

– Presentation sheet :

UMR CNRS 6023 Laboratoire Microorganismes : Génome et Environnement, Université Clermont Auvergne (Didier DEBROAS)

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Crossing the human blood-brain barrier by neurotropic enteroviruses: investigation of possible mechanisms with in vitro cell co-culture models

Enteroviruses display a large genetic diversity and are the main cause of acute meningitis in children and adults. Specific enterovirus types are also associated with infrequent cases of encephalitis and acute flaccid paralysis. The initial transmission route is through the oral mucosa. During a short viremia, the virus is disseminated through the blood to different organs and tissues. The nervous system is infected through a nervous route or by crossing the blood-brain-barrier.

The main aim of the project is to implement in the laboratory an existing model of cell co-culture to mimic the human blood-brain-barrier in vitro. In this model, the endothelial cells were differentiated from pluripotent stem cells. After validation, the model will be used to test different hypotheses related to crossing of enteroviruses through the endothelial barrier. In this project, we will specifically investigate three possible crossing mechanisms by comparing different infectious strains of enterovirus type A71.

Volle et al (2015). Differential permissivity of human cerebrovascular endothelial cells to enterovirus infection and specificities of enterovirus 71 in crossing an *in vitro* model of human blood brain barrier. *J Gen Virol.* 96: 1682-95.

Lafolie et al (2018). Assessment of blood enterovirus PCR testing in paediatric populations with fever without source, sepsis-like disease, or suspected meningitis: a prospective, multicentre, observational cohort study. *Lancet Infect Dis.* 18:1385-96.