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Research Seminar

3:00 pm in CBLL-16, Sept 11th, 2023

Liquid Chromatography-Mass Spectrometry Based Omics

Different types of molecules are present in a biological system. Multiomics analyzes multiple groups of these molecules and integrates data acquired in different omic groups to gain a comprehensive picture of the biological system. Liquid chromatography-mass spectrometry (LC-MS) is a powerful platform in multiomics and two approaches have been developed, untargeted and targeted analyses. Untargeted omics focuses on global analysis to quantify as many molecules as possible, while targeted omics analyzes a set of known molecules. In my research seminar, I will present my works in LC-MS-based metabolomics, lipidomics, and epitranscriptomics.

1. Metabolomics
   a. *Caffeine metabolism dysregulated in alcohol-associated liver disease (ALD) patients*[1] After collecting 64 human urine samples from healthy control, patients with non-severe ALD and severe alcohol hepatitis (AH), we extracted polar metabolites and analyzed them using both untargeted and a newly developed targeted metabolomics approach. The caffeine metabolites have significant concentration differences between the healthy control and patients. Paraxanthine, 5-acetylamino-6-amino-3-methyluracil and 1-methylxanthine decreased with the increase of ALD severity, and they may serve as biomarkers for ALD diagnosis.
   b. *Altered tryptophan metabolic pathway in ALD patients*[2] Tryptophan (Trp) plays significant roles in many mammalian physiological processes. However, Trp metabolism in ALD is still an ongoing research area. Our untargeted metabolomics data showed that Trp pathway was perturbed in ALD. I then developed a targeted metabolomics method to quantify the Trp and its metabolites. The urinary Trp has no change between healthy control and patients with ALD. However, the increase of quinolinic acid and the decreasing indoxyl sulfate are highly correlated with different stages of ALD.
2. Lipidomics

We developed a comprehensive two-dimensional LC-MS (2DLC-MS) platform for lipid profiling. The lipids extracted from biological samples are first separated on a hydrophilic liquid chromatography (HILIC) column (^{1}D) and then further separated on a reversed phase column (^{2}D). I first developed analysis software, *Lipid Wizard*, for lipid assignment and quantification using precursor ion m/z matching, ^{1}D and ^{2}D retention time filtering. The overlapping lipids are quantitatively deconvoluted by iterative linear regression. We applied *Lipid Wizard* to study the lipid changes in the livers of mice fed with alcohol and show that *Lipid Wizard* can qualify the lipids in biological samples[3].

3. Epitranscriptomics (in progress)

I am developing a comprehensive stop-flow 2DLC-MS for the separation and quantification of oligonucleotides (OGNs), where OGNs are digested from the RNAs by RNase T1. My current configuration of the comprehensive 2DLC system is configured as a ^{1}D anion exchange column connected with a ^{2}D reversed phase column.

References:

1. Xu, R.; He, L.; Vatsalya, V.; Ma, X.; Kim, S.; Mueller, E. G.; Feng, W.; McClain, C. J.; Zhang, X. *Am J Physiol Gastrointest Liver* **2023**, 324 (2), G142-G154.
2. Xu, R.; Vatsalya, V.; He, L.; Ma, X.; Feng, W.; McClain, C. J.; Zhang, X. *Alcohol Clin Exp Res* **2023, in press**.
3. Xu, R.; Liu, H.; Yuan, F.; Kim, S.; Kirpich, I.; McClain, C. J.; Zhang, X. *Anal Chem* **Submitted.**