New insights into the role of salivary glands in Sjögren's disease

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Sjögren's disease primarily affects the salivary and lacrimal glands, resulting in tissue inflammation characterized by the formation of tertiary lymphoid structures (TLS), and a loss of glandular

function—resulting in dryness of the eyes and mouth, fatigue, and poor health-related quality of life.

It is also known that salivary gland epithelial cells (SGEC) play a pathogenic role in Sjögren's disease. Two abstracts presented at the 2024 congress of EULAR—The European Alliance of Associations for Rheumatology—looked at Sjögren's disease, specifically around furthering our understanding of the role of the salivary glands.

TLS are accumulations of lymphoid cells that share similar cellular compartments, organization, and function as secondary lymphoid organs. Importantly, the presence of these structures in inflamed salivary glands associated with active disease, increased autoantibody production, and malignancy risk.

"To treat patients effectively, comprehensive understanding of the salivary gland microenvironment is needed," said Saba Nayar, "but current profiling efforts often struggle to capture high-plex 'omics data while preserving the spatial architecture of the tissue."

To address this, the team mapped both identified cell types and novel populations, clustering tissue architectural features to define eight so-called neighborhoods. Some of these were enriched with epithelial cells, but others were associated with different immune cell populations.

One neighborhood was enriched with IgA plasma cells, and was associated with myeloid populations—in contrast to other IgG plasma cells niches. This novel spatial mapping work—presented in a basic abstract session on new pathways in Sjögren's disease—has the potential to reveal novel cellular landscape and their interactions, aiding therapeutic and discoveries for the management of Sjögren's disease.

A second abstract focused on SGEC, which are already known to play a

pathogenic role in Sjögren's disease. Research is underway to develop and characterize differentiated organoids of SGEC derived from minor salivary gland biopsies of both patients and sicca controls.

Organoids were shown to form and differentiate in both groups, with comparable self-renewal capacity of organoids for long-term culture. The organoids expressed epithelial ductal and acinar markers and recapitulated the epithelial diversity.

Exposure to pilocarpine induced increased calcium levels—suggesting a capacity to secrete saliva in response to a cholinergic stimulation—but this effect was reduced in organoids derived from Sjögren's patients compared to controls.

In conclusion, Loïc Meudec said "additional characterization investigations are ongoing to develop immuno-organoids that can be used to study the crosstalk between epithelial cells and immune cells and to test the effect of drugs on this crosstalk."

Drug development for Sjögren's disease has predominantly focused on suppressing aberrant immune cells, but this approach has not shown efficacy in clinical studies, and there are no approved biologic therapies that directly target the underlying pathogenesis.

Comprehensive understanding of the salivary gland may help change this picture in the future.

More information: S. Nayar et al, OP0199 Spatial insights into the salivary glands of patients with Sjögren's disease, *Scientific Abstracts* (2024). DOI: 10.1136/annrheumdis-2024-eular.5434

L. Meudec et al, OP0329 Development of salivary gland organoids to study Sjögren's disease, *Scientific Abstracts* (2024). DOI:

10.1136/annrheumdis-2024-eular.1959