Analytical Seminar

The NeuCode Mouse: Multiplexed Proteomic Analysis Reveals Tissue Specific Effects of Deubiquitinase Deletion

Stable isotope labeling by amino acid in mammals (SILAM) is a popular technique for comparing proteomes of model systems, typically mice. In traditional SILAM, light peptides from experimental samples are compared to heavy-labeled reference material in 2-plex experiments. In that context, incomplete isotopic labeling of the reference sample yields peptides which interfere with the unlabeled experimental peptides, requiring costly multi-generational labeling. Utilizing variations of lysine with different neutron signatures (NeuCode), we perform NeuCode-SILAM and demonstrate protein quantification after only 10 days of labeling. This multiplexed, quantitative *in vivo* metabolic labeling strategy reduces labeling time and enables simultaneous analysis of up to four animals. Using this technology we characterized tissue-specific protein changes following deletion of BAP1, a deubiquitinase whose loss is associated with myelodysplastic syndrome and cancer. Combining results from 4-Plex and 2-Plex experiments >8,000 proteins from nine tissues of wild-type and BAP1 KO mice were interrogated. We conclude that NeuCode SILAM enables direct comparison of mammals without a heavy reference sample, while decreasing labeling time and increasing multiplexing capabilities.

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12:15 p.m. in 1315 Chemistry