

Single-Cell Metabolomics: Towards Applications in Cancer and Aging

PI: Prof. Huiyong Yin Co-I: Prof. Mengsu (Michael) Yang, Prof. Liang Zhang

Project Summary

Cellular metabolism is a highly regulated and dynamic process in which cells rely on to fulfil biological functions, and dysregulation of metabolism has been associated with various pathological processes including metabolic diseases, cancer, and aging. Although conventional research tools have been instrumental in deciphering the metabolic mechanisms, emerging single-cell omic technologies, such as transcriptomics, proteomics and metabolomics, may offer unprecedented advantages in studying the heterogeneity and dynamics of metabolism at single cell levels. Comparing to other single-cell omic techniques, single-cell metabolomics poses enormous challenges due to the complexity of the metabolic processes and extremely low levels of metabolites with tremendous structural diversities. The past decade has witnessed impressive progress in the development of various single-cell metabolomics, however, this technique is far from maturation for addressing the complex metabolic mechanisms underlying various physiological and pathophysiological processes.

In this application, we propose to develop and optimize single-cell metabolomic protocols utilizing targeted and untargeted metabolomics, in combination with microfluidic technology, nano-liquid chromatography with high resolution mass spectrometry (MS). The team led by the principal investigator of this application has over 20 years of experience in developing MS-based metabolomics in investigating mechanisms in various metabolic diseases, including cardiovascular disease, hyperuricemia, and cancer. This application will focus on the technical challenges in MS-based single-cell metabolomics, from single cell isolation, sample preparation, metabolite separation, to MS detection and bioinformatics. In collaboration with research teams led by Professor Michael Yang and Zhang Liang, we will leverage their experience and expertise with the microfluidic single-cell isolation and proteomics to develop single-cell metabolomic work flow. This powerful technique will be applied to further our understanding on the molecular mechanisms we have obtained in bulk studies using various mouse models and human samples. Three specific aims are proposed:

Specific Aim 1 To establish a single-cell metabolomics workflow using microfluidic single-cell isolation and MS detection by optimizing the liquid chromatography, MS ionization and interface.

Specific Aim 2 To profile the single-cell metabolomes in cancer cell lines and cell models in the context of aging.

Specific Aim 3 To profile the metabolomes of circulating tumor cells (CTCs) from breast cancer patients and identify potential metabolic biomarkers for early diagnosis, subtyping, and metastasis.

Successful execution of this proposal will greatly enable the metabolic research in metabolic diseases, cancer and aging.