

In Conversation:

Postdoctoral Fellow John Simmons, Ph.D.

CCR: You've been training in CCR labs for several years—as an undergraduate and graduate student and now as a Postdoc. Congratulations on completing your Ph.D. in April, through the NIH Graduate Partnership Program with Georgetown University. Could you tell us about your thesis?

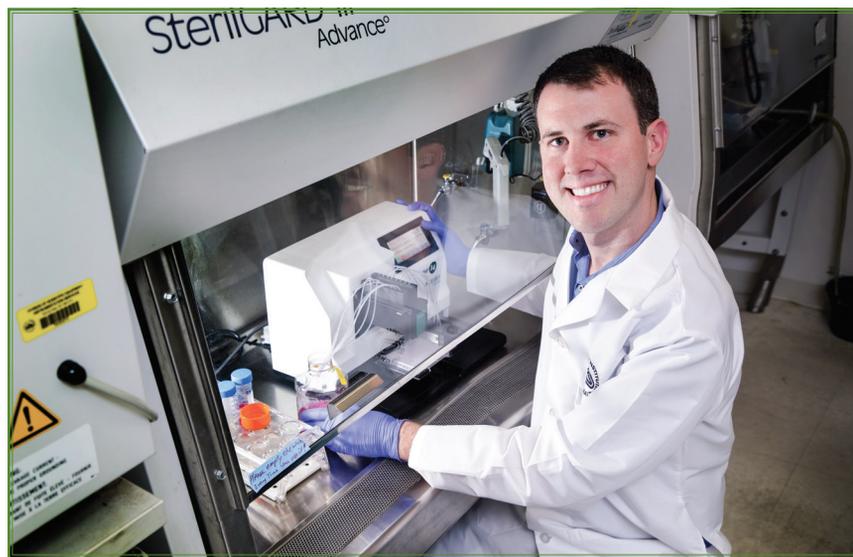
John: I focused on drug combinations to treat multiple myeloma. In 2009, I started working with Beverly Mock, Ph.D., Deputy Chief of CCR's Laboratory of Cancer Biology and Genetics. Her laboratory was trying to understand the synergistic interactions between inhibitors of two anticancer targets: mTOR and HDACs. We discovered that the drug combination actually had a synergistic effect on destabilizing the MYC protein.

CCR: How did you figure out that MYC was involved?

John: Working with a bioinformatician, Staff Scientist Aleksandra Michalowski, Ph.D., we evaluated drug synergy at the molecular level using transcriptomics. Instead of looking at changes in gene expression one gene at a time, we looked for correlations between gene expression changes. We found a network of genes that were affected by the drug combination and were correlated with improved prognosis in patient data. We discovered the relationship of this network to MYC protein regulation through data mining tools and then verified this finding *in vitro* and in mouse models.

CCR: That sounds like a lot of serious bioinformatics. Was that challenging?

John: I didn't have a lot of training in statistics and no training in any of



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the programming languages like R, but early on, I made a commitment to at least understand the principles behind all the different types of analyses. At this point, though, I mainly focus on the biology. These data sets are increasingly so large that it's not a place to really get your feet wet, so to speak.

CCR: Are you continuing this work as a Postdoctoral Fellow in Dr. Mock's laboratory?

John: Yes, in part, but I have expanded my focus beyond the particular drug combination that I focused on in my thesis. While still a grad student, I participated in a translational science training program run by the NIH Office of Intramural Training and Education (OITE). I wrote a proposal for how my thesis could benefit from the high-throughput screening capabilities at National Center for Advancing Translational Science (NCATS). In a collaboration with their Chemical Genomics team, we started looking at drug sensitivities in 70 genetically defined multiple myeloma cell lines. We incorporated

a subset of compounds to evaluate the cell lines in combination with a panel of 2,000 drugs. Along the way, I submitted a career development grant to the Multiple Myeloma Research Foundation, which was recently funded. We are particularly interested in drug combinations that are active in cell lines resistant to standard of care.

CCR: It sounds as though your focus as a cancer researcher is firmly rooted in translation.

John: Well, I've always had an interest in science, even as a child. But my interest in cancer came when an aunt was diagnosed with multiple myeloma when I was in middle school. She went on a clinical trial at Duke and lived about three years after diagnosis. It was the first time I'd ever heard of clinical research. I grew up in rural southern Virginia, so being interested in science, the obvious career option was medicine. It wasn't until I started interning at CCR as an undergraduate that I got a great appreciation of translational research and its potential impact.

(Photo: B. Branson)