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A carboxylated Zn-phthalocyanine inhibits the fibril formation of Alzheimer's amyloid β peptide

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Amyloid β ($A\beta$), a 39 to 42 amino acid long peptide derives from amyloid precursor protein, is deposited as fibrils in Alzheimer's disease (AD) brains and considered as main cause of the disease. We have investigated the effects of a water-soluble Zn-phthalocyanine [$ZnPc(COONa)_8$], which have near infrared optical property, on *in vitro* $A\beta$ fibril formation process. The ThT fluorescence assay demonstrated that $ZnPc(COONa)_8$ significantly inhibited $A\beta$ fibril formation, as evident by increasing the lag time and dose-dependently decreasing the fibril levels at the plateau. Moreover, it increased the destabilization of the preformed $A\beta$ fibrils and consequently increased monomer, dimer and trimer species of $A\beta_{1-40}$ in a dose-dependent manner. Immunoprecipitation using $A\beta$ -specific antibody followed by near infrared scanning demonstrated the binding of $ZnPc(COONa)_8$ to $A\beta_{1-42}$. As a result, the hydrophobicity of the $A\beta_{1-42}$ fibril formation microenvironment was decreased. Further, SDS-PAGE and dot blot immunoassay showed that $ZnPc(COONa)_8$ delayed the reduction of low molecular weight and appearance of higher molecular weight oligomer species of $A\beta_{1-42}$. The toxicity of $ZnPc(COONa)_8$ on the culture of a neuronal cell line (A1) was evaluated by MTT cell viability assay. The result showed, that $ZnPc(COONa)_8$ did not decrease the viability, rather protected A1 cells from $A\beta_{1-42}$ -induced toxicity. Thus our results demonstrated that $ZnPc(COONa)_8$ bound to $A\beta$ and decreased the hydrophobicity of fibril formation microenvironment. This change of microenvironment consequently inhibited oligomer and fibril formation process.

Biography

Atsushi Nagai has acquired medical doctor's license in 1988 and completed his PhD at 1997 from Shimane Medical University and postdoctoral studies at University of British Columbia, Canada. He is currently the Professor of Department of Laboratory Medicine at Shimane University Faculty of Medicine. He has published more than 50 papers in reputed journals.

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