

MisingLink

**Identification and structural characterization of the primordial cytotoxic conformers of the amyloidogenic cascade:
Ideal prevention/diagnostic/therapeutic targets in neurodegeneration.**

Amyloidogenic Neurodegenerative Diseases (ND) such as Alzheimer's or Parkinson's are one of the major causes of disability and death in Europe. At present, there are no effective treatments for any ND. Given the societal, personal and financial impact of the burden of NDs, determining their primary cause has become a major focus of basic and clinical research in order to efficiently tackle prevention, early diagnosis and treatment.

In recent years, new pathological protein aggregates involved in NDs have been discovered and their components have been identified. MisingLink postulates that among these components, the hyper-mechanostable (hM) conformers, or their precursors, are the "missing link" and represent the first committed step towards disease (primary cause).

This project proposes a single-molecule approach to detect the missing events that turn these small proteins into neurotoxic components at the start of the pathological cascade. We expect that this research will lead to the development of ideal biomarkers for earlier diagnosis and to the design of better small-molecule therapeutics. Thus, MisingLink will use the state-of-the-art technology to define a new paradigm to understand, prevent, diagnose and treat NDs based on the neurotoxic proteins conformers that cause these types of pathologies.

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