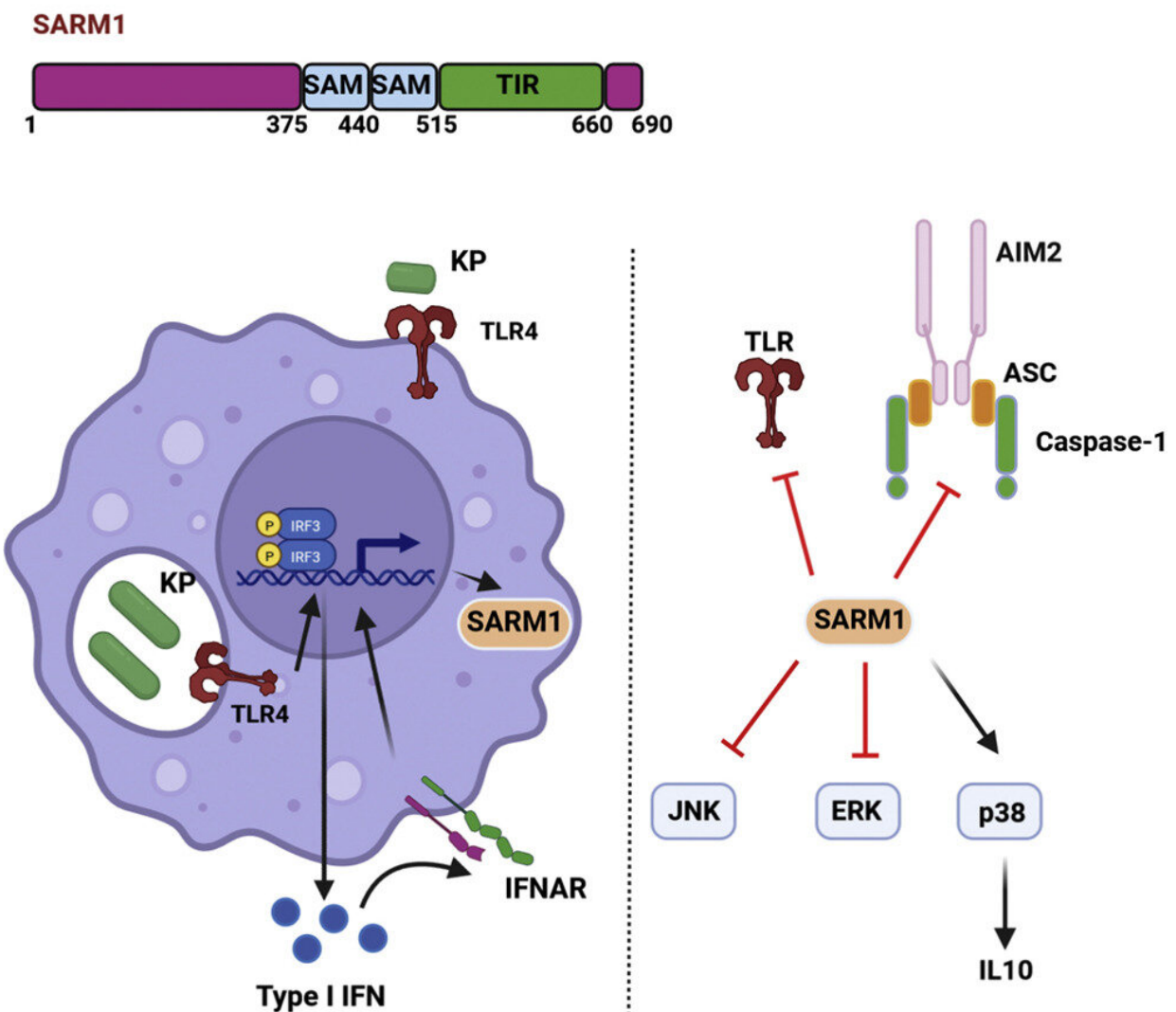


How antibiotic resistant microbes protect themselves from attack of body's defenses

August 25 2022



Graphical abstract. Credit: *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111167

Klebsiella pneumoniae can cause deadly infections such as pneumonia, wound or bloodstream infections, that are becoming untreatable due to the lack of effective antibiotics due to antibiotic resistance (AMR).

