Label-free observation of supported lipid bilayer disruption induced by protein aggregates

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There are increasing evidences that specific types of protein aggregates, involved in the pathogenesis of the so-called conformational diseases, can damage the cell membrane and consequently involve in cytotoxic action. Here, we show the lipid membrane disruption derived from the amyotrophic lateral sclerosis (ALS)-associated Cu/Zn-superoxide dismutase (SOD1) aggregates, adapting supported lipid bilayer (SLB) that mimics cellular membrane, and employing the label-free characterization methods, such as atomic force microscopy (AFM) and surface plasmon resonance spectroscopy (SPR). Using these surface-sensitive tools, we directly cross-checked the loss of ca. 80% from the pre-existed SLB coverage. Based on control tests with native-state proteins, we postulate that changes of SLB integrity are resulted from the alterations in bilayer structure by aberrant properties of SOD1 aggregates, such as conformational and superficial variation of native state. This in vitro observation reported here is regarded as meaningful approach to comprehend cellular component-mediated cytotoxic actions generated in vivo and has implicated in the membrane-mediated cytotoxicity of protein aggregates.