Title: Mimicking nature to switch the host specificity of phages

Congress Theme: Phage Therapy
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Summary

Phages are subject to rapid evolution given their short replication cycle and high turnover rate. While the accumulation of small genetic changes (vertical transfer) allows for gradual adaptive evolution, horizontal transfer, or the exchange of genetic fragments, is the most disruptive evolutionary force driving this process. Phages encode receptor-binding proteins (RBPs) to initiate infection by reversible binding to the receptor on the bacterial surface. These proteins have a modular build-up with structural domains for attachment of the RBP to the phage tail machinery and specificity domains to bind to the corresponding receptor. While some phages have a single RBP, other can have multiple RBPs, requiring elaborate systems to organize all RBPs. Evolution of RBPs is shaped by intense horizontal transfer events where mainly the specificity modules are exchanged to switch phage specificity. We study the natural modularity of these RBPs and apply synthetic biology tools to mimic horizontal transfer on a lab scale. As such we develop synthetic phages with swapped receptor-binding proteins in standardized scaffolds.