

# Long-term effect of chemogenetic suppression of excitatory hippocampal neurons on spontaneous seizures in a rat model for temporal lobe epilepsy

M.G. GOOSSENS<sup>1</sup>, K. VONCK<sup>1</sup>, C. VAN DEN HAUTE<sup>2</sup>, V. BAEKELANDT<sup>2</sup>, W. WADMAN<sup>1</sup>, C. VANHOVE<sup>3</sup>, P. BOON<sup>1</sup>, R. RAEDT<sup>1</sup>

<sup>1</sup> 4BRAIN, Department Head and Skin, Ghent University - Ghent, Belgium.

<sup>2</sup> Leuven Viral Vector Core, Centre for Molecular Medicine, KU Leuven - Leuven, Belgium

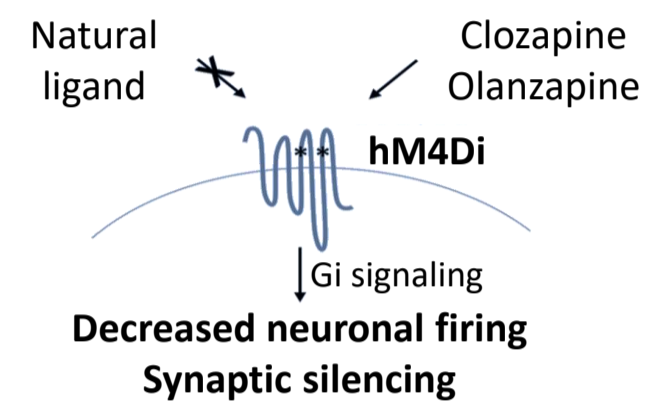
<sup>3</sup> MEDISIP, Department of Electronics and Information Systems, Ghent University - Ghent, Belgium



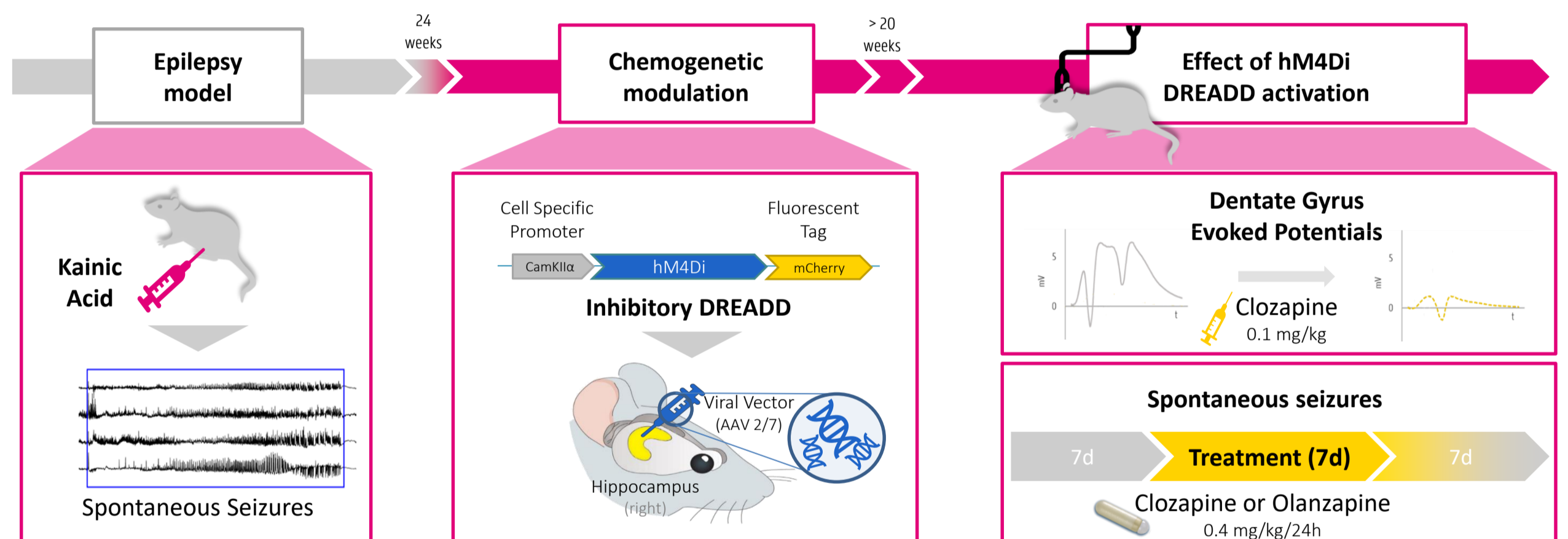
Corresponding author: MarieGabrielle.Goossens@UGent.be

