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Mycobacteriophages and their host interactions

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Mycobacteriophages are natural predators of *Mycobacterium* strains. We have gained insights into mycobacteriophage biology through science education programs such as PHIRE and SEA-PHAGES, in which many students have collected over 30,000 phages, half of which infect Mycobacterium. This set of phages isolated on a single bacterial strain (*M. smegmatis* mc2155) reveals the amazing genetic diversity of the phage population. These phages has provided insights into the mycobacteria and facilitated development of tools that are broadly useful for the *Mycobacterium* research community. Elucidating phage diversity and development of engineering tools enable first therapeutic phage intervention for treating an *M. abscessus* infection. We now have received 650 requests for phage evaluation of NTM strains, which we have screened with a phage panel, although the phage repertoire is limited. Most strains are *M. abscessus*, of which about 50% have smooth colony morphotypes and are rarely killed efficiently by any phages. The other 50% have rough colony morphotypes, and we can identify one or more phages that infect and kill about 50% of these efficiently. To date we have provided phage preparations for clinical treatment of over 50 patients, providing insights into the opportunities and challenges for *Mycobacterium* phage therapies. However, a serious challenge to broadening therapeutic use is the narrow host preference of the phages and unpredictability of phage infection profiles. This likely arises from a diverse set of integrated prophages prevalent in *M. abscessus* strains, a rich and varied plasmid repertoire, and an abundance of known phage defense systems in genomic islands.

Reference #1

Reference #2

Reference #3

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