A fascinating and potentially revolutionary new concept is emerging in several neurodegenerative diseases. It involves the propagation of RNA-protein aggregates from cell to cell during the onset and progression of diseases. It now appears that many "protein-folding" diseases, such as Alzheimer’s and Parkinson’s diseases, can be transmitted between cells by a prion-like mechanism.

RNA-binding proteins affect pre-mRNA processing and are transported with the mRNA to the cytosol, where they are removed by translation-dependent and independent mechanisms for recycling into the nucleus. Once into the cytoplasm, when mRNAs are not engaged in translation, they assemble into P bodies or Stress Granules (SGs).

Prion mechanism as clinical strategy? - Diseases caused by proteins with excess of activity - Pathogens

**Prion Mechanisms**

Cellular stress induces FUS/TLS or HNRNPD incorporation into stress granules, which form through the ordered aggregation of several RNA-binding proteins complexed RNA molecules. This physiologic reaction to cellular stress may be an initial trigger for pathogenic inclusion formation, given that the increased local protein concentration and RNA scaffolding molecules may facilitate ordered aggregation of FUS/TLS or HNRNPD. In this context, the functional conformational changes of these two proteins associated with their physiological roles in stress granule formation may transform into pathogenic, self-perpetuating, irreversible aggregation upon chronic cellular stress and defects in stress granule disassembly occurring with aging. Possible cell-to-cell spread of prion-like aggregates may underlie or contribute to disease spread from a focal initiation.

**Concluding Remarks**

Why neurodegenerative diseases?

**Figure 9** Model for the Selective Sensitivity of Neurons to Altered Ribosomes [1]

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