

Antivirals for preemptive therapy of BK polyomavirus infection in transplant recipients and interference with in-host virus evolution - ANTIPOLE

Initiative: Innovative Ansätze in der antiviralen Wirkstoffentwicklung

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Reactivation of latent viral infection poses a significant threat to immunosuppressed patients in transplantation medicine. BK polyomavirus (BKPyV) is an underexplored virus responsible for nephropathy or hemorrhagic cystitis in a significant number of kidney or allogeneic hematopoietic stem cell transplant recipients. Currently, there is no vaccine, and drugs are urgently needed for preemptive treatment to prevent organ damage. This interdisciplinary project addresses the major challenges that have hindered drug development against BKPyV. The project team synergistically combines specific expertise in small DNA virus immuno- and cell biology, cutting-edge genomics and translational drug discovery to identify drug candidates from unique compound libraries disrupting viral key processes. The team has developed a novel BKPyV replication assay for drug screening and will use complex human 3D culture models for preclinical validation, such as BKPyV-infected renal proximal tubule organoids, organotypic 3D cultures integrating immune cells and organ-on-a-chip models. To gain molecular insight into drug resistance development and develop counter strategies, the researchers will use innovative BKPyV specific next generation sequencing-based technologies to monitor viral genetic adaptation and in-host evolution. With these combined approaches the team aims to advance both, a straightforward translational approach to drug repurposing in transplant patients, and the development of entirely new drug classes against BKPyV.

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