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THE SAHLGRENSKA ACADEMY
INSTITUTE OF MEDICINE

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Announcement - scholarship at postdoctoral level

The Department of *Rheumatology and Inflammation Research* at the Institute of Medicine hereby announces a scholarship at postdoctoral level in B cell biology.

Plan for advancement
Subject: The role of IgD nanodomains in human B-cell tolerance and autoimmunity.

Background: Up to 40% of newly formed human B cells are self-reactive upon leaving the bone marrow, yet most fail to cause disease due to peripheral tolerance mechanisms. Transitional B cells co-express two surface receptors, IgM and IgD, which recognize the same antigen but differ in structure, signaling strength, and membrane organization. IgD resides in cholesterol-rich membrane nanodomains alongside specific co-receptors, while IgM is largely excluded from these structures. Disruption of this nanoscale organization may allow self-reactive B cells to escape deletion and produce autoantibodies, contributing to autoimmune diseases. Using the Proximity Network Assay (Pixelgen Technologies) and Fab-based proximity ligation assay (Fab-PLA), we have already mapped IgD nanodomain composition across B-cell subsets in healthy donors, establishing high-resolution reference maps of protein organization at nanoscale resolution. These data now form the foundation for the project proposed here.

Purpose: This project aims to determine how specific co-receptors within the IgD nanodomain regulate B-cell fate decisions and which perturbations of this nanodomain allow self-reactive immature B cells to escape tolerance checkpoints and produce autoantibodies. The long-term goal is to identify molecular targets for restoring peripheral tolerance in autoimmune disease.

Method: (aim1) The co-receptors identified from the completed nanodomain mapping will be knocked out or knocked in using CRISPR gene editing in antigen-specific Ramos B-cell lines. Their impact on IgD signaling will be quantified by calcium flux, phosphorylation assays (Syk, Btk, ERK, Akt), activation, inhibition, and apoptosis. Findings will be validated in primary B cells from healthy donors. **(aim2)** Immature B cells will be cultured and exposed to the IgD stimulation and co-receptor perturbation conditions to mimic tolerance checkpoint failure. Cells surviving these conditions will be driven toward antibody-secreting cells, and autoantibody output will be measured by ANA indirect immunofluorescence on Hep-2 cells and by ENA multiplex screening.

Time plan: Aim 1 begins immediately, with optimization of gene editing in the Ramos cell line in year 1, followed by primary B-cell assays in years 1–2. Aim 2 runs in parallel from year 1, with culture conditions and perturbations informed by early Aim 1 results, and autoantibody readouts completed in year 2.

Outcome: This project will define which IgD nanodomain co-receptors tune signaling strength to enforce or fail peripheral tolerance in immature B cells, and will directly link specific nanodomain perturbations to autoantibody production. These results will provide a mechanistic framework for developing targeted strategies to selectively silence self-reactive B cells in autoimmunity without impairing protective immune responses.

Period

2026-05-01 – 2028-04-30

Financing

A total of 624000 SEK will be paid for the whole period.

If you require any further information, please contact Alessandro Camponeschi, alessandro.camponeschi@rheuma.gu.se, supervisor.

Application

To apply please fill out the form" Application for a scholarship at postdoctoral level" and send it to Alessandro Camponeschi, alessandro.camponeschi@rheuma.gu.se, supervisor.

Please attach a copy of your PhD certificate with the application. PhD must be completed within three years of the application deadline.

Closing date is 2026-04-03.