ABSTRACT: Complex human diseases such as cardiovascular disease, diabetes, and neurodegenerative disorders involve multi-scale alterations and re-organization at molecular, cellular, and tissue levels. Technological advances in the past decade are enabling an outpour of multi-omics big data to assist with our understanding of complex human diseases, but also pose challenges to multi-scale data integration. In this talk, I will introduce i) systems genomics approaches and tools to accommodate diverse omics data types from different species for network modeling of pathophysiological systems, and ii) applications of these methods in metabolic and brain disorders. These efforts have led to the elucidation of cell-specific and tissue-specific networks and critical regulators either specific to individual diseases or shared between diseases. The systems and network level insights can help guide the development of novel network-based medicine for common complex human diseases.