Ming-Han Tsai

Dr.sc.hum.

Identification and phenotypic characterization of a highly pathogenic Epstein-Barr virus strain

Promotionsfach: DKFZ (Deutsches Krebsforschungszentrum)

Doktorvater: Prof. Dr. med. Dr. rer. nat Henri-Jacques Delecluse

The Epstein-Barr virus (EBV) is found in a variety of tumors whose incidence greatly varies around the world. Many epidemiological studies showed that host genetics and environmental factors might contribute to this phenomenon; however, whether particular strains of EBV play a role in tumor progression is poorly understood. In this study, we compared M81 EBV strain, which was isolated from a nasopharyngeal carcinoma (NPC) patient in a high incidence region, to B95-8 strain, which is common in western countries with an extremely low incidence of NPC. The genetic analysis of M81 shows its remarkable similarity to other EBV isolates found in NPC patients but is divergent from all other known strains. M81 exhibited a reversed tropism relative to B95-8 with a reduced ability to infect B cells and a high propensity to infect epithelial cells, which is in agreement with its isolation from carcinomas. Importantly, M81 elicited spontaneously lytic replication in B cells in vitro and in vivo and epithelial cells in vitro at unusually high levels, in conformity with the elevated viral replication commonly observed in NPC patients. On a molecular level, the composition of virions and polymorphisms within viral proteins could partially explain epitheliotropism and spontaneous lytic replication observed in M81 in this study. In summary, our results suggest that M81 and its closely related isolates from NPC patients should be considered as a distinct EBV subtype with enhanced pathogenic potential.