9th International Annual Conference

Phages 2019

Bacteriophage in Medicine, Food and Biotechnology

11TH – 12TH September 2019

The Edward Boyle Auditorium, JdP, St Hilda's College
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Bacteriophages as a smart tool to target Alzheimer's Disease

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Alzheimer's disease is an irreversible, progressive and age-dependent neurodegenerative disorder affecting millions of people worldwide. In our brain, a small sized amyloid-beta (Abeta) peptide, when in excess, progressively aggregates into soluble oligomers and fibrils, to finally deposit and accumulate as insoluble amyloid plaques. The still-soluble Abeta oligomers and fibrils are sufficient to corrupt synaptic function and trigger memory loss, emphasizing the importance to find diagnostic tools targeting the soluble forms of Abeta. Specific amyloidogenic motifs were described to react with AB fibrils: AB30-39, and with fibrils and oligomers: AB33-42. However, the blood-brain-barrier (BBB), is a major bottleneck for effective brain applications. To overcome this limitation, bacteriophages (phages) and phage display technology may represent an interesting tool as delivery vehicles to shuttle its cargo across this BBB. To examine this possibility, peptides AB30-39 and AB33-42 were cloned into the M13 filamentous phage genome, and the binding ability of AB phages towards Abeta-oligomers and fibrils was tested *in vitro*. Our results show that these Abeta-specific phages inhibit oligomers and fibril formation as well as promote fibril disaggregation. Moreover, results revealed the specificity of recognition of each engineered phage. AB-phages were also tested *in vivo* to characterize their biodistribution in disease mouse models and preliminary results suggest that AB30-39 is able to recognize amyloid-beta in the brain of these animals. For future work, this system will be tested to assess its therapeutic potential to restore the synaptic function and memory formation. This approach may provide phage-based tools for Alzheimer's early diagnose and therapy.