2018 Helmholtz – OCPC – Program
for the involvement of postdocs in bilateral collaboration projects

PART A

Title of the project:

"Analyzing the Functional Cooperation of Nufip2 and Roquin in the Immune System"

Helmholtz Centre and Institute:
Helmholtz Zentrum München, Research Unit Molecular Immune Regulation

Project leader:
Prof. Dr. Vigo Heissmeyer
Helmholtz Zentrum München, Research Unit Molecular Immune Regulation
Marchioninistr. 25, 81377 München
Web-address:
https://www.helmholtz-muenchen.de/amir/index.html

Description of the project (max. 1 page)**:**

Scientific background

The Roquin family proteins serve critical functions in the prevention of autoimmunity. These factors keep naive T cells in their quiescent state and inhibit the differentiation of activated T helper cells into pro-inflammatory Th17, Th1 and Tfh subsets. On the molecular level, the cytoplasmic Roquin-1 and Roquin-2 proteins inhibit gene expression by binding to the 3′-UTR of target mRNAs at specific stem-loop structures and by inducing mRNA decay. Our most recent work has demonstrated that Roquin-dependent recognition of mRNAs is supported by the Nufip2 protein, which we identified in a targeted siRNA screen for cofactors of Roquin-dependent ICOS regulation. Nufip2 was also shown to interact with the FMRP protein, but its function remained unclear. We demonstrated that Nufip2 forms a ternary complex with Roquin and RNA, enhances the affinity of the complex for the stem-loop containing response elements of the 3′-UTRs of ICOS and Ox40 and promotes Roquin-dependent mRNA decay. These findings involve Nufip2 as a novel cofactor of Roquin that may either be required for the efficient interaction of Roquin with all or with a subset of targets.

Scientific questions

In the proposed project we will ask these specific questions: What is the function of Nufip2 in immune cells? Which mRNAs does Nufip2 bind in T cells? Does Nufip2 regulate its target set in cooperation with Roquin or also with other RNA binding proteins? What is the phenotype of mice with Nufip2 deficiency in T cells or in the hematopoietic system and how can we molecularly explain these phenotypes?

Work packages

1. Generating a conditional Nufip2 knockout by CRISPR Cas9-mediated gene editing.
We will employ a homology-directed repair strategy to establish a conditionally targeted Nufip2 allele in the mouse germline.

2. Determining the relative expression levels of Nufip2 in immune cells.
Within a knockout/wild-type comparison, we will determine the relative expression levels of Nufip2 in different cells of the hematopoietic system.

3. Analyzing cooperative Nufip2/RNA binding sites in the transcriptome of T cells.
Using the PAR-CLIP technology we will determine Nufip2 specific binding sites in the transcriptome of T cells by comparing WT to Roquin-1/Roquin-2 DKO or Fmr1-/- T cells.

4. Phenotyping of Nufip2-deficient mice.
We will determine phenotypes that arise from Nufip2 deletion in the hematopoietic system or in peripheral T cells.

5. Elucidating the molecular mechanisms of Nufip2 functions.
We will identify the Nufip2-regulated target genes and determine their regulation by Nufip2, Roquin or FMRP.

Description of existing or sought Chinese collaboration partner institute (max. half page)**:**

Our research unit is currently building up collaborations with several research groups in China. I have close interactions with researchers in Xiamen University, Xiamen and Tongji Medical College, Huazhong University of Science and Technology, Wuhan working on post-transcriptional gene regulation in T cells. During the 6th Chinese-German Symposium on Immunology in Hangzhou, where I have been invited to, I interacted with the community of Chinese immunologists and I would be happy to receive a postdoc from this network.

Required qualification of the post-doc:

We are searching for a highly-motivated postdoctoral research fellow with enthusiasm for molecular immunology. She or he should have

- a PhD in biology, biochemistry or molecular medicine
- experience in immunology, biochemistry and molecular biology
- interest in studying immune responses in mice
- the ability to work independently in an international team
- good skills in English (speaking and writing)

PART B

Documents to be provided by the post-doc, necessary for an application to OCPC via a postdoc-station:

- Detailed description of the interest in joining the project (motivation letter)
- Curriculum vitae, copies of degrees
- List of publications
- 2 letters of recommendation
- Proof of command of English language

PART C

Additional requirements to be fulfilled by the post-doc:

- Max. age of 35 years
- PhD degree not older than 5 years
- Very good command of the English language
- Strong ability to work independently and in a team