Activity based Proteomics in Lipid Research

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Lipids are the major energy source of humans. Their digestion, transport, formation, intracellular storage and mobilization are tightly controlled processes to ensure overall energy balance. Overall, a vast number of molecular components are involved in the regulation of lipid mobilization and absorption. Many of these components have been identified and characterized, but not all are yet known. Moreover, the interaction and regulation of these enzymes by, e.g. hormones, coenzymes/activators, post-translational modifications (e.g. phosphorylation), product inhibition (e.g. free fatty acids) and especially substrate accessibility, remain to be studied in full detail. One quickly evolving tool to investigate protein-small molecule interactions are activity based probes (ABP). These probes are able to target a specific class of enzymes based on the catalytic mechanism in the active site of the prey enzyme. Combined with various reporter tags and/or affinity tags these probes allow efficient detection, purification and quantification of whole enzyme classes in highly complex proteomes. The labelled enzymes can then be analysed employing various mass spectrometric methods. A set of new ABP for *in vivo* tagging of lipolytic enzymes was developed. The tuneable selectivity of these probes as well as their highly adaptable reporter tags allows customization of the probes to the sample of interest. As an example the lipolytic proteome of 2 mouse adipocyte cell lines is shown. These novel ABP allow to identify low abundant lipolytic enzymes in a wide variety of different samples *in vivo*. Future aims are the development of ABPs for relative and absolute quantitation of lipolytic sub-proteomes.