The lack of genetic factors in sporadic forms of Alzheimer and other neurodegenerative diseases (NDs), the deposition of a toxic conformer of a cellular protein and a missing involvement of DNA in the propagation of the aetiological agent has led to the construction of “protein-only” disease concepts in which the toxic protein is the aetiological agent. However, none of these concepts can conclusively explain any of the diseases.

**Aim:** To find a general and simple concept applicable to all forms of all NDs.

We have screened the sequences of genes linked to a particular ND by pedigree for additional complete genes, and tested for their expression (mRNA, protein) using clinical samples. Biochemical features of the protein products were predicted by computerized analysis. The protein related to transmissible spongiform encephalopathies (TSE) was tested experimentally for disease-related function, particularly the capacity to convert cellular prion protein (PrP\(^C\)) to disease-like conformers.

We have identified nested genes randomly located within genes linked to Alzheimer, Parkinson, TSE, Down syndrome and Huntington. Clinical studies suggested disease-specific, pre-symptomatic expression of the nested genes. Furthermore, auto-antibodies against the protein products were present in individuals affected by the particular disease. Various toxic behaviours were predicted for all protein products including membrane and transcriptional activity, nucleo-cytoplasmic shuttling (NES-signal) and the ability to competitively inhibit processing and activity of the protein product of the host gene. The TSE-specific toxic protein reacted with PrP\(^C\), producing insoluble, partly proteinase K-resistant PrP\(^\text{27-30}\).

**Conclusion:** The nested genes disease concept may apply to most NDs.