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Engineered phage banks: targetable nanodevices as a functional answer to bacteriological threats

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Abstract:

The emergence and re-emergence of bacterial diseases together with ever increasing antibiotic multi-resistances constitute significant medical a bio-security problems. The capacity to rapidly and efficiently detect and destroy any bacterial pathogen without using antibiotics or vaccines is urgently needed. Bacteriophages do provide some solutions, but their use is limited by rapid development of resistances in bacterial target populations and the inefficiencies of selecting new phage strains from nature. To define the most appropriate approaches, we used systems biology to build models of phage-hosts co-evolution. These led to the development of novel phage engineering technologies allowing to systematically counter bacterial escape strategies. The phage host-targeting proteins are stochastically engineered to encode hyper-variable regions interspersed between constant domains. Each engineering step generates millions of variants and when several proteins are being thus manipulated, the number of variants generated nears practical infinity. Thus, starting from a single phage, this results in the creation of a huge diversity of specificities from which phage subsets capable of detecting and eradicating any given bacterial population can be rapidly isolated and amplified. Furthermore, since a multitude of non-bacterial components can also be targeted, this effectively transforms phages and phage envelopes into targetable nanodevices.

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