BACHD transgenic rats

QPS Austria collaborates with University Tuebingen, Germany, in the EU-supported Marie-Curie project:

Switching the disease off:
Effects of spatial and temporal inactivation of mutant huntingtin in Huntington disease

The goal of this Industry-Academia Partnerships and Pathways project aims to investigate the role of mutant huntingtin (mhtt) in the striatum and hypothalamus by downregulating mhtt in these brain regions at different disease stages using lentiviral delivery of CRE recombinase into the unique BACHD rat. For the first time, this method will allow to analyze which mhtt containing brain region is causing which Huntington disease symptom. Translation of these results to the human disease will allow the development of more specific treatments against Huntington disease.

The group of Nguyen, H.P., University Tuebingen, Germany, already successfully characterized the BACHD transgenic rat model with 97 CAA-CAG repeats (Fig.1) in detail, showing that the animals have severe motor deficits as analyzed by RotaRod (Fig.2) and gait analysis. Furthermore, animals show hyperactivity and strong metabolic changes [**1**].

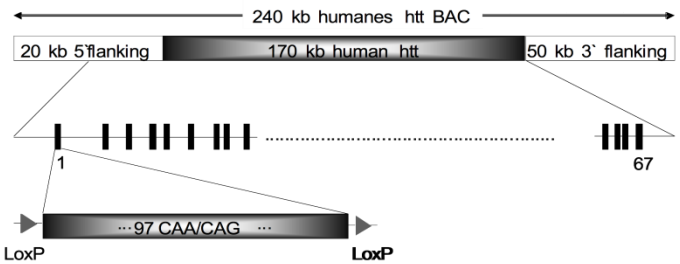

Fig.1: BACHD construct was designed using a BAC containing the entire 170kb of the HTT genomic locus with ~20 kb upstream and 50 kb downstream flanking sequences. The mutant HTT exon 1 including 97 CAA-CAG trinucleotide repeats in place of endogenous HTT exon 1 is flanked by two loxP sites [**1**].

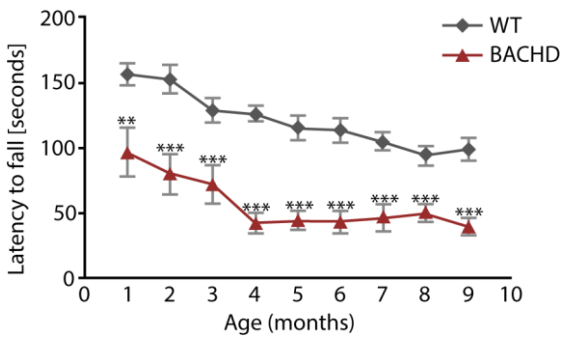

Fig.2: Longitudinal analysis of BACHD rats on an accelerating rod (4-40 rpm in 4 min; n=12) [**1**].

Histopathological analyses of BACHD rats revealed spatio-temporal accumulations of neuropil aggregates as well as nuclear accumulations in the amygdala and cortex starting at 3 and 9 months, respectively Fig.3 [**1**].

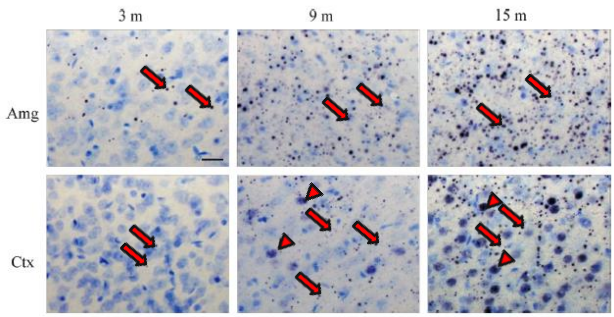

Fig. 3: Spatiotemporal accumulation of mhtt in amygdala (Amg) and cortex (Ctx) of BACHD rat brains. Neuropil aggregates (arrows). Nuclear accumulations of mhtt (arrowheads). Scale bar, 20 µm [**1**].

Based on the detailed BACHD rat characterization by Nguyen and colleagues, we are convinced that the collaboration project will be of great success and results of this project will support the scientific community in finding a cure against Huntington disease.

[1] Yu-Taeger et al., A novel BACHD transgenic rat exhibits characteristic neuropathological features for Huntington disease. J Neurosci, Oct 31, **2012**, 32(44):15426-15438.

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