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Proteomics: translating genes into cellular functions to understand biology and disease

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The sequencing of the human genome has provided a privileged envision of our own biology. However, much remains to be explored to fully define a complete map of cell functions, their regulatory mechanisms and the alterations participating in disease. As proteins are primary effectors of cellular pathways, the study of the proteome based on a systems biology strategy has opened new perspectives in biomedical research. Proteome complexity, the wide dynamic range of its components as well as their inherent physicochemical nature precludes the coverage of the entire protein set of a living organism on a single experiment. However, the astonishing progress in protein/peptide fractionation combined with mass spectrometry in the past decade allow unprecedented proteome coverage and measurement accuracy. Proteomics emerges, therefore, as an exciting tool in biomedical research. In this seminar basic concepts and state of the art methods in proteomics will be revised as well as their application to the analysis of complex cell and tissue proteomes.

One carbon metabolism (1CM) was prioritized as a central pathway associated to the progression of liver disorders. Impairment of the methylation capacity of liver cells lead to the identification of 216 differential proteins that suggest deregulation of cellular pathways as those mediated by ERK or NFκB. R-methyl proteome analysis lead to the identification of 74 differentially methylated proteins, including 116 new methylation sites. Inhibition of RNA binding proteins methylation is especially relevant. Moreover, quantification of 1CM enzymes by SRM in the liver revealed a tissue specific expression profile as well as a significant remodelling in mice upon CCl4 induced liver injury and in liver tumours.

It is then tempting to suggest that impairment of 1CM is a bad prognostic hallmark in cancer. The systematic monitorization of one carbon metabolism in the liver may probe its usefulness for the assessment of liver parenchymal cells homeostasis.