Spatio-temporal protein dynamics during autophagy

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CELLULAR processes are generally carried out by proteins. Thus, the analysis of spatio-temporal protein dynamics allows exciting insights into cellular decision finding. Quantitative mass spectrometry (MS) has become the method of choice for the analysis of protein dynamics ranging from posttranslational modification changes to changes in subcellular localizations of proteins. We are using stable isotope labeling by amino acids in cell culture (SILAC) in combination with quantitative MS-based proteomics to analyze protein dynamics during autophagy. The autophagosomal/lysosomal pathway is next to the proteasome/ubiquitin system responsible for the majority of cellular degradation. Autophagy is an evolutionary conserved process wherein catabolism of cytoplasm generates energy which allows cell survival under condition of reduced nutrient availability. It is thought to be important for the turn-over of whole organelles and long-lived proteins. Deregulation of autophagy has been shown to be important in several diseases ranging from cancer to neurodegenerative diseases. Autophagy is regarded as an unspecific bulk degradation process. However, using unbiased proteomic approaches we could show that during long-term amino acid starvation organelles are degraded in an ordered fashion via autophagy. The analysis of autophagosomes showed stimulus-dependent changes in autophagosome composition varying over time. In addition, ample cross-talk between the proteasome system and the autophagosomal/lysosomal system became evident. Thus, our data implies that during stress responses degradation via autophagy is more specific than anticipated so far.