# PhD project description (to be shown on the URI-website)

## ONE page

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| **Scientific Area** | Hematopoiesis and development and Immune-related diseases |
| **Two project titles** | A) Understanding T cell population homeostasis<br>B) How to achieve tolerance to auto- and allo antigens while maintaining anti-pathogen immunity |
| **Host country** | University of Basel, Basel, Switzerland |
| **Supervisor, institution** | Jean Pieters |
| **Co-Supervisor, institution** | A) N. N.<br>B) N. N. |
| **Mentor, institution** | A) and B) N. N. |
| **Secondment institution** | A) and B) xxx |

**Short description of the supervisor's lab with introduction to the topic**

Maintenance of appropriate and clonally diverse T cell numbers in peripheral lymphoid organs is fundamental to the proper functioning of the immune system, yet the underlying mechanisms remain undefined. Our laboratory is investigating the role played by members of the coronin protein family in the establishment and regulation of the peripheral T cell population. Coronin proteins are highly conserved, widely expressed in the eukaryotic kingdom, and deletion or mutation of coronin 1, a coronin abundantly expressed in T cells results in peripheral T cell paucity in both mice and men.

**Topic description, including techniques to be used**

**Project A): Understanding T cell population homeostasis**

Peripheral T cells are being maintained long-term (several months in mice and up to decades in humans), but the mechanisms underlying such longevity remain unclear. Naive T cell survival in peripheral lymphoid organs has been proposed to be regulated through pMHC:TCR and IL-7 signaling, but the essential roles for these pathways in thymic output and T cell proliferation has made it virtually impossible to assign a specific role for these pathways in T cell survival. We recently found that the WD repeat-containing protein coronin 1 is dispensable for thymic selection and output and regulates naïve T cell survival in a manner that is independent of TCR and IL-7 signaling. The purpose of this project is to dissect the molecular mechanisms underlying peripheral T cell survival.

**Project B): How to achieve tolerance to auto- and allo antigens while maintaining anti-pathogen immunity**

Defining pathways that differentially regulate graft-reactive versus anti-microbial T cell responses could facilitate more precise manipulation of immune responses in the context of organ and tissue transplantation. We have identified a coronin-1-PDE4-cAMP axis that, when perturbed, results in the induction of autoimmune and transplantation tolerance while maintaining anti-microbial immunity. The goal of this project will be to analyze the mechanisms underlying coronin 1-dependent regulatory axis in T cells important for auto and allo immunity.

**Recommended applicant's training (technical expertise and knowledge)**

The candidate should have a strong background in biochemistry, cell biology and molecular biology and ideally be familiar with both in vitro and in vivo techniques; Furthermore, the candidate should exhibit team spirit, be highly motivated, self-driven and creative.

**Maximum two relevant publications**

Pieters, J. (2013). On guard: coronin proteins in innate and adaptive immunity. *Nat. Rev. Immunol.* 13: 510-18.

Jayachandran et al., (2019). Disruption of coronin 1 signaling in T cells promotes allograft tolerance while maintaining anti-pathogen immunity. *Immunity* 50:152-165.

The EURIdoc programme has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement number 101034170.

# Ethics description

| Name of the supervisor |
|---|
| **Jean Pieters** |
| **PhD project title** |
| A) Understanding T cell population homeostasis<br>B) How to achieve tolerance to auto- and allo antigens while maintaining anti-pathogen immunity |
| |
| Please fill out **Ethics self-assessment.** If you answer YES to any of the questions, please provide additional information about how these issues will be addressed in your research by providing an ethics approval with your proposal.<br><br>You may consult the Horizon 2020 Programme Guidance "How to complete your ethics self-assessment" for further information on how to address ethical issues in your research proposal. |
| **Note**: Please update ethics approvals throughout the programme by informing EURIdoc ethics officer Marta Rizzi (marta.rizzi@uniklinik-freiburg.de) |

**Please send your project description together with the ethics self-assessment and ethics approvals (if you already have them) to Angelika Reichinger:**

**angelika.reichinger@bioss.uni-freiburg.de**

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**Ethics self-assessment**

Please complete the ethical assessment below by indicating yes or no in the corresponding box.

| | |
|---|---|
| **1. Human Embryos/Foetus** | |
| Does your research involve Human Embryonic Stem Cells (hESCs)? | YES ☐ / NO ☒ |
| Does your research involve the use of human embryos? | YES ☐ / NO ☒ |
| Does your research involve the use of human foetal tissues / cells? | YES ☐ / NO ☒ |
| **2. Humans** | |
| Does your research involve human participants? | YES ☐ / NO ☒ |
| Does your research involve physical interventions on the study participants? | YES ☐ / NO ☒ |
| **3. Human Cells /Tissues** | |
| Does your research involve human cells or tissues (other than from Human Embryos/ Foetuses, i.e. section 1)? | YES ☒ / NO ☐ |
| **4. Personal Data** | |
| Does your research involve personal data collection and/or processing? | YES ☐ / NO ☒ |
| Does your research involve further processing of previously collected personal data (secondary use)? | YES ☐ / NO ☒ |
| **5. Animals** | |
| Does your research involve animals? | YES ☒ / NO ☐ |
| **6. Third Countries** | |
| In case non-EU countries are involved, do the research related activities undertaken in these countries raise potential ethics issues? | YES ☐ / NO ☒ |
| Do you plan to use local resources (e.g. animal and/or human tissue samples, genetic material, live animals, human remains, materials of historical value, endangered fauna or flora samples, etc.)? | YES ☐ / NO ☒ |
| Do you plan to import any material - including personal data - from non-EU countries into the EU? | YES ☐ / NO ☒ |
| Do you plan to export any material - including personal data - from the EU to non-EU countries? | YES ☐ / NO ☒ |

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| In case your research involves low and/or lower middle income countries, are any benefits-sharing actions planned?<br>List available here: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519 | YES ☐ / NO ☐ |
| Could the situation in the country put the individuals taking part in the research at risk? | YES ☐ / NO ☒ |
| 7**. Environment & Health and Safety** | |
| Does your research involve the use of elements that may cause harm to the Environment, to animals or plants? | YES ☐ / NO ☒ |
| Does your research deal with endangered fauna and/or flora and/or protected areas? | YES ☐ / NO ☒ |
| Does your research involve the use of elements that may cause harm to humans, including research staff? | YES ☐ / NO ☒ |
| **8. Dual Use** | |
| Does the research have potential for military applications? | YES ☐ / NO ☒ |
| **10. Misuse** | |
| Does this research have the potential for malevolent/criminal/terrorist abuse? | YES ☐ / NO ☒ |
| **11. Other Ethics Issues** | |
| Are there any other ethics issues that should be taken into consideration?<br>If yes, please specify in your ethics statement (see below) | YES ☐ / NO ☒ |
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