Antisense oligonucleotide mediated exon skipping to remove the expanded polyQ repeat from the ataxin 3 protein in Spinocerebellar Ataxia 3

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Country

Netherlands

Title of project or programme

Antisense oligonucleotide mediated exon skipping to remove the expanded polyQ repeat from the ataxin 3 protein in Spinocerebellar Ataxia 3

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Hersenstichting

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€ 130,000

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01/01/2013

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4

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Research Abstract
Polyglutamine disorders are caused by expansion of a CAG repeat, encoding a stretch of glutamine amino acids (hence polyglutamine). For each disorder the repeat is located in a different protein. Huntington Disease and Spinocerebellar Ataxia 3 (SCA3) are the most

frequent polyglutamine (polyQ) disorders with current treatments limited to symptomatic relief. The prevalence of the SCAs varies significantly according to race and place of birth. International prevalence estimates vary from 0.3 to 3.0 per 100,000. Patients with a CAG repeat above a certain threshold will develop the disease, symptoms become apparent around mid-life and gradually worsen over time.
The ataxin-3 protein has important functions within the cell and complete removal might not be beneficial. The current project proposes an approach for antisense oligonucleotide (AON) mediated therapy in SCA3 that should reduce protein toxicity without lowering protein levels, by removing the polyQ repeat from the protein through in-frame exon skipping. AONs will be directed at the exons that encode the polyQ repeat, this will result in the formation of a shorter ataxin-3 protein that should retain most of its important wild type functions without changing the ataxin-3 protein levels. The most promising AONs will be selected in cultured cells and then tested in an animal model of SCA3.

Further information available at:

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Investments < €500k

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Netherlands

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