

An implication from the molecular structure principle for the anti-prion drug GN8

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Prion diseases, traditionally referred to as transmissible spongiform encephalopathies (TSEs), are invariably fatal and highly infectious neurodegenerative diseases that affect a wide variety of mammalian species, manifesting as scrapie in sheep and goats, bovine spongiform encephalopathy (or 'mad-cow' disease) in cattle, chronic wasting disease in deer and elk, and Creutzfeldt-Jakob diseases, Gerstmann-Strussler-Scheinker syndrome, fatal familial insomnia, and kuru in humans, etc. These neurodegenerative diseases are caused by the conversion from a soluble normal cellular prion protein (PrP^C) into insoluble abnormally folded infectious prions (PrP^{Sc}). However, the precise mechanism of the conversion is still not known well. In PrP^C, the average distance between Asn159 and Glu196 is 1.54 nm, but in PrP^{Sc} the distance is more than 4.5 nm. GN8 is a therapeutic anti-prion compound to fix the above distance at 1.54 nm, and experiments show that this chemical chaperone can stabilize the PrP^C conformation and identify the hot spots to stop the pathogenic conversion from PrP^C to PrP^{Sc}. We found an important salt bridge between Arg164 and Asp178 will contribute greatly to the structural stability of PrP^C. Implied from the molecular structure principle for GN8, is it possible to design an anti-prion chemical compound to fix the distance between Arg164 and Asp178 at the salt bridge distance? In This talk we will discuss this potential drug target.

Biography

Jiapu Zhang is an Australian-based research scientist. He finished his Ph.D. degree in the Universities of Melbourne and Ballarat and then a CSIRO (Commonwealth Scientific and Industrial Research Organisation) Postdoc training in Australia. CSIRO has a world-wide reputation for excellence and achievement in basic and applied research; the successful drug Relenza® for influenza was designed by CSIRO with its partners. He was trained by CSIRO in protein structure-based drug design, materials. He has investigated the secret of prion diseases and other neurodegenerative diseases, and served as an editor, a reviewer for many academic journals, as a committee member for many academic conferences, workshops and seminars.

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