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Sjögren's Syndrome Foundation Research Grant

LAY ABSTRACT

The Lay Abstract is for publicity purposes and should use simple language summarizing the proposed research and its significance.

Proteins of complexes from the cells' nucleus, (NP), are the main group of SS autoantigens and play important roles in biogenesis and quality control processes. Stress conditions cause impairment of these functions, and let SS NP travel into stress granules, a step which may influence their release from cells, and their potential to become antigens. This project aims to identify binding partners, which influence the localization of SS NP and could contribute towards autoimmunity.

We will identify SS NP binding partners under stressed and unstressed conditions in patients and in healthy controls using blood samples, develop methods to isolate and characterize stress granules, and study their formation and disassembly in cells. Once established, we will try to identify which components that contribute to immune stimulation.

Our approaches potentially allow to detect genetic changes in patients, which may provide a better understanding of autoimmunity and an improve diagnosis of SS.

SCIENTIFIC ABSTRACT

The Scientific Abstract is written for SSF reviewers and a professional audience.

Nuclear proteins (NP), major antigens in Sjögren's syndrome (SS), play important roles in RNA-polymerase-III-based noncoding-RNA biogenesis and quality control. Stress-mediated translocation of SS NP into cytoplasmic stress granules may influence their immunogenic potential and / or influence their release from cells, potentially triggering autoimmunity. Aiming to study effects influencing their localization, dynamics and immunogenicity, we will identify SS NP interaction partners by crosslinking and high-throughput RNA sequencing techniques and mass spectroscopy, and compare interactions in patients and healthy controls. Furthermore, we will develop methods to isolate and characterize stress granules, and study their dynamics in live cells using GFP-fusion proteins. Interaction partners of SS NP and isolated components from stress granules will be tested for their immunostimulatory potential using interferon and cytokine activation assays.

Genetic variations detected in SS patients may serve as biomarkers, and could provide an enhanced understanding of innate and adaptive immune activation, inflammatory pathways, and regulation of tolerance.