ePOSTER:

Towards bacteriophage therapy in infections with multidrug resistant *Klebsiella pneumoniae*

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Summary: The emergence of multi drug resistant (MDR) *Klebsiella pneumoniae* (*Kp*) strains are a serious challenge for public health and force protection, as MDR associated treatment failures cause high mortality rates in septicemia caused by contaminated wounds and in nosocomial infections. Hence, bacteriophage (phage) therapy has resurfaced as a promising strategy for battling MDR infections as phages have the innate ability to specifically infect and lyse bacteria.

Methods-Results: *Kp* specific phages use the host's capsule, a major virulence factor of *Kp*, as receptor for adsorption. To date, 80 different *Kp* capsule types (K-serotypes) have been described with predominant capsule types varying between different countries and continents. Therefore, therapeutic phages need to be customized according to the locally prevailing variant(s). In a retrospective study we capsule-typed 168 *Kp* strains from clinical samples of the military hospital in Tunis (MHT). We found that *Kp* K64 was not only the most predominant strain at MHT but also associated with high mortality rates, especially at the MHT intensive care unit (ICU). We isolated and described the phage TUN1 isolated in the MHT ICU, which specifically infects and lyses *Kp* K64 strains [1].

Conclusions: Highly capsule type specific phage for the *Kp* type most common at MHT were identified. Our next goals are to expand the host range of phage TUN1 (e.g. via phage engineering informed by the Appelmans protocol [2]) and to conduct a prospective study using phage produced following best practice guidelines [3] at the MHT in Tunisia with wildtype or recombinant Kp-phages to treat patients suffering from infections with MDR *Kp* strains.

References:

1. Eckstein S, Stender J, Mzoughi S, Vogele K, Kühn J, Friese D, Bugert C, Handrick S, Ferjani M, Wölfel R, Millard A, Ben Moussa M, Bugert JJ. Isolation and characterization of lytic phage TUN1 specific for Klebsiella pneumoniae K64 clinical isolates from Tunisia. BMC Microbiol. 2021 Jun 21;21(1):186. doi: 10.1186/s12866-021-02251-w. PMID: 34154528; PMCID: PMC8215767.
2. Würstle S, Stender J, Hammerl JA, Vogele K, Rothe K, Willy C, Bugert JJ. Practical Assessment of an Interdisciplinary Bacteriophage Delivery Pipeline for Personalized

Therapy of Gram-Negative Bacterial Infections. Pharmaceuticals (Basel). 2022 Feb 2;15(2):186. doi: 10.3390/ph15020186. PMID: 35215298; PMCID: PMC8879309.

3. Jakob N, Stender J, Friese D, Hammerl J, Filippov AA, Swierczewski BE, Ellison DW, Wölfel R, Bugert, JJ. Modified Appelmans protocol for in vitro Klebsiella pneumoniae phage host range expansion - Poster submitted to the 44. ICMM, Brüssels, September 5-9, 2022.