

Metabolic and Immune Regulation of the Gonadal Niche: Decoding Germline-Soma Crosstalk in Fertility

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Infertility affects approximately one in six people worldwide. While research often focuses on germline-intrinsic factors, germ cell development occurs within a specialized gonadal somatic environment that plays an instructive role during sexual differentiation and gametogenesis. Furthermore, reproduction is under strict hormonal regulation and is tightly linked to the overall physiology and metabolic state of the organism.

A significant challenge in reproductive medicine is understanding how extrinsic factors—such as nutrition, immune signalling, and systemic ageing—impact the germline. Traditional models often overlook this "germline-soma crosstalk," leaving a gap in our ability to treat idiopathic infertility or mitigate the effects of lifestyle on reproductive health.

The Project

The primary goal of this PhD is to investigate the role of the gonadal niche and systemic physiology in maintaining reproductive fitness. The project combines genetic approaches, nutritional interventions, spatial transcriptomics, in vivo mouse models as well as in vitro generated 3D germline-soma organoid models to dissect how inter-tissue communication influences the germ line.

The student will employ a transdisciplinary approach, integrating spatial transcriptomics, advanced imaging, and functional assays to address two key pillars:

1. **Metabolic Signalling & Dietary Impact:** We will test the effects of dietary interventions, such as high-fat diets and fasting, on embryonic (in utero) germline development as well as on adult germline function
2. **Immune-germline interactions:** We will investigate the role of immune cells in the gonadal niche and how their dysfunction contributes to "inflammageing" and age-related fertility decline.

The student will join the **LMS Team Science initiative** "Reproductive health and fertility: aging, sex, and the environment," a highly collaborative environment involving three postdoctoral researchers and two additional PhD students. This project bridges the expertise in epigenetic reprogramming and germline development (Hajkova), immunometabolism (Gallage), and computational genomics (Vaquerizas).

We seek a highly motivated student with a background and keen interest in **reproductive biology, epigenetics** or **immunology** and a strong interest in functional studies of the gonadal niche. You will receive world-class training in imaging, transcriptomics, and 3D organoid assays. The long-term vision of the project is to generate lifestyle guidelines and therapeutic strategies to promote reproductive health.