2026 PILOT GRANT

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Spatially Resolved Metabolic Biogeography of the Neuro-Epithelial-Immune Interface in Salivary Glands for Dissecting the Dietary Interventions on Sjögren's Disease

Abstract: Sjögren's disease (SjD) is defined by a debilitating loss of salivary function that often precedes significant glandular destruction, suggesting a functional signaling blockade at the neuro-epithelial interface. While healthy glands rely on precise crosstalk where autonomic fibers release neuropeptides to trigger secretion, chronic inflammation in SjD creates a "neuro-metabolic desert" that silences this circuit. This proposal addresses the 2026 Sjögren's Foundation priority of neuro-immunological mechanisms by constructing a Spatially Resolved Neuro-Epithelial Metabolic Response Framework to elucidate how dietary interventions can restore glandular function. Leveraging our established Salivary Gland Atlas (SjöMap) of 50 donors, we will utilize spatially resolved metabolic biogeography to map the spatio-chemical "niches" where the Tryptophan-Kynurenine (TRP-KYN) shunt and other metabolic regulators (Purinergic, oxidative stress, and neurotoxic lipid remodelling) suppress neuropeptide maintenance. We introduce a first-in-class Neuro-Metabolic Index (NMI) to quantify the signaling readiness of the gland at the cellular level. To move beyond observational data, we will employ a cutting-edge "Diet-on-a-Chip" platform—a 3D co-culture of acinar cells, autonomic neurons, and patient-derived PBMCs. This model allows for the testing of spatial and temporal dietary combinations (e.g., specialized pro-resolving mediators and antioxidant pulses) to identify the precise metabolic kinetics required to "unmute" the neuro-salivary signal. By integrating high-resolution mass spectrometry imaging with mechanistic organ-on-a-chip validation, this pilot project will provide the first evidence for diet-driven neuro-metabolic restoration. This work establishes a foundation for precision nutritional prescriptions, transforming dietary management from a lifestyle suggestion into a molecularly targeted therapy to reclaim salivary function and improve quality of life for SjD patients.

For more information, please contact the Sjögren's Foundation at research@sjogrens.org.