Endogenous Cerebellar Stem Cells and their Potential Neuroregenerative Role in Inherited Ataxias

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Scientific summary

Inherited ataxias, such as cerebellar ataxias are generally heterogeneous conditions. However, clinical and pathological features are often rather similar. In particular, variable degrees of neuronal loss and atrophy of the cerebellum are well known common features of several of these conditions. Promoting regeneration and repair in the cerebellum would therefore have a significant impact on these diseases.

Endogenous neural stem cells are multipotent cells that can give rise to a differentiated progeny as well as self-renew. They have been isolated from several regions of the postnatal mammalian brain and they have been shown to significantly contribute to regeneration and plasticity of the adult brain.

The aim of this study is to isolate and characterise, molecularly and functionally, neural stem cells from the postnatal human cerebellum. Currently, such cells have been isolated and characterised in mice but it is an essential first step of any future translational application of this knowledge to provide proof of principle that similar cells also exist in humans.

The basic scientific knowledge obtained from this project will provide the basis for experiments aimed at assessing whether fine tuning of self renewal capacity of cerebellar neural stem cells can be a viable approach to increase the available stem cell pool to sustain repair and regeneration in inherited ataxia conditions.

Lay summary

Inherited cerebellar ataxias are neurodegenerative conditions that are associated with a variable degree of neuronal loss and atrophy of the cerebellum. Recent discoveries in neuroscience have shown that cells with stem-like features exist in the adult brain. These cells can either maintain themselves or differentiate into mature brain cells such as neurones. Therefore they can be considered as a reservoir of cells which can replenish damaged cells if appropriately stimulated.

Here we would like 1) to assess whether stem-like cells are present in the adult human cerebellum, 2) to study their cellular properties (maintenance and

differentiation) and 3) to provide proof of principle that these properties can be manipulated to increase the stock of these cells and to induce them to differentiate.

Understanding how the life of these cells is regulated will allow us to set the basis for a potential future development of new treatments aiming at increasing regeneration and repair in currently incurable neurodegenerative brain conditions such as the ataxias.

For more support or information please contact: Ataxia UK, Lincoln House, Kennington Park, 1 – 3 Brixton Road. London SW9 6DE

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