VICTORIE

Virulence and pathogenesis

COOPERATION

COORDINATED BY THE VIROSCIENCE LAB OF ErasmusMC

Virulence and pathogenesis

VECTORIE addresses the need for understanding how the different WNV lineages circulating in Europe differ in their capacity to cause severe disease and for understanding the pathways involved in WNV and CHIKV neuroinvasive disease. These studies will lead to novel knowledge that will enable us to improve our ability to monitor spread of these infections in Europe. In addition, they will lead to diagnostic and prognostic tools as well as novel strategies to treat infected patients.

Tasks for virulence and pathogenesis

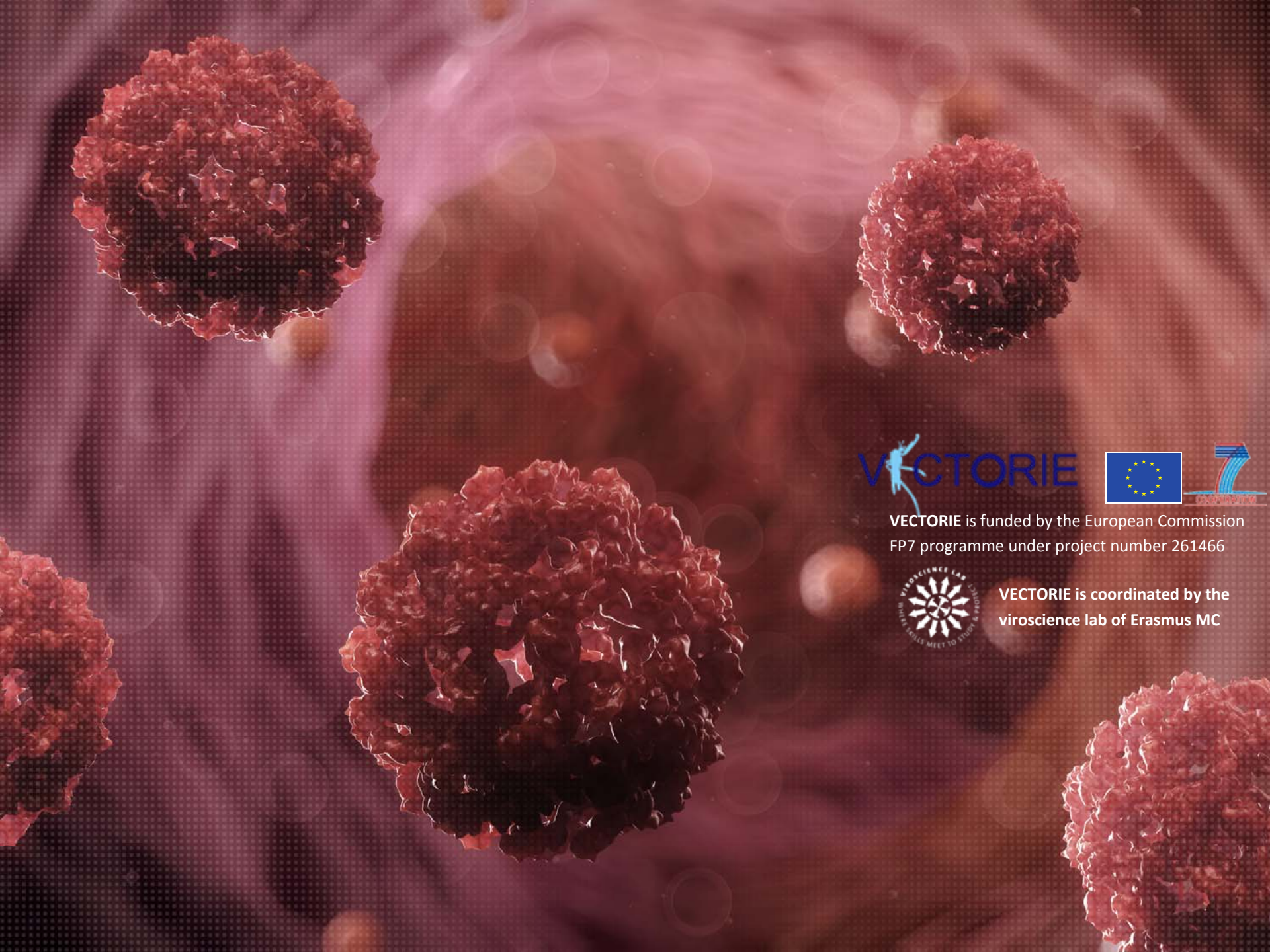
Determine markers of virulence and the pathogenicity of the four WNV lineages in mice

Four different lineages of WNV circulate in Europe, based on differences at the genome level. These four lineages are assumed to be associated with differences in virulence. The WNV lineage 1 and 2 strains, which have emerged in Italy and Hungary respectively are neuroinvasive and neurovirulent and therefore pose a significant threat to humans that may spread throughout Europe with so far unpredictable consequences. It is therefore important to understand how the different WNV lineages circulating in Europe differ in their capacity to cause severe infections as this will contribute to the development of an effective early warning system for Europe, for instance by stratifying areas into risk categories. In addition, the strains that are relevant for Europe will be defined and targeted for subsequent vaccine development. Furthermore, in order to interpret findings of a WNV surveillance program and to be able to take effective measures in case of a WNV outbreak, it is important to be able to predict the spreading and disease causing capacity of the strain involved in the outbreak. In this study virulence factors associated with increased transmission and morbidity of different WNV strains will be identified, at the molecular level, which can eventually assist in the development of virulence assays.

Virulence and pathogenesis

Study the pathways involved in WNV and CHIKV neuroinvasive disease

The emergence of CHIKV in previously unaffected areas and the increase in incidence of central nervous system involvement in a considerable proportion of symptomatic cases pleads for a better understanding of the pathogenesis of neuroinvasive disease. However, the mechanism of neuronal damage *in vivo* is not completely understood. Understanding the pathogenesis of WNV and CHIKV neuroinvasive disease using state-of-the art technology will allow for the identification of biomarkers and leads for novel treatment protocols. Although there is a dramatic improvement in the management of viral encephalitis, our limited knowledge of the pathogenesis at the cellular and molecular level still hampers the development of intervention strategies to reduce mortality and long-term functional deficits in survivors of encephalitis. The knowledge obtained from these studies will allow for the development of novel therapies that can be tailored to resolve specific pathophysiologic derangements. In addition, markers that are associated with and may have predictive value for development of severe disease will be identified. Furthermore, the results will lead to development of an individual risk assessment score system that allows selection of patients who need intensive monitoring and treatment. Such a system will contribute to better patient management, decrease of mortality and reduction of cost associated with effective patient management.



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