

## THE EFFECT OF HDAC4 REDUCTION POST-WEANING ON HD-RELATED PHENOTYPES IN R6/2 MICE

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### Background

We have previously shown that constitutive heterozygosity for *Hdac4* results in a delay in the formation of HTT aggregates in the cytoplasm, rescues electrophysiological defects, improves rotarod impairment and delays end stage disease. However, the beneficial consequences of decreasing *Hdac4* levels after weaning, thereby more closely mimicking a potential pharmacological trial, are unknown.

### Aims

To test the effect of a temporal reduction in *Hdac4* levels in R6/2 mice.

### Methods

The tolerability of tamoxifen dosing regimens in wild type and R6/2 mice was investigated at 4, 6 and 8 weeks of age. Mice expressing a tamoxifen inducible ubiquitously expressed Cre transgene (pCAG-Cre<sup>ERT2</sup>) were crossed to mice that are heterozygous for a conditional *Hdac4* knock-out allele (*Hdac4* flox) and the extent of recombination across the floxed *Hdac4* allele was established using PCR and qPCR assays. The triple cross between pCAG-Cre<sup>ERT2</sup>, *Hdac4* flox and R6/2 was set up and the effect of *Hdac4* reduction on aggregation levels at 4 weeks of age was measured using the Seprion ligand ELISA.

### Results

Tamoxifen administration at 85 mg/kg was tolerated by R6/2 and wild type mice aged 4 and 6 weeks of age and this led to recombination across the floxed *Hdac4* gene in the five brain regions examined. The triple cross between pCAG-Cre<sup>ERT2</sup>, *Hdac4* flox and R6/2 has been performed and the tissues are in the process of being analysed.

### Conclusions

The results of this study will be presented.

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