



## EFIS-IL Study Group proposal - Immune Sex Differences

### Summary

Sex and gender differences in the immune system have gained increased attention over the past years, and are fundamental for the understanding of immune variation. The main aim of our proposed Immune Sex Differences study group is to advance and promote research in the field of immune sex differences. The study group will serve as a forum for scientific discussions, exchange of expertise, and networking, and will also advocate for studying immune sex differences within the immunological societies.

### 1. Research area

Morphological and behavioral characteristics that differentiate males and females (sexual dimorphism) are prevalent in the animal kingdom. The mammalian immune system also presents sexual dimorphism. At the phenotypic level, the outcome and survival rates from infectious diseases, sepsis, trauma or injury are better in females than in males. On the other hand, women are at greater risk than men to acquire most autoimmune diseases. At the molecular level, females have stronger humoral and cellular immune response, higher proportions of activated CD4 and CD8 T-cells, higher levels of certain Immunoglobulins and more rapid rejection of allografts compared to males.

Several possible explanations are invoked to account for the immunologic disparity between sexes. First, different sex hormones have different immunosuppressive or immune stimulating effects. Second, there are differences in the dosage of specific X and Y-chromosome genes, and several chromosome X genes escape X inactivation. Third, there is increased exposure of females to stimulation during pregnancies, via the semi-allogeneic fetus. Fourth, in human, socio-cultural reasons may lead to gender differences in exposure to various types of antigens, access to health providers and other immune modulating factors. However, the molecular mechanisms responsible for sex differences of immunity remain poorly understood. As a consequence, most treatments and prevention strategies in medicine are sex- and gender-blind.

The research of immune sex differences spans over multiple immunological and non-immunological disciplines. Accurate identification of sex-biased molecular phenotypes and the mechanisms behind those phenotypes is crucial for understanding the current state and evolution of the genomic architecture and mechanisms producing sexual dimorphism in the immune system.

### 2. The core group of proponents

The field of sex differences in the immune system has grown dramatically in recent years, as evident in the two newly founded meetings focused on this field - the Biennial Meeting Sex Differences in the Immune System, which was held for the third time on 2024 (<https://www.sex-differences-immunology.com/>), and the Gordon Research Conference Sex Differences in Immunity, held for the first time in 2023

(<https://www.grc.org/sex-differences-in-immunity-conference/>). In those meetings we got to know each other, and realized the commonalities between our separate research projects, and the advantages of discussing them in early research stages. Hence, we propose to initiate a study group, whose core participants will be the European researchers of these two communities, but will increase with time.

The study group will include research groups that study the topic of sex and gender immune differences in various organisms and aspects. The study group will include PhD, postdoctoral researchers and medical professionals. Acknowledging the social and medical importance of gender, the study group will aim to recruit groups researching the aspect of gender and non-binary scenarios, e.g., the four core genotype mouse model and gender-affirming hormone therapy.



### 3. Organization of study group meetings and financing

The aims of the immune sex differences study group is to facilitate exchange of research ideas among the fields of genetics, genomics, and immunology; train young scientists as experts in sex and gender roles in the immune system function; initiate collaborative research; enhance inclusion of sex and gender in immunological research, and establish large research groups that will apply for funding by the European Union.

**I. Regular online meetings:** Such meetings do not require any fundings and will be organized on rotation basis among the study group committee and volunteers from the study group itself. The meeting will be held in different formats, such as:

- a. **Seminars:** 1-2 members of the study group will present ongoing works
- b. **Thematic Panel Discussions:** researchers from different groups present findings or perspectives on a specific topic. Each panelist can give a short presentation followed by interactive Q&A sessions to foster dialogue and exchange of ideas.
- c. **Virtual Workshops or Breakout Sessions:** focused on specific research methods or emerging trends in the study of immune sex differences. Participants can choose sessions based on their interests and actively engage in discussions, share insights, and brainstorm potential collaborations.

The meetings will provide the opportunity for both advanced as well as PhD and postdoctoral researchers to extend their knowledge on the topic, exchange ideas, receive crucial feedback on their research and provide the opportunity for collaborations.

### II. Yearly in-person meeting

The in-person meeting for the study group will take place as a satellite meeting of the ECI, in one of the immunological societies annual meetings, such as the DGfI annual meeting, which are held at a central European city at an institute affiliated with one of the study group members. Financing of the meetings will be covered by a contribution from the EFIS and will require participants to cover their own expenses.

### 5. Anticipated outcomes

We anticipate that our study group will strengthen the European network on sex and gender aspects of immunity. This study group will become a platform for scientific ideas and expertise exchange, will serve as the basis for future research cooperations, provide networking opportunities for young researchers that will secure opportunities for career development, such as short-term scientific stays. The active exchange of ideas is foreseen to provide the tools for an increased and sustainable inclusion of sex and gender topics in immunological research. This will be in the form of a White paper "Sex and gender aware research: a guideline for immunologists" and a Special Issue of *Immunology Letters* covering the topic of immune sex differences.

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