Guo-Ping Zhou, J Proteomics Bioinform 2018, Volume 11
DOI: 10.4172/0974-276X-C2-114

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The study of the misfolding mechanism of the prion protein by incorporating the Wenxiang diagrams into NMR spectroscopy

The conversion of a normal native helix rich prion protein (PrPC) to an abnormal polymeric ß-sheet rich configuration (PrPSc) is a misfold-ing process. PrPSc is a disease associated fibril-forming isoform such as transmissible spongi-form encephalopathies (TSEs) or prion diseas-es, a deadly disease occurred in both humans and many vertebrate animals. Our NMR stud-ies have indicated that the misfolding process from PrPc to PrPsc is related to the unwinding and stability of the original α-helix structures in PrPc protein. Recently, we have also built up the Wenxiang diagrams of all three helices (H1-H2-H3) of PrPC and observed that most hydrophobic residues of the all three helices (H1-H2-H3) in PrPC are distinctly distributed in one half of the Wenxiang diagram of each helix and most hydrophilic residues are dis-tributed in the other half of the Wenxiang dia-grams. Similarly, most residues formed salt bridges or ionic pairs in a helical structure are close to each other in a Wenxiang diagram plane. According to these features, the helix-helix interactions, stability of alpha helical structure, as well as possible interactions be-tween the helix and residues outside the helix (the residues in loops) can be quickly inferred and further verified by incorporating NMR spectroscopy. Our results explain why H1 is the most stable helix and H2 is the most unsta-ble helix during the formation process of prion disease. Thus, the incorporation of the Wen-xiang diagrams into NMR may provide more insight on the molecular mechanisms of the protein misfolding diseases.

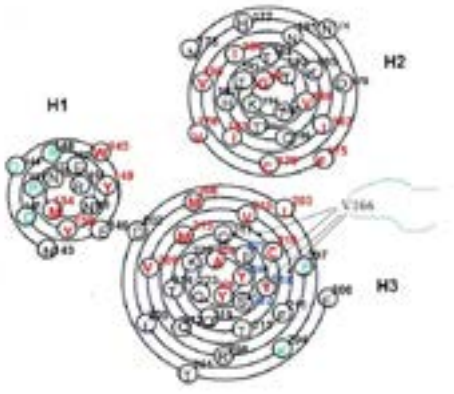

Figure 1: Wenxiang diagram of the helices H1, H2 and H3. The names of all hydrophobic residues are labeled by red. The sequence number of Y218, E221, S222 and Y225 are labeled by blue, which in close contact with loop residue V166.

Biography

Guo-Ping Zhou is a current Professor of Gordon Life Science Institute. He is also an Adjunct Professor of several academics in both USA and China. He received his PhD in Biophysics from University of California at Davis and completed his Postdoctoral training at Stanford University and Harvard University, respectively. He has determined the 3D NMR structures of some im-portant biomolecules, and successfully introduced the novel diagram approach to elucidate the mechanisms of the protein-biomolecule interactions, and protein misfolding diseases observed by NMR. His current research is focused on the molecular mechanism of neural cell adhesion molecule polysialylation using NMR and biophysical approaches. In addition, he has also edited some special issues on the fields of Structural Biology and Medicinal Chemistry for several in-fluential scientific journals as an Editorial-Board Member and Guest Editor.