Salivary gland epithelial cell in Sjögren’s syndrome: Metabolic shift and altered mitochondrial morphology toward an innate immune cell function

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Objectives: Salivary gland epithelial cells (SGEC) are the main targets of the autoimmune reactivity in Sjögren’s syndrome (SS). This study aimed to investigate the core proteomic differences between SS and Control- (Ct) -derived SGEC and to recognize ultrastructural alterations of the cells, possibly related to proteomic differences.

Materials and methods: Proteome analysis of cultured SGEC from five SS patients and four Ct was performed in a label-free quantitation format (LFQ). Electron microscopy was applied for analysis of the mitochondrial ultrastructure of SGEC in minor salivary gland sections from six SS patients and four Ct.

Results: Four hundred seventy-four proteins were identified differentially abundant in SS- compared to Ct-SGEC. After proteomic analysis, two distinct protein expression patterns were revealed. Gene ontology (GO) pathway analysis of each protein block revealed that the cluster with highly abundant proteins in SS-SGEC showed enrichment in pathways associated with membrane trafficking, exosome-mediated transport and exocytosis as well as innate immunity related mainly to neutrophil degranulation. In contrast, the low abundance protein cluster in SS-SGEC was enriched for proteins regulating the translational process of proteins related to metabolic pathways associated to mitochondria. Electron microscopy showed decreased total number of mitochondria in SS-SGEC, which appeared elongated and swollen with less and abnormal cristae compared to Ct-SGEC mitochondria.

Conclusions: This study defines, for the first time, the core proteomic differences of SGEC between SS and Ct, substantiates the metamorphosis of SGEC into an innate immune cell and reveals that these cells are translationally shifted towards metabolism rewiring. These metabolic alterations are related mainly to mitochondria and are mirrored *in situ* with heavy morphological changes.

Keywords: Sjögren’s syndrome Salivary gland epithelial cells Mitochondria Metabolism Innate immunity

**Acknowledgment:** This project has been funded by the H2020 project HARMONICSS; H2020-SC1-2016 (GA: 731944). S.K is supported by a MSCA individual fellowship, H2020-MSCA–IF–2019 (GA: 897821). MS and GS are supported by the project pMedGR (MIS 5002802). K.M. is supported by the HFRI under the PhD Fellowship grant (GA: 1642). We like to thank Professor Haralampos M. Moutsopoulos for his valuable input and feedback on this project and for his continuous inspiration and guidance.

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Biography: Professor Fotini N. Skopouli, MD, PhD, FRCP, Internist-Immunologist, has specialized in Internal Medicine /Autoimmune Diseases /Immunology in the Medical School, Ioannina, Greece, Bath, UK and NIH, USA. She taught Medicine and Immunology, in the Medical School, University of Ioannina, and in Harokopio University, Athens, Greece. She directs the Internal Medicine /Autoimmune Diseases Department of Euroclinic in Athens. Her research is focused on the clinical manifestations and pathogenetic aspects of Sjögren’s syndrome (SS). She has published more than 130 scientific publications (Citations: 17495, h index: 53). Her recent important scientific contributions include: the identification of metabolic alterations of salivary gland epithelial cells (SGEC) of SS patients, the impact of endoplasmic reticulum (ER) stress in intracellular autoantigens relocation and the metamorphosis of SS SGECs into innate immune cells that are translationally shifted towards metabolism rewiring. At present, she studies, in vitro, how stress can initiate and perpetuate the autoimmune reactivity in SS.