

Pierre-Yves Bochud – abstract

Immunogenetics of infectious diseases

Immunogenetics of infections due to human herpes simplex viruses

Herpes simplex encephalitis (HSE) is a rare, sporadic form of encephalitis caused by HSV-1 (occasionally HSV-2) which occurs in 2-4 individuals per million per year and has a mortality rate of >70% if untreated. It mainly occurs in children (e.g. as a result of primo-infection) and adults >50 years old (e.g. as a result of reactivation).

The reasons why HSV-1 causes such a devastating disease in a very limited number of individuals have long been unknown. In fact, susceptibility to HSE in children results from mutations in genes belonging to the “Toll-like receptor 3 (TLR3) /interferon (IFN) axis”, an immune pathway involved in viral detection, production of type-1 and type-3 interferons, and subsequent interferon-stimulated genes (ISGs) activation. However, such variants explain only a subset of HSE among children and limited data support the role of such variants in adults HSE.

The goal of this study is to extend our knowledge on genetic variants associated with HSE and to determine to which extent the same genetic variants (or variants in the same immune pathways) can explain the disease in both children and adults.

It includes the identification, by whole exome sequencing, of rare genetic variants associated with HSE in children and/or adults and their functional characterization by using a combination of in vitro and ex- vivo experiments.