

Neuronal Ageing

Proteomics

Neuronal Ageing

Axonal Transport

Mollusc

Effects of Age on Neuronal Protein Expression

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The Investigation

Objectives

Increasing age is associated with changes in the number and strength of synaptic connections a neuron makes with a target cell¹. As such the age-related changes are believed to lead to cognitive decline and decreased independence. This project will provide an initial screen on the effects of age on the proteome (entire protein complement) using the nervous system of the pond snail *Lymnaea stagnalis* to assess the functional significance of protein changes within the ageing phenotype.

Plan

Extracted CNS samples are prepared and separated using conventional proteomic tools including 1D and 2D gel electrophoresis followed by subsequent identification of peptides using analytical mass spectrometry (see Fig1). LC-MALDI MS/MS² and ESI MS/MS techniques will be used and the two methods compared to maximise sensitivity in identifying the differentially expressed proteins.

The functional significance of candidate proteins will be assessed by designing a degenerate primer for PCR and subsequently cloning the complete cDNA. Knockdown will be achieved in the isolated CNS by injecting specific neurons with the dsRNA, while cultured neurons will be incubated in the dsRNA (10 µgml⁻¹).

Resources

Mass spectrometry, electrophysiology, PCR, proteomics facility, ageing snail population

References

- Morrison JH, Hof PR
Life and death of neurons in the ageing brain
Science 1997 278 (5337): 412-9
- Perlson E et al
Differential proteomics reveals multiple components in retrogradely transported axoplasm after nerve injury.
Molecular & Cellular Proteomics 3: 510-520, 2004

Potential Benefits

For older people

Brain ageing is a complex process involving a deterioration of several biological processes leading to cognitive decline. A number of pathways are being investigated however the triggers and consequences of age-related changes at the protein level remain unclear. In this study we aim to identify key proteins regulating some of these pathways which could be used as therapeutic targets against age-related decline.

For society

This study will provide new information concerning the role of changes in protein expression in neuronal ageing and has the potential to identify novel targets involved in the ageing process.

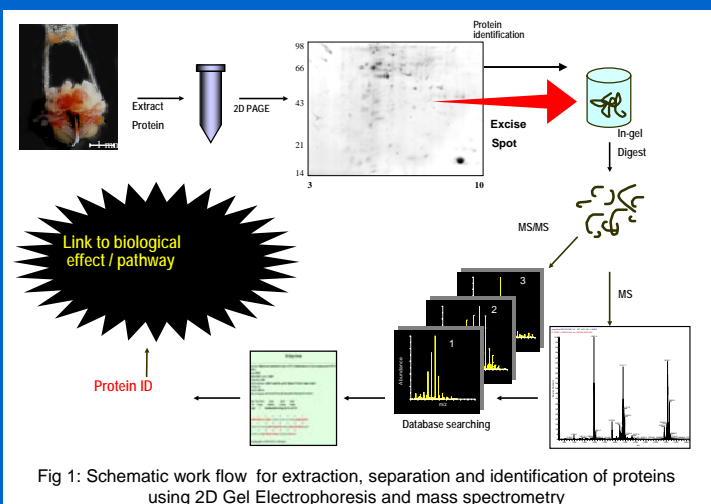


Fig 1: Schematic work flow for extraction, separation and identification of proteins using 2D Gel Electrophoresis and mass spectrometry



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