Understanding Cellular Proteolysis with Proteomic Approaches

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Proteolysis affects every protein through limited processing or degradation. Unlike other post-translational modifications, proteolysis is irreversible and occurs intra- and extracellularly. Limited proteolysis regulates cytokine function, zymogen activation, membrane shedding, and assembly of structural proteins. The large number of genetically encoded proteases in man (> 560) illustrates the involvement of proteolysis in most physiological and pathological processes. However, the in vivo substrate profiles of most proteases have remained elusive; presenting a major hurdle to understanding and therapeutically exploiting protease function in health and disease.

System-wide, unbiased identification of protease substrates has long been inaccessible but is now enabled by recently developed proteomic strategies for the quantitative determination of neo N– and C–termini together with high-content screening of in vitro protease specificity. The seminar will introduce these novel techniques and highlight how they can be applied to better understand proteolytic processing in the cellular context.