T7 Adaptation to Antibiotics

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Abstract

Bacteriophages provide one of the few hopes for treating drug-resistant bacteria. Rather than replacing antibiotics, however, phages will likely complement treatment for patients already on drugs. A challenge with the use of dual treatment is that antibiotics may inhibit the growth of phages by inhibiting growth of their bacterial hosts, possibly limiting phage efficacy. But might phages be adapted to grow in the drugs and thus offset any negative effect? Here, a wildtype T7 was separately adapted to grow in partially-inhibitory concentrations of chloramphenicol (Cm, 2ug/ml) or kanamycin (Kn, 8ug/ml) as well as in a no-drug control. The timeframe for adaptation was fifty hours as a compromise between experimental discovery and expediency that would be dictated by patient treatment demands. Of the three phage lines separately adapted to each environment, growth rate was elevated over ancestor for all lines, albeit to profoundly different degrees, suggesting that pre-adaptation of phages might translate to enhanced treatment. One striking result was that all evolved phages improved fitness in both the Cm and no-drug environments regardless of their selective environment, suggesting that a substantial component of selection was merely for better growth. A second general result was that the Kn environment remained highly suppressive of all phages. These limited data support the idea that antibiotics will inhibit phage growth. They also suggest that phage pre-adaptation could improve treatment but that such adaptation will not erase inhibitory effects of drugs.

Keywords: Bacteriophage, phage therapy, adaptation, evolution, fitness.