

Modifying the exosomal release of alpha synuclein as a potential target to prevent disease progression in Parkinson's

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United Kingdom

Title of project or programme

Modifying the exosomal release of alpha synuclein as a potential target to prevent disease progression in Parkinson's

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Parkinson's UK

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20/07/2015

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2

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Research Abstract

Alpha-synuclein along with other proteins, mRNA and microRNAs can be released from cells in exosomes which can be transferred to neighbouring cells. While this may not be detrimental under normal conditions we have demonstrated that when lysosomal function is compromised alpha-synuclein oligomerises and there is an increased alpha-synuclein release in exosomes. We have identified the pathway leading to alpha-synuclein transfer to exosomes which is

dependent upon hsc70 interaction. Mutant 98AA99 alpha-synuclein does not bind hsc70 and is not released in exosomes. We have generated a model that explains why alpha-synuclein is channelled to exosomes under conditions of lysosomal dysfunction, and why specific defects associated with PD may also increase exosomal alpha-synuclein release from cells. In this project we will utilise the 98AA99 mutation to confirm the relevance of the exosomal release of alpha-synuclein to the cell to cell transmission of alpha-synuclein aggregation. In addition we will explore the possibility that alpha-synuclein aggregation may lead to microRNA dysregulation and subsequent changes to microRNA content of the exosomes. If neighbouring cells are exposed to exosomes containing modified alpha-synuclein and altered microRNA expression these could promote alpha-synuclein aggregation in the recipient cells.

Further information available at:

Types:

Investments < €500k

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United Kingdom

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