ST4. Bacteriophages – a bio sustainable solution to tackle Alzheimer´s disease

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Introduction: Amyloid-beta (AB) is a prime suspect to cause Alzheimer's disease (AD), an irreversible, progressive and age-dependent neurodegenerative disorder affecting millions of people worldwide. An accumulation of AB in the brain leads to its aggregation into soluble oligomeric and fibrillar clusters, which are the culprits to impair synaptic function and memory formation in mice models.

Currently, we lack diagnostic tools to detect AB oligomers (ABOs) in the brain, all the methods used provide a late diagnosis when there are already symptoms. Moreover, the existence of the blood-brain-barrier (BBB) is the major bottleneck for reaching the brain. To overcome this, bacteriophages (phages: bacterial viruses) are a solution, once they posses the capacity to cross the BBB.

Aims: Hence, our main goals were the development of a solution to 1) detect ABOs in the brain and monitor AD progression and 2) delay or prevent the onset of the symptoms.

Methods: We resorted to phage engineering with AB-targeting peptides described to recognize ABOs and fibrils with high affinity. These were tested for their capacity to detect ABOs in tissues samples and their effect on AB aggregation.

Results: The engineered phages are able to detect the early and toxic forms of AB in brain tissue of APP/PS1 transgenic mice and human donors. Moreover, these phages also possess a high therapeutic potential by inhibiting the aggregation process of AB.

Conclusion: We provide a highly versatile bio-inspired solution based on phages displaying AB peptides to detect early soluble AB oligomers in the brain, and possibly prevent, or delay, the onset of the symptoms, consequently inhibiting AD progression.

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