Profiling drugs by chemical proteomics

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Identifying the targets of a drug can be done by immobilizing an analogue of the small molecule and proceeding to a competition experiment of the free drug versus the immobilized drug in a lysate. This is known as a compound-centric approach. When the targets of many drugs need to be identified, this approach suffers from the lengthy process of synthesizing at least one analogue per drug. To circumvent this limitation, an unselective matrix for a sub-proteome of interest can be generated. With such a tool, competition assays between the drugs and the matrix will pinpoint all the targets of the drugs within the enriched native sub-proteome.

The workshop will focus on the conceptual and practical aspects of generating such matrices and using them for drug profiling. These topics will be detailed and exemplified:

- How to design an affinity probe
- How to generate an affinity probe
- How to combine affinity probes to obtain a sub-proteome enriching matrix
- How to obtain a relevant repertoire of native proteins
- How to perform affinity pulldown experiments
- How to identify and quantify proteins by mass spectrometry
- How to convert drug competition data into K_d values for identified targets