

A mirror-phage display selected D-peptide and its derivative eliminate Abeta oligomers in vitro and decelerate cognitive and motoric impairments of transgenic AD mice in vivo

Tina Dunkelmann, Oleksandr Brener, Lothar Gremer, Janine Kutzsche, Dagmar Jürgens, Ewa Mirecka, Antje Willuweit, Karl-Josef Langen, Luitgard Nagel-Steger, Dieter Willbold

Institute of Complex Systems (ICS-6), Research Center Jülich

Several lines of research provide strong evidence for a central role of amyloid-beta (Abeta) oligomers in the pathogenesis of Alzheimer's disease. Investigations on Abeta oligomer interference, however, are impeded by the lack of a quantitative assay to measure substance-induced effects on Abeta oligomers. We have developed a comprehensive, fast and reliable in vitro assay to quantify the removal of Abeta oligomers by any potential drug, for example D3 and its dimeric form, denominated D3D3. This multivalent D3 molecule was expected to have enhanced efficacy due to increased avidity. Therefore we wanted to investigate if there is a correlation between the removal of Abeta oligomers by D3 and D3D3 and positive effects on cognitive and motoric performance in transgenic AD animal models.