LS24-059 - Deconstructing and Reconstructing Anelloviruses

Zusammenfassung

Anelloviruses are a family of small, single-stranded DNA viruses that infect vertebrates. Most humans acquire them after birth, and remain infected life-long with a variety of viral strains. Anelloviruses are not known to cause any pathology in humans, making them commensal members of our virome. They elicit only a minimal antibody response, and are controlled by cellular immunity. Viral titers spike upon immunosuppression.

The causes and functional consequences of the viral sequence diversity and how it relates to the host's immune state are active areas of research. The cell biology of anelloviruses is almost completely unexplored: The mechanisms of entry, replication and egress, and most molecular aspects of interactions with host factors are poorly understood. A major challenge is the lack of laboratory strains and experimental infection models.

To answer these open questions, we will combine clinical virology and synthetic biology: We will sequence the anellomes in our expansive biobank of organ transplant recipients. In parallel, we will develop a suite of assays that each reconstruct an individual aspect of viral cell biology. First, will comprehensively map interactions between viral factors and host proteins and conduct pseudovirus and replicon screens to determine functional dependencies. Next, we aim to establish the production of recombinant replication-competent viruses, opening up many avenues of investigation. Ultimately, we want to deploy our synthetic biology pipelines to functionally characterize many viral sequences, spanning the spectrum of diversity found in humans. Our results will traverse biological scales by connecting the properties of individual viral molecules and their behavior in a cell, with the immunological state and the virome of the patient from which the sequences were derived.

Our proposal has transformative potential to open up the field of molecular anellovirology and inform translational applications of engineered anelloviruses.

Wissenschaftliche Disziplinen:
Virology (60%) | Cell biology (20%) | Systems biology (20%)

Keywords:
VirologyMicrobiologyAnellovirusesTorque teno virusvirus/host interactionssystems biologysynthetic biologyCRISPR screeningviral repliconspseudotypingprotein interaction mapping

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Status: Vertrag in Vorbereitung

Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter
https://wwtf.at/funding/programmes/ls/LS24-059/