## Introduction

The hippocampus is believed to play a crucial role in seizure generation in **temporal lobe epilepsy** (TLE). Chemogenetic inhibition of excitatory neurons in the hippocampus using hM4Di, an inhibitory **Designer Receptor Exclusively Activated by Designer Drugs (DREADD)**, can be used to suppress hippocampal excitability. In this study, we evaluated the potential of ligand-based activation of DREADD, selectively expressed in excitatory hippocampal neurons, as a tool to suppress epileptic activity in a **rat model** for TLE.

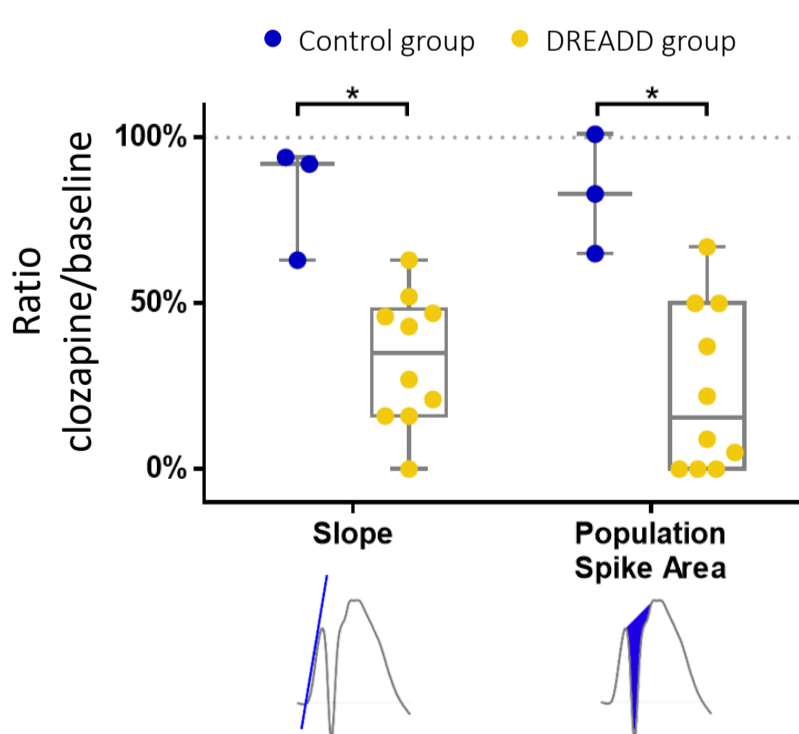


## Methods



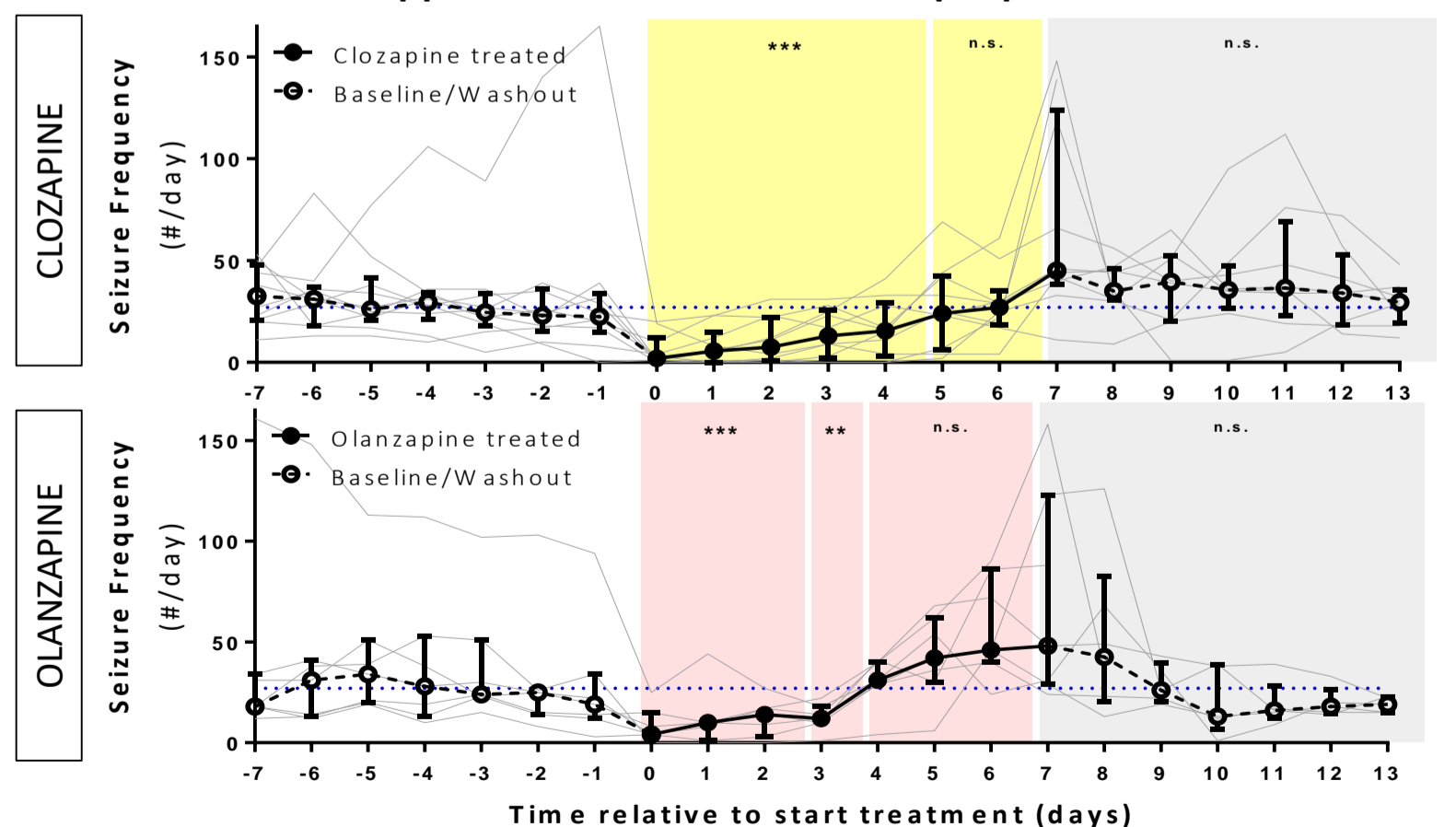
## Results

### Activation of hM4Di DREADD suppresses evoked potentials in epileptic rats



Shown ratios calculated at I<sub>70</sub>. Median ± IQR, symbols correspond to individual animals. Control: n=3, DREADD: n=10

### Continuous activation of hM4Di DREADD suppresses chronic seizures in epileptic rats



Median ± IQR, lines correspond to individual animals. Clozapine: n=10, olanzapine: n=7. \*\*: p < 0.01, \*\*\*: p < 0.001

## Conclusion



### Chemogenetic inhibition in an epilepsy model:

- ✓ Activated by subpharmacological doses of clozapine or olanzapine
- ✓ Suppression of dentate gyrus evoked potentials
- ✓ Reduction of seizures in IPKA rat model for TLE
- ✗ Observed tolerance towards end of treatment
- ✗ Further optimization is required