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(54) Title: MATERIALS AND METHODS RELATING TO PROTEIN AGGREGATION IN NEURODEGENERATIVE DISEASE

(57) Abstract: Disclosed are methods of proteolytically converting a precursor protein (e.g. tau) to a product fragment (e.g. a 12 kd fragment) in a stable cell line, wherein the precursor protein is associated with a disease state in which the precursor protein aggregates pathologically (e.g. a tauopathy), and the methods comprise:(a) providing a stable cell line transfected with nucleic acid encoding: (i) a template fragment of the precursor protein such that the template fragment is constitutively expressed in the cell at a level which is not toxic to the cell; and (ii) the precursor protein, which protein is inducibly expressed in the cell in response to a stimulus, whereby interaction of the template fragment with the precursor protein causes a conformational change in the precursor protein such as to cause aggregation and proteolytic processing of the precursor protein to the product fragment. The method is preferably used to screen for modulators of the aggregation process by monitoring production (or modulation of production) of the product band or bands. Also provided are materials for used in the assays, plus medicaments, and related uses and processes, based on compounds which show high activity in the assay of the invention e.g. reduced diaminophenothiazines.

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