Pan-genotypic neutralizing human monoclonal antibodies with enhanced effector function as therapeutic option for Hepatitis E virus infection

Initiative: Innovative Ansätze in der antiviralen Wirkstoffentwicklung

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The hepatitis E virus (HEV) is a small, positive-stranded RNA virus, which consists mainly of 4 genotypes pathogenic for humans belonging to the genus of Orthohepevirus A. It is the leading cause of acute virus-associated hepatitis in Germany and worldwide. Genotypes 3 and 4 are zoonotic infections with their main reservoir in swine resulting in high infection rates particularly in Germany of up to 420.000/year. Moreover, in addition to acute infections these genotypes can cause chronic infections in immunocompromised hosts contributing to high morbidity and mortality. Recently, another HEV strain from rats has shown it's potential to cross the species barrier and was detected in patients after organ transplantation. The importance of this potential medical threat for immunocompromised individuals is not fully understood. Importantly, no approved treatment for HEV is available. This project aims at identifying and evaluating pan-genotypic monoclonal antibodies (mAbs) targeting the HEV capsid as therapeutic option. Utilizing recombinant soluble capsid proteins, the researchers will isolate HEV specific memory B-cells of convalescent patients. After Next Generation Sequencing of the corresponding B-cell receptors, antibody fragments will be synthesized and tested in vitro for their ability to bind and neutralize HEV viruses from different genotypes. The best candidates will be generated as full antibodies and their Fc-part optimized in order to enhance NK-cell mediated effector function. Finally, the team will provide strategies to evaluate this treatment option in a humanized animal model and to develop the product in a clinical program in collaboration with industrial partner.

Projektbeteiligte

Dr. Patrick Behrendt
TWINCORE
Zentrum für Experimentelle und
Klinische Infektionsforschung GmbH
Experimentelle Virologie
Translationale Virologie
Hannover

Prof. Dr. Heiner Wedemeyer
Medizinische Hochschule Hannover
Zentrum Innere Medizin
Klinik für Gastroenterologie, Hepatologie und
Endokrinologie
Hannover

Prof. Dr. Thomas Krey
Universität zu Lübeck
Institut für Biochemie
Lübeck