EFIS-IL Study Group proposal - Lymphoid Structures: Orchestrators of Immunity

Summary
Lymphoid structures serve as central hubs of immune coordination, integrating signals from hematopoietic and stromal compartments to regulate adaptive immunity. Beyond their well-established roles in vaccination and infection control, they are key players in cancer, autoimmunity, transplantation, infection and immune aging. The rapid expansion of research in this area has led to groundbreaking discoveries that challenge long-held beliefs about lymphoid structure function and organization. Advancing our understanding of these structures requires innovative experimental models, including 3D cultures and organoid systems, to better capture their complex microenvironment. This EFIS-IL Study Group will bring together experts to explore lymphoid structure biology, experimental models, and translational opportunities, fostering innovation in diagnostics and therapy.

1. Research area

Lymphoid structures play a critical role in immune coordination, regulating responses in both homeostasis and disease. The field of lymphoid structure immunology is undergoing rapid advancements, challenging traditional views on their function. For instance, while booster vaccinations were previously believed to primarily rely on memory B cells, new evidence suggests a dominant role for naive B cells in this process (L. Mesin et al., Cell, 2022), with antibodies from the primary immune response potentially limiting memory B cell recruitment (J. Tas et al., Immunity, 2022). Additionally, the spatial organization of cells within lymph nodes plays a crucial role in immune function, particularly in age-related immune decline, where structural disruptions contribute to impaired responses (A. Silva-Cayetano et al., Nat Immunol, 2023).

Beyond classical secondary lymphoid organs, lymphoid structures can form de novo in response to chronic inflammation, giving rise to tertiary lymphoid structures (TLSs). These formations appear in diverse settings, including infections, autoimmunity, and tumors, and their presence is linked to immune modulation. They represent a powerful hub for the induction of T and B cell immune responses with a dual role, i.e. a favorable impact (prognostic and predictive biomarker) in cancers and deleterious in autoimmune diseases and transplantation. However, the mechanisms regulating their formation and functional specialization remain poorly understood.

Much of our current knowledge is based on murine models, emphasizing the need for comparative translational studies and the advancement of experimental systems, such as organoid-based lymphoid structures and 3D culture models. This study group will integrate expertise in lymphoid tissue organization, immune cell-stromal interactions, and experimental modeling to deepen our understanding of the fundamental biology of lymphoid structures. Moreover, we will be able to assess mechanistic insights from in vitro models in clinical trials where lymphoid samples can now be collected using advanced sampling methods such as fine needle aspiration. By fostering interdisciplinary collaboration, we aim to refine concepts of lymphoid tissue function and regulation, ultimately advancing the field of immunology.

2. Core Group of Proponents, Coordinator, and Participants

The study of lymphoid structures has gained significant momentum, reflected in dedicated research efforts and specialized scientific meetings. Notably, the "Lymphatic Tissues and Germinal Centers in Immune Reactions" conference in July 2024, highlights the increasing focus on this area.

Core Group of Proponents

Country	Collaborators & Affiliations
Netherlands	T. van den Broek (Coördinator, UMC Utrecht), S. Jochems & M. Coppola (UMC Leiden), R. Mebius & L. de Winde (Amsterdam UMC)
United Kingdom	A. Denton (Imperial College London), J. Fergusson (Jenner Institute), M. Bombardieri (Queen Mary University London)
France	M.C. Dieu-Nosjean (CIMI), C. Sautes-Fridman (University Paris-Descartes)
Italy	P. Nistico (Regina Elena Cancer Institute), M. Tazzari (IRCCS-IRST)

Belgium	K. Willard-Gallo (HU Bruxelles)
Switzerland	K. Silina & N. Pikor (ETH Zurich)
Denmark	S. Degn (Aarhus University)
Sweden	A. Dimberg (Uppsala University)

The core group represents a diverse cohort of junior and senior scientists with expertise in lymphoid structure immunology across various disciplines. The study group will include additional researchers and medical specialists specializing in lymphoid structures from multiple European countries, ensuring broad scientific and demographic representation.

3. Organization of study group meetings and financing

The aim of the lymphoid structures study group is to foster interdisciplinary exchange between immunology, stromal biology, and tissue organization. It will support the training of young scientists, promote collaborative research efforts, and enhance the integration of lymphoid tissue dynamics into immunological studies. Additionally, the group will serve as a platform to establish large research consortia capable of securing European Union funding to advance the field.

- **Regular online meetings:**

To ensure ongoing engagement, the study group will hold regular virtual meetings, which do not require dedicated funding. These meetings will be organized on a rotating basis by the study group committee and volunteer members and will provide a valuable platform for early-career and senior researchers to expand their expertise, refine research projects through peer feedback, and establish new collaborations. Our goal is to hold one online session per month featuring two speakers, following the current model of the EFIS Study Group T Cell Connect. Simon Jochems has already initiated a national lymph node working group, which provides a platform for both junior and senior scientists to present and discuss scientific data. Sessions will take various formats to accommodate different research interests, including:

- **Seminars** – Featuring presentations of ongoing work by study group members.
- **Thematic Panel Discussions** – Researchers from different groups presenting findings on a shared topic, followed by interactive Q&A sessions.
- **Virtual Workshops and Breakout Sessions** – Focused on specific research methods or emerging trends, encouraging discussion, knowledge exchange, and potential collaborations.

- **Yearly in-person meeting**

An in-person meeting will be held annually as a satellite event of the European Congress of Immunology (ECI) or one of the annual meetings of an EFIS-affiliated immunological society. The location will rotate among central European cities at institutions affiliated with study group members. EFIS funding will contribute to organizational costs, while participants will be responsible for covering their own travel and accommodation expenses.

4. Anticipated outcomes

This study group will strengthen the European research network focused on lymphoid structures in immunity. By facilitating the exchange of scientific ideas and expertise, it will lay the foundation for future research collaborations. Additionally, it will provide networking opportunities for young researchers, supporting career development through short-term scientific stays and mentorship programs.

The active exchange of knowledge will drive innovation in understanding lymphoid structures in both health and disease. As key outcomes, we aim to develop:

- **A Seminar Paper**, titled "Lymphoid Structures in Immunity: From Fundamental Insights to Translational Advances," to serve as a guideline for researchers in the field.
- **A Special Issue of Immunology Letters**, dedicated to recent advances in lymphoid structure research, compiled from contributions of study group participants.

By fostering collaboration across disciplines and experimental systems, this EFIS-IL Study Group will play a crucial role in advancing lymphoid structure immunology and its applications in immunotherapy, vaccine development, and immune regulation.