PRESS RELEASE

Veni Vidi Vici: How natural killer cells conquer the superbug *Klebsiella*

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Multidrug resistance of microbes poses a serious global threat to human health. Such resistant strains of *Klebsiella pneumoniae* significantly reduce therapeutic options for the treatment of *Klebsiella*-induced, potentially fatal pneumonia or sepsis. Pavel Kovarik and his team at the Max F. Perutz Laboratories (MFPL), a joint venture of the University of Vienna and the Medical University of Vienna, together with colleagues at Queen's University Belfast now report new insights into how immune cells communicate at the site of infection and join forces in the fight against *Klebsiella* infections. Their results, published in the journal *PLOS Pathogens*, might be used for the development of alternatives to ineffective anti-microbial drugs.

The inappropriate or excessive use of anti-microbial agents in past decades has propelled the emergence and spread of multidrug resistant microbial pathogens. According to the European Centre for Disease Prevention and Control and the European Medicines Agency, each year about 25.000 patients in the EU die from infections with multidrug-resistant bacteria. Globally, 700.000 people per year die due to antimicrobial resistance.

The rise of superbugs

Earlier this year, the World Health Organization (WHO) published a report on anti-microbial resistance, with a special emphasis on antibiotic resistance of so-called "superbugs". Such bacteria pose the greatest threat to human health due to their resistance to several different antibiotics. Among these superbugs is *Klebsiella,* which can cause severe and often fatal infections of the bloodstream and lungs. *Klebsiella* has been reported to be resistant to common classes of antibiotics and to a great extent also to carbapenems, the last resort to treat severe nosocomial infections.

Treatment options beyond common antibiotics

The researchers around Pavel Kovarik at MFPL and Jose Bengoechea at Queen's University Belfast now discovered how immune cells arriving at the site of infection communicate and join forces to eradicate *Klebsiella* during lung infections. Their study suggests that future therapies of severe *Klebsiella* infections could target the immune system, rather than the pathogen itself.

Natural killer cells keep bacterial growth in check

The scientists report the mechanism of how natural killer cells, important cells of the innate immune system, control the growth of *Klebsiella* during lung infection.
Klebsiella induces critical immune response regulators, type I interferons (IFNs), which act as middlemen in the crosstalk between alveolar macrophages (immune cells that engulf and "eat" microbes) and natural killer cells. Type I IFNs help activate natural killer cells, which in turn license macrophages to launch an antibacterial program.

"Type I IFNs are used by the immune system to transport messages between immune cells to orchestrate a perfect defense. Natural killer cells represent the conductor of the defense orchestra, whereas macrophages are the bacteria-killing instruments," explains Masa Ivin, first author of the study and PhD student in the Kovarik lab at the MFPL.

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Future perspectives
Pavel Kovarik and his team are optimistic that their new found results will contribute to the development of urgently needed novel therapeutics against multidrug resistant pathogens. "If drugs fail to kill the pathogen, we should help the immune system do the job. Our current study identifies new and feasible ways how to support the immune system in fighting superbugs."
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About the MFPL
The Max F. Perutz Laboratories (MFPL) are a center established by the University of Vienna and the Medical University of Vienna to provide an environment for excellent, internationally recognized research and education in the field of Molecular Biology. The MFPL are located at the Vienna BioCenter, one of the largest Life Sciences clusters in Austria, and host on average 60 independent research groups, involving more than 500 people from 40 nations.