CDCS
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IN NATURAL SCIENCES

OPENING SYMPOSIUM 2022

Universität Hamburg
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DESY.

TUHH

Contribution ID: **76** Type: **Poster**

Bottom-up proteomics to study pathogenic RNA(+) viruses

Viral infections by RNA viruses emerged in the past decade as a global health challenge, given their enormous epidemic potential and their severe pathological outcomes. Despite a relatively high genetic similarity and overall conserved replication strategies, these viruses evolved finely tuned and divergent mechanisms of host exploitation, resulting in extraordinarily distinct tropisms and pathogeneses. To establish efficient replication and transmission, viruses need "entry points", in order to access specific cellular functions or evade dedicated defense mechanisms. This is often accomplished through direct binding of specific cellular proteins (i.e. protein-protein interactions), perturbation of the proteostasis of a subset of cellular proteins (i.e. turnover rate/stability) or modulation of the activity of entire cellular pathways through chemical modification of key signalling components (i.e. post-translational modifications).
Our group uses cutting-edge mass-spectrometry-based discovery tools in combination with molecular and biochemical approaches to systematically identify how pathogenic RNA(+) viruses (i.e. DENV, ZIKV, WNV, SARS-CoV-2) perturb protein and proteome homeostasis at all levels. In this talk, I will describe specific applications in which we have used these approaches to understand the complex regulatory processes perturbed by pathogenic RNA+ viruses *in vitro* and *in vivo*. The ultimate aim of these efforts is to shed light on the molecular mechanisms of virus-host adaptation, thereby exposing, categorizing and characterizing novel molecular targets.

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Session Classification: Poster session with buffet

Track Classification: CDL3 (Systems Biology)