PhD project No. 10, Prof. Häcker

Scientific Area	Innate and adaptive immunity
Two project titles	A) Regulation of inflammasomes by post-translational modifications. B) RIP kinase regulated metabolism and its impact on inflammation.
Host country	Germany
Supervisor, institution	Prof. Georg Häcker Medical Center - University of Freiburg, Germany University of Freiburg, Germany
Co-Supervisor, institution	A) Romeo Ricci – IGBMC Strasbourg B) Romeo Ricci – IGBMC Strasbourg
Mentor, institution	A) to be determined later B) to be determined later
Secondment institution	A) and B) University of Strasbourg, France

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

The Häcker lab has had long running focus on apoptosis and inflammation both at the basic level, but also how it is regulated during infection. There has been a particular focus on mitochondrial apoptosis and more recently, how mitochondria can regulate immune signalling at various levels including inflammasome activation and other inflammatory pathways.

Topic description, including techniques to be used

Project A)

Inflammasomes are important regulators of inflammation and also cell death and they are tightly regulated by various post translational modifications including ubiquitylation. During activation, certain cytokines can modulate the ubiquitylation of various inflammasome components. We aim to determine the nature of post-translational modification events on inflammasome proteins and their regulation to understand how this influences the outcome of inflammatory signalling.

Techniques: Cell culture, cloning, microscopy, Western blotting, mass spectrometry.

Project B)

RIP kinases such as RIPK3 are integral to activation of necroptosis, but there is evidence that they are also involved in regulating mitochondrial metabolism and inflammasome activation. Mitochondrial metabolism is central to triggering inflammatory behaviour in cells such as macrophages as well as other important processes such as Reactive Oxygen Species production that can have wide-ranging effects. Exactly how RIP kinases can regulate mitochondrial metabolism and the downstream effects of this will be the focus of this study, with particular emphasis on ROS generation, inflammasome signalling and metabolic regulation.

Techniques: Cell culture, flow cytometry, cloning, western blotting, CRISPR-Cas9 gene knockouts, metabolite analysis, mitochondrial activity assay (seahorse).

Recommended applicant's training (technical expertise and knowledge)

Techniques: general lab techniques including molecular cloning, Western blotting, cell culture, flow cytometry.

Knowledge: basic knowledge of innate immune signalling pathways, inflammation, signal transduction, mitochondrial homeostasis.

Maximum two relevant publications

Vince JE et.al., 2012, Immunity.
Brokatzky D. etal., 2019, EMBO J.

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

1. Humans	
This research involves human participants.	YES ☐ / NO ☒
This research involves physical interventions on the study participants.	YES ☐ / NO ☒
2. Human Cells /Tissues	
This research involves human cells or tissues, such as blood.	YES ☐ / NO ☒
3. Personal Data	
This research involves personal data collection and/or processing.	YES ☐ / NO ☒
This research involves further processing of previously collected personal data (secondary use).	YES ☐ / NO ☒
4. Animals	
This research involves animals, such as mice.	YES ☐ / NO ☒

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