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Zoonotic flaviviruses, including tick-borne encephalitis virus (TBEV), represent an increasing threat to European countries. Patients infected with strains of the European TBEV subtype show a wide spectrum of disease manifestations, ranging from flu-like symptoms to meningitis and severe encephalitis, which in 35% of the cases translates in long-term morbidity. Despite intensive efforts, the exact pathological mechanisms driving acute neurological manifestations remain poorly understood.

We postulate that the extent of the damage and the long-term sequelae of neurotropic flavivirus infections are influenced by their ability to invade the central nervous system, to efficiently replicate in various cell types, and to induce high inflammation and damages. This hypothesis will be tested by applying complementary ex vivo and in vivo approaches with the aim to compare different TBEV strains in terms of: neuro-invasiveness, neurovirulence, and neuronal pathomechanisms. Furthermore, different antiviral candidates will be tested for their ability to improve the outcome of the disease.

CONCLUSION

Cerebellar and hippocampal organotypic cultures, together with tissue clearing staining, are a well-suited model to investigate cellular tropism of flaviviral infection. Both viruses (LGTV and TBEV) are able to proliferate in different regions of the brain: in the cerebellum the proliferation take place mainly in the Purkinje cells and probably also in the granule cells, while in the hippocampus the cells infected by the two viruses have still to be identified. The quantification via TCID50 is only partially in line with the immunohistochemistry results and needs to be improved.