Multitarget drugs against prion diseases

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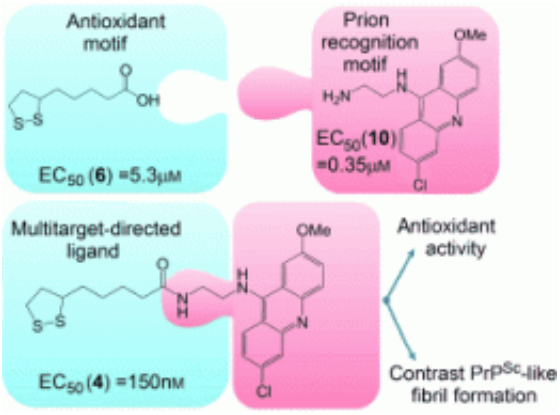

The central nervous systems of humans and cattle alike are attacked by prions (abnormal insoluble amyloidogenic proteins) when they suffer from Creutzfeldt–Jakob disease (CJD) or bovine spongiform encephalopathy (BSE).

This causes a steady deterioration of neurological function and ultimately leads to death. There is no currently approved treatment for prion diseases, and no drug candidates are expected to enter clinical trials soon. In *ChemMedChem*, Maria Laura Bolognesi (University of Bologna, Italy) and colleagues argue in support of a multitarget drug discovery strategy as an alternative way to develop effective anti-prion agents.

Under the dominant drug discovery paradigm "one disease, one target, one molecule," which ignores the polyetiological nature of prion diseases and similar maladies, developing anti-prion therapies is a particular challenge; indeed, this paradigm could be a factor in the ongoing failure of current neurotherapeutic drugs.

Bolognesi and colleagues now describe the discovery of rationally designed molecules endowed with various activities relevant for combating prion neurodegeneration. A new series of chimeric molecules were generated by linking the antioxidant fragment of lipoic acid to heteroaromatic prion-recognition motifs. These compounds effectively counter both prion fibril formation and oxidative stress in a cell culture model of prion replication.

The reported in vitro results make these compounds effective candidates for further in vivo investigations into their multiple biological properties against prion diseases.

More information: Maria Laura Bolognesi, Hybrid Lipoic Acid Derivatives to Attack Prion Disease on Multiple Fronts, *ChemMedChem*, dx.doi.org/10.1002/cmdc.201100072

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