JUNE 2015

CZ09 Czech-Norwegian Research Programme

7F14308 - HUNTINGTON

norway grants

JAN MOTLÍK, Institute of Animal Physiology and Genetics

Comparative study of Huntington's disease using biochemical, immunocytochemical and molecular genetic methods on the mouse, minipig and human tissues and cells

Huntington's disease (HD) is a fatal progressive neurodegenerative disorder that is inheritedin an autosomal dominant manner and is caused by a polymorphic trinucleotide CAG repeat expansion in exon 1 of huntingtin gene (HTT). The findings from animal model studies have helped to elucidate important pathways that are disrupted in HD and have provided important insights into the pathogenesis of this disease. However, an exact mechanism, how mutant HTT induces selective neurodegeneration, still remains to be elucidated. The grant proposal is based on comparative studies of tissues (mainly from brain), somatic cells (skin fibroblasts) and germ cells (spermatozoa) isolated from mice (R6/2) and minipigs transgenic for N-terminal part of human mutated HTT (TgHD) as well as HD patients. The unique biological material will be examined by a complex set of biochemical, immunocytochemical and molecular genetic methods in cooperation of four laboratories: Institution of Animal Physiology and Genetics AS CR, First Faculty of Medicine- Charles University in Prague, Deparment of Molecular Medicine- Oslo University Hospital, Department of Medical Biochemistry- University of Oslo.CAG instability will be studied in DNA from tissues of R6/2 mice, F2 and F3 generations of TgHD minipigs.

The complex methodological approach to mitochondrial functions and Golgi complex proteins will be applied to R6/2 mouse and minipig (F2 generation) brain tissues and to mouse, minipig and human cells. Mutant HTT aggregation process will be investigated on mouse and minipig (F2 generation) brain tissues and F0 and F1 generation minipig cells.

"The Programme enables collaboration, discussion, and exchanges of students and scientists. It reinforces methodology and science of all partners. Common meetings help to focus our effort to publish high quality papers. "

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