# Detailed insight into stressed cells

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When cells are stressed, they initiate a complex and precisely regulated response to prevent permanent damage. One of the immediate reactions to stress signals is a reduction of protein synthesis (translation). Until now, it was difficult to measure such acute cellular changes. As reported in the latest online issue of the renowned journal *Molecular Cell*, researchers at Goethe University have now developed a method overcoming this hurdle.

The team led by biochemist Dr. Christian Münch, who heads an Emmy Noether Group, employs a simple but extremely effective trick: When measuring all proteins in the mass spectrometer, a booster channel is added to specifically enhance the signal of newly synthesised proteins to enable their measurement. Thus, acute changes in protein synthesis can now be tracked by state-of-the-art quantitative mass spectrometry.

The idea emerged because the team wanted to understand how specific stress signals influence protein synthesis. "Since the amount of newly produced proteins within a brief time interval is rather small, the challenge was to record minute changes of very small percentages for each individual protein," comments group leader Münch. The newly developed analysis method now provides his team with detailed insight into the molecular events that ensure survival of stressed cells. The cellular response to stress plays an important role in the pathogenesis of many human diseases, including cancer and neurodegenerative disorders. An understanding of the underlying molecular processes opens the door for the development of new therapeutic strategies.

"The method we developed enables highly precise time-resolved measurements. We can now analyse acute cellular stress responses, i.e, those taking place within minutes. In addition, our method requires little material and is extremely cost-efficient," Münch explains. "This helps us to quantify thousands of proteins simultaneously in defined time spans after a specific stress treatment." Due to the small amount of material required, measurements can also be carried out in patient tissue samples, facilitating collaborations with clinicians. At a conference on Proteostatis (EMBO) in Portugal, Ph.D. student Kevin Klann was recently awarded with a FEBS journal poster prize for his presentation of the first data produced using the new method. The young molecular biologist demonstrated for the first time that two of the most important cellular signaling pathways, which are triggered by completely different stress stimuli, ultimately results in the same effects on protein synthesis. This discovery is a breakthrough in the field.

**More information:** Kevin Klann et al. Functional Translatome Proteomics Reveal Converging and Dose-Dependent Regulation by mTORC1 and eIF2α, *Molecular Cell* (2019). DOI: 10.1016/j.molcel.2019.11.010

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