The vast array of functions within our body is performed by proteins, which are biomolecules. Proteins are made constantly in our cells by a specialized complex, the ribosome. The eukaryotic ribosome itself consists of ~82 proteins (ribosomal proteins). Since its discovery in the 1950s, it was believed that each ribosome complex is identically built. Only recent advances in technology helped to reveal that this view of the ribosome as a static machine needs to change. So-called "specialized ribosomes" have been identified that contain different stoichiometry of ribosomal proteins, a variety of ribosome-associated proteins, and other regulatory elements. "Specialised ribosomes" allow the cells to regulate what kind of proteins will be produced and this can depend on the type of cell, developmental stage of the organism, or whether the cell is exposed to a hazardous condition.

Mitochondria, the energy-producing organelles of the cell, are built of proteins that are produced on ribosomes outside of the organelle and these proteins need to be transported into mitochondria. We found that if this transport is disrupted ribosomes decrease overall protein production but maintain the ability to produce specific proteins that might help to overcome the defect in the mitochondria. We identified at least one candidate ribosomal protein whose abundance changes rapidly upon such mitochondrial defect and could modulate ribosome function. Thus, we hypothesize that "specialized ribosomes" can be formed upon mitochondrial dysfunction in order to change the output of protein production to help to restore mitochondrial function. We propose to use global approaches including proteomics, transcriptomics, and in-depth biochemical analysis to uncover changes in ribosomal proteins, competence in protein production and feedback mechanisms to restore mitochondrial function.

Our research will uncover fundamental mechanisms of cellular stress responses and in particular maintenance of mitochondrial function, which is essential for overall health of cells. In humans, impaired ribosome formation and function is the underlying cause of diseases called ribosomopathies. Ribosomopathy has been linked to the pathology of various malignancies and several ribosomopathies are associated with an increased rate of cancer. Thus, fundamental studies on the function of ribosomal proteins will also increase knowledge of human pathologies.