[ID: 396] Engineered M13-bacteriophages to target amyloid-β peptide in oligomeric/fibrillar form for Alzheimer´s Disease diagnosis

Ivone Martins [1], Ana Silva [1], Joana Azeredo [1], Helmut Kessels [2]

[1] Centre of Biological Engineering - University of Minho, Braga, Portugal
[2] Center for NeuroSciences, Swammerdam Institute for Life Sciences - University of Amsterdam, Amsterdam, Netherlands

Alzheimer´s Disease (AD) is an age-dependent neurodegenerative disease with very high incidence worldwide and detrimental consequences. Manifests as a decline in cognitive functions and memory loss, characterized at molecular level by an increased deposition of amyloid-beta (AB) plaques. Nevertheless, it is AB in the still-soluble oligomeric/fibrillar form that impairs synaptic function and memory encoding [1]. Therefore, new tools that selectively target AB oligomers/fibrils in the brain hold great potential to halt AD at an early stage.

Specific amyloidogenic peptide motifs grafted into an antibody, were described to react with AB fibrils: AB30-39, and with fibrils and oligomers: AB33-42 [2]. However, the blood-brain-barrier, by sheltering the central nervous system from the systemic circulation, is a major bottleneck for peptide- and antibody-based applications. To overcome this limitation, bacteriophages and phage display can be applied [3,4].

We have successfully cloned peptides AB30-39 and AB33-42 into the M13 filamentous phage genome. The binding ability of AB-specific phages towards AB-oligomers was tested ex vivo and in vitro in mouse AD-tissue and AB42 peptide, respectively. Results showed that AB36-39 peptide selectively target AB-protofibrils, but not plaques, in brain slices from AD-model mice and not from wild-type (WT) littermate. In addition, control phage (carrying no AB-selective peptide), did not stain AD or WT tissue.

For future work, this system will be tested in AD-mouse models to assess the inhibition of the oligomeric AB-mediated synaptic loss and memory impairment.

The outcomes will allow the development of novel phage-based tools for the detection/treatment of early AD, with a direct impact on society and well-being, minimizing the economic burden due to late AD diagnosis and consequent medical treatments.

[1] Kessels H.W., et al. PNAS, 2013. 110: p.4033-8.
[2] Perchiacca, J.M., et al. PNAS, 2012. 109: p.84-9.
[3] Pasqualini, R. & Ruoslahti, E. Nature, 1996. 380: p.364-6.
[4] Dabrowska, K. et al. J Appl Microbiol, 2005. 96: p.7-13.