



2026 HIGH IMPACT GRANT

Teja Kapoor, MD

Director, Columbia Sjögren's Program

Department of Medicine

Columbia University

Mechanistic Endotypes of Neuro-Autonomic Sjögren's Disease

Abstract: Neuro-gastrointestinal and autonomic manifestations in Sjögren's disease (SjD), including orthostatic intolerance, dysmotility, fatigue, and small fiber neuropathy (SFN), are common, disabling, and biologically heterogeneous. Although these complications significantly contribute to functional impairment and reduced quality of life, the mechanisms behind this variability remain poorly understood. Current paradigms centered on conventional serologies fail to explain why some patients develop severe neuroautonomic dysfunction while others do not. We hypothesize that neuro-autonomic SjD consists of three mechanistically distinct endotypes: (1) autoantibody-mediated neuronal dysfunction targeting autonomic receptors; (2) Fcγ receptor (FcγR)-mediated innate immune dysregulation characterized by an imbalance between activating and inhibitory FcγRs; and (3) non-inflammatory neural dysfunction marked by structural impairment. To test this framework, we will integrate targeted neuroimmune autoantibody profiling, high-dimensional FcγR phenotyping of innate immune cells, and objective assessments of autonomic and small-fiber neuropathy in 30 SjD participants from our cohort with and without neuroautonomic symptoms. We will determine whether immune signatures correlate with physiologic dysfunction and structural nerve loss, thereby defining biologically anchored subgroups. By linking molecular immune signatures with objective autonomic and neuropathic phenotypes, this framework will identify biologically distinct subgroups within SjD. Establishing these endotypes will enable a precision medicine approach to guide more rational selection of IVIG, B-cell-targeted therapies, or neuroprotective strategies, moving beyond empiric management toward mechanism-based care.

©2026 Sjögren's Foundation. All rights reserved. This abstract is provided for informational purposes only and may not be reproduced, distributed, published, or transmitted, in whole or in part, without the prior written permission of the Sjögren's Foundation and the author(s).

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