PhD Studentship in Molecular Virology, University of Zurich

Laboratory of Prof. Dr. Benjamin G. Hale (hale.ben@virology.uzh.ch)

Human Innate Immune Defences Against Virus Infection: Interferon Responses

The Hale laboratory is focused on understanding, at the molecular level, how human cells defend themselves against infection, particularly against respiratory viruses such as influenza viruses and SARS-CoV-2. We are interested in mechanisms by which a cell recognises that it is infected by a pathogen and uses the interferon cytokine system to trigger antiviral gene expression and block infection. We seek to exploit knowledge in these areas to identify and understand host factors that contribute to infectious disease susceptibility.

The human interferon (IFN) system constitutes a major innate immune barrier to zoonotic virus transmission, and is essential to limit the severity of new pandemic viruses. At the molecular level, host-encoded sensors of 'non-self' **viral RNA (e.g. RIG-I) signal through a MAVS-TBK1-IRF3 axis to induce secretion of IFNs, which act as cytokines to activate specific receptor-mediated signalling events canonically involving phosphorylation-dependent JAK/STAT activation, nuclear translocation, and transcription of antiviral interferon-stimulated genes.**

Recently, our group has sought to dissect the molecular details of the human antiviral interferon system further. We described that influenza virus infection triggers a post-translational SUMO switch in a host genomic repressor molecule, TRIM28, which leads to de-repression of endogenous retroviral RNAs (Domingues et al, Cell Reports, 2015; Schmidt et al, PNAS, 2019). Surprisingly, these 'self' RNAs are sensed by the **cell as foreign, and activate potent antiviral interferon responses. We are now seeking to understand: (i) the molecular mechanisms by which this TRIM28-SUMO switch is triggered during infection; (ii) precisely how these endogenous retroviral RNA sequences are recognised as foreign; (iii) whether this pathway is activated by other viruses; and (iv) whether some viruses have evolved strategies to evade or block this newly described antiviral pathway. A PhD project would be available in this area to tackle some of these, or related, questions.**

The ideal student should have recently completed (or be about to complete) a Masters' **degree in a relevant topic, have a strong theoretical or experimental background in molecular biology, be highly organised with excellent presentation skills, and be motivated to join a friendly, international research team consisting of the Principal Investigator, 1-2 postdoctoral researchers, 4-5 PhD students and a technician. Prior knowledge in virology, though desirable, is not essential as extensive training in modern molecular virology and cell biology will be provided. The group is also experienced in successfully utilising technologies such as protein biochemistry, interaction and post-translational modification proteomics, transcriptomics, fluorescence microscopy, CRISPR/Cas9-mediated genome editing and screening, medium-high throughput screening, and Next-Generation Sequencing. The PhD student can develop skills in these areas as required.**

The Hale laboratory is located within the Institute of Medical Virology at the University of Zurich (Irchel Campus), and has excellent close working relationships with neighbouring groups interested in virus entry (Stertz), antibody responses (Trkola) and viral metagenomics (Huber), as well as clinical colleagues in Infectious Diseases based at the University Hospital Zurich. The Institute's infrastructure, which includes **state-of-the-art research equipment and modern Biosafety Level 2 & 3 facilities, is outstanding. Some recent work from the group on influenza viruses, SARS-CoV-2, and interferon signalling includes:**

https://www.biorxiv.org/content/10.1101/2021.02.04.429732v1
https://www.biorxiv.org/content/10.1101/2020.10.22.350207v1
https://mbio.asm.org/content/11/5/e01928-20
https://msphere.asm.org/content/5/4/e00423-20
https://www.pnas.org/content/116/35/17399.short
https://www.nature.com/articles/s41467-019-11388-2

More details about the group, and a link to the full list of group publications, can be found on the group website: http://www.virology.uzh.ch/research/ghale.html

Please send letters of motivation and CVs to: hale.ben@virology.uzh.ch