Study to Evaluate the Efficacy and Safety of Elagolix in Combination with Estradiol/Norethindrone Acetate for the Management of Heavy Menstrual Bleeding Associated with Uterine Fibroids in Premenopausal Women.
Dr. Ronica Neuhoff - Obstetrics and Gynecology
## IRB Corner

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## Contact Us

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