A Multiomics Method Enabled by Sequential Metabolomics and Proteomics for Human Pluripotent Stem Cell-Derived Cardiomyocytes

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Human pluripotent stem-cell-derived cardiomyocytes (hPSC-CMs) show immense promise for patient-specific disease modeling, cardiotoxicity screening, and regenerative therapy development. However, thus far, hPSC-CMs in culture have not recapitulated the structural or functional properties of adult CMs in vivo. To gain global insight into hPSC-CM biology, we established a multiomics method for analyzing the hPSC-CM metabolome and proteome from the same cell culture, creating multidimensional profiles of hPSC-CMs. Specifically, we developed a sequential extraction to capture metabolites and proteins from the same hPSC-CM monolayer cultures and analyzed these extracts using high-resolution mass spectrometry. Using this method, we annotated 205 metabolites/lipids and 4319 proteins from 106 cells with high reproducibility. We further integrated the proteome and metabolome measurements to create network profiles of molecular phenotypes for hPSC-CMs. Out of 310 pathways identified using metabolomics and proteomics, 40 pathways were considered significantly overrepresented (false-discovery-rate-corrected $p \leq 0.05$). Highly populated pathways included those involved in protein synthesis (ribosome, spliceosome), ATP generation (oxidative phosphorylation), and cardiac muscle contraction. This multiomics method achieves a deep coverage of metabolites and proteins, creating a multidimensional view of the hPSC-CM phenotype, which provides a strong technological foundation to advance the understanding of hPSC-CM biology.

Biography:

Elizabeth is an Analytical Chemistry Ph.D. candidate under the supervision of Dr. Ying Ge at the University of Wisconsin - Madison. She earned a BA in Chemistry from Smith College in 2014. Prior to graduate school, Elizabeth spent four years as part of Analytical R&D at Pfizer in Groton, CT where she specialized in late-stage drug development. She is pioneering the use of multi-omics in the Ge lab by integrating high resolution mass spectrometry-based proteomics and metabolomics to study human pluripotent stem cell cardiomyocyte (hPSC-CM) maturation. Elizabeth also studies top-down proteomics and metabolomics of human cardiac tissue.