Quantitative proteomics by mass spectroscopy: a new tool for 21th century's biology and for diagnostics

Studies in young mammals on the qualitative and quantitative molecular effects of food restriction (RES) and of re-feeding are scarce. Whereas RES may lead to growth and developmental deficits in children, it is a proven treatment to prolong adult life in all tested animals.

Our aim here is to describe how, using mass spectroscopy techniques and high-throughput quantitative proteomic of whole rat livers, we could address the molecular basis for the apparent life-prolonging effect of the RES regimen.

Using at least six independent biological repeats for each conditions, the method could identify and precisely quantify more than 1800 common proteins in the livers of *ad libitum* (AL), RES- and AL re-fed rats after RES, which summed up into being over 92% of the total protein mass of the liver cells. Compared to RES, AL cells contained significantly less mitochondrial catabolic enzymes and more cytosolic and ER HSP90 and HSP70 chaperones, which are typical hallmarks of heat- and chemically-stressed tissues.

The quantitative and qualitative protein values thus clearly indicated that the RES regimen is less stressful than the unlimited feeding regimen. RES needed only minimal amounts of HSP-chaperones to maintain optimal protein homeostasis and to sustain a lengthy life span. In contrast, the elevated levels of HSP-chaperones in rapidly growing AL tissues were characteristic of a chronic stress applied on the protein quality control machineries of the liver cells, which in the long term could cause early aging and shorten life span.