Project 9.3. RNA-Protein Interactions in Human Health and Disease (NCN/DIOSUCRI)

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Laboratory: Laboratory of RNA-Protein Interactions

www: https://www.iimcb.gov.pl/en/press-office/news/highlights/1073-gracjan-michlewski-will-establish-a-dioscuri-centre-of-excellence-at-the-iimcb

Background:

RNA-binding proteins (RBPs) are key molecules that control gene expression through RNA-protein interactions. Consequently, they contribute to cellular homeostasis, normal development and majority of human diseases. Importantly, new RBPs are being discovered by high-throughput proteomics, but we still have a limited understanding of their function.

RNA viruses have caused several epidemics in the 21st century. Taking influenza A virus (IAV) infection as an exemplar, it kills 250,000 to 500,000 people annually and generates a significant global socioeconomic burden. Importantly the emergence of COVID-19 pandemic caused by an RNA virus SARS-CoV-2 continue to have catastrophic consequences on public health and world economy. Thus, a detailed molecular understanding of host-virus interactions is imperative in order to know how best to inactivate these viruses and prevent major disruptions in the future.

We have recently discovered and started characterising novel RNA binding protein – E3 ubiquitin ligase TRIM25 (Choudhury et al. 2014; Choudhury et al. 2017). TRIM25 belongs to a large family of tripartite motif-containing proteins (more than 80), most of which have E3 ubiquitin ligase activity. Many of TIRIMs are positive or negative regulators of innate immune response pathways. Importantly, TRIM25 is emerging as a key factor in the innate immune response to RNA viruses (including IAV, CoV, dengue virus and many others). Despite the essential involvement of TRIM25 in viral RNA-induced innate immunity, its RNA-binding functions are still poorly understood.

Aim:

With this project, we aim to take advantage of an assembled multi-disciplinary team to uncover the roles of the novel RNA-protein interactions in the antiviral response to selected RNA virus infections. We hypothesise that TRIM25 binds directly to viral RNAs to restrict virus propagation. We also hypothesise that other members from TRIM family bind RNA. Finally, we hypothesise that specific host RBPs bind to virus derived RNAs and inhibit or augment innate immune response. In summary, this project has the potential to make crucial contributions to understanding the innate immune response to RNA viruses and provide a platform for the development of novel, RNA-based antiviral therapeutics.

Requirements:

- MSc degree in biology, biochemistry or related field
- solid knowledge of the principles of cell and molecular biology, virology
or biochemistry
- hands-on experience in laboratory work and is familiar with basic cell and molecular biology techniques
- prior experience in virus handling and analysis, cell culture, mass spectrometry

or bioinformatics will be an advantage

- proficiency in written and spoken English
- excellent interpersonal skills, initiative and ability to work independently and in a high-performance team