**Call:** 6th transnational call for the JPIAMR within the ERA-NET JPI-EC-AMR:
Innovations against antibiotic-resistant bacteria: New targets, compounds and tools

**Title**: Advancing CRISPR antimicrobials to combat the bacterial pathogen Klebsiella pneumoniae

**Acronym**: CRISPRattacK

**Consortium composition**

| Type | Name | Institute | Country |
|---|---|---|---|
| Coordinator | Chase Beisel | Helmholtz Institute for RNA-based Infection Research | Germany |
| Partner | Udi Qimron | Tel Aviv University | Israel |
| Partner | David Bikard | Pasteur Institute | France |
| Partner | Sylvain Brisse | Pasteur Institute | France |
| Partner | Strowig Till | Helmholtz Center for Infection Research | Germany |

**Abstract**
The increasing incidence of multidrug-resistant bacterial infections and the trickling pipeline of novel antibiotic classes demand a new generation of antimicrobials. One promising avenue has been the development of antimicrobials based on CRISPR-Cas immune systems. These systems can be programmed to specifically and efficiently eliminate cells harbouring multi-drug resistance genes without impinging on resident microbiota. However, CRISPR antimicrobials remain to be advanced from a few proof-of-principle demonstrations to established therapeutics that can effectively combat the most pressing pathogens. Here, we propose to advance this antimicrobial platform to selectively kill *Klebsiella pneumoniae*, a major cause of multi-drug resistant, nosocomial infections worldwide. We have devised a series of experimental approaches that will identify the most active CRISPR nucleases and DNA target sites for programmed killing, engineer bacteriophage delivery vehicles that can efficiently deliver CRISPR to a large fraction of clinical isolates, and evaluate the efficacy of the most promising therapeutic candidates in mouse infection models. Once demonstrated, the resulting optimised CRISPR antimicrobials will represent a large leap forward for the development of novel antimicrobials against *Klebsiella*, and they will provide a framework to develop similar antimicrobials against other high-priority pathogens associated with multidrug resistance.