

The department of Clinical Genetics plans to appoint a

PhD Student (OIO) (fulltime)

The department

The department of Clinical Genetics is involved in the search for genes involved in human disease as the starting point for molecular, biochemical and cell biological studies to unravel the mechanisms of the disorder. One research line focuses on neurogenetic diseases.

The department has a modern infrastructure and has access to all the facilities needed for the realization of the project.

The position

The topic of this project is: **Experimental approaches towards therapeutic intervention for Fragile X-associated Tremor Ataxia Syndrome (FXTAS).**

Fragile X-associated tremor/ataxia syndrome (FXTAS) is a late-onset neurodegenerative disorder affective carriers of premutation forms of the *FMR1* gene. FXTAS results in progressive development of tremor, ataxia and neuropsychological problems, including anxiety, memory impairment and dementia. Both the gene and the pathogenic trigger (RNA toxicity) responsible for FXTAS are known. Development of an effective therapy requires a thorough understanding the cellular mechanisms of the disease, identification of molecular targets for therapy, and development of novel therapeutics that can reach those targets. This project proposes to characterize valid mouse models of FXTAS that will allow us, in concert with other projects, to systematically explore the underlying disease mechanisms of FXTAS and to identify molecular targets for new therapies. Specifically, we will use transgenic mice that are constructed to model the gene mutation that causes FXTAS (i.e., expanded CGG trinucleotide repeat). We will then use these mice to (1) define critical periods in development for disease onset, (2) identify therapeutic windows for treatment, (3) establish the potential for halting or reversing FXTAS by targeted gene therapies, and (4) test novel therapeutics in mice for their potential to prevent or reverse the development of FXTAS. Inducible (tet-on) transgenic mice models have been developed and will enable us to turn off activation of the mutant CGG trinucleotide repeat during development to establish when suppression of abnormal gene expression can halt or reverse disease progression, as well as identify the specific cell types and mechanisms that cause FXTAS. In addition, we have developed inducible *in vitro* cellular models (mouse embryonic fibroblasts; MEFs) to test novel gene-targeted (i.e., antisense oligonucleotides, RNAi) and pharmacological treatments.

Job requirements

We are looking for an enthusiastic and motivated young scientist who has recently completed his/her MSc in (medical)Biology, Medicine or similar disciplines. The candidate should preferably have some knowledge and experience with molecular biology, cell biology or biochemistry techniques and have interests in the molecular mechanisms of human brain diseases. English language skills are essential.

Conditions of employment

We offer you an appointment as a PhD student (oio) for a period of 4 years. You are an employee of the Erasmus MC. The conditions of employment are in accordance with the Collective Bargaining Agreement for University Medical Centres (CAO UMC).

Information

For more information about this position, please contact dr. Rob Willemsen, tel. +31 10 – 7043152 or by email r.willemsen@erasmusmc.nl