



Next-gen Sequencing

Zhao leverages HPC in classroom, lab



With assistance from the Ohio Supercomputer Center (OSC), Research Scientist Yue Zhao, Ph.D., leads several classroom and lab sessions for an introductory bioinformatics course taught at The Ohio State University by Lijun Cheng, Ph.D., assistant Professor of biomedical informatics. The class introduces students to basic topics of bioinformatics, including sequence analyses, proteomics, microarrays and associated genomics and genetics databases. In her sessions, Zhao introduces future biologists and physicians to next-generation sequencing techniques and data-analysis methods, such as RNA-seq analysis, differential gene expression analysis and mutation calling.

Zhao's class sessions require up to 10 software packages, so she reached out for some assistance from OSC's physical Help Desk location on campus, which Zhao subsequently visited numerous times leading up to her class sessions. The experts there were able to help her get all her software installed and operational in short order.

"The staff working at OSC helped me set up a class project and assigned student pass codes," said Zhao. "I am delighted the way the students in the classroom can get approved almost immediately and are allowed to manage their own accounts."

Zhao also leverages the Center's Owens Cluster to help conduct her own sequencing research into therapies to combat prostate cancer, a project led by Xiaoqi Liu, Ph.D., professor and chair of toxicology and cancer biology at the

University of Kentucky, and Lang Li, Ph.D., professor and chair of biomedical informatics at Ohio State. Initial therapies that many doctors employ against prostate cancer attempt to lower levels of 'male hormones'—mostly testosterone and androstenedione—called androgens. For patients whose cancer keeps growing despite therapies, doctors employ a hormone therapy that targets a protein—an androgen receptor—that regulates the transfer of testosterone and related hormones into the cell's nucleus.

A second-generation androgen receptor drug, enzalutamide, has shown encouraging clinical effectiveness in patients whose cancer doesn't respond to the initial androgen-lowering treatments. Yet, despite early success, a majority eventually develop a resistance. Zhao is utilizing a computational tool called MAGeCK to identify important genes from the CRISPR-Cas9 knockout screens and to then examine the molecular events behind the resistance development.

"Our study demonstrates a new research strategy to investigate the mechanism underlying the drug resistance at whole-genome level," said Zhao. "Genes and signaling networks identified through CRISPR-Cas9 screening further expand our understanding of the androgen signaling network and provide valuable insight on new therapy development." •

PROJECT LEAD // Yue Zhao, Ph.D., The Ohio State University
RESEARCH TITLE // Genome CRISPR-Cas9 knockout screens reveal new mechanism of enzalutamide resistance in prostate cancer
FUNDING SOURCE // The Ohio State University
WEBSITE // medicine.osu.edu/bmi/people/research/yue_zhao/Pages/index.aspx