AMR is a major global health threat, accounting for more than five million deaths a year. Public Health England has warned that the lack of effective antibiotics could result in three million routine operations becoming life-threatening.

These findings, published in *Cell Reports*, represent a step change in the fight against the global pandemic of antibiotic resistant infections and was led by researchers from the Wellcome-Wolfson Institute for Experimental Medicine at Queen's University Belfast and the Trinity Biomedical Sciences Institute at Trinity College Dublin.

The research demonstrates that *Klebsiella* hijacks a protein from our cells, SARM1, to limit the activation of protective inflammation. Previously, SARM1 was shown to be involved in neurodegenerative disease.

Now, researchers demonstrate that *Klebsiella* induces the expression of SARM1 in macrophages, a type of white blood cell that are crucial for controlling infections. Macrophages kill microorganisms, remove dead cells, and stimulate the action of other immune system cells, to blunt inflammation and to survive inside macrophages, resulting in a protective niche to the action of antibiotics. These findings reveal one of the Achilles heel of our defenses exploited by *Klebsiella* to survive.

Importantly, researchers have demonstrated that the absence of SARM1 facilitates the clearance of Klebsiella without need of antibiotics in a translational model of human pneumonia. There are anti ASMR1 drugs already under investigation and this research will be the foundation of testing them to treat Klebsiella infections alone or as add-on of antibiotics.

Professor Jose Bengoechea, a world leader in the deadly Klebsiella pneumoniae infection at the Wellcome-Wolfson Institute for Experimental Medicine at Queen's University Belfast, and the lead of the project, explains: "This new research is of great relevance in our understanding of AMR, and marks an advance into the development of so dearly needed future therapeutics.

"Our research uncovered how [deadly infections](#) manipulate our cells for their own benefit but, on the other hand, revealed a new target, SARM1, to combat these infections. This research was possible by funding across the island of Ireland, expanding our research capabilities and strengthen the area of infection and immunology, which the recent pandemic has proven to be of critical importance in public health."

Professor Andrew Bowie, Professor of Innate Immunology at Trinity College Dublin and a world expert on innate immunity who has been working to unlock the role of SARM1 in the regulation of inflammation, added: "The surprising and unexpected discovery that Klebsiella manipulates SARM1 to counteract host defenses came about from uniting our different expertise and perspectives on pathogens and host defense which was made possible by the joint North-South funding that myself and Professor Bengoechea received from Science Foundation Ireland and Biotechnology and Biological Sciences Research Council."

Dr. Colin Miles, AMR Lead at Biotechnology and Biological Sciences Research Council (BBSRC), said: "AMR is a major area of research

interest to BBSRC and U.K. Research and Innovation (UKRI) as a whole. It has significant societal implications and I'm pleased to see that a BBSRC funded collaboration with the Science Foundation Ireland, led by Queen's, has been able to discover a fundamental biological process that may ultimately translate into the reduced use of antibiotics in certain clinical cases. This is a positive outcome not only for BBSRC, but for the U.K. Government's 20-year vision for AMR."

More information: Claudia Feriotti et al, *Klebsiella pneumoniae* hijacks the Toll-IL-1R protein SARM1 in a type I IFN-dependent manner to antagonize host immunity, *Cell Reports* (2022). [DOI: 10.1016/j.celrep.2022.111167](https://doi.org/10.1016/j.celrep.2022.111167)

Provided by Queen's University Belfast

Citation: How antibiotic resistant microbes protect themselves from attack of body's defenses (2022, August 25) retrieved 27 April 2024 from <https://phys.org/news/2022-08-antibiotic-resistant-microbes-body-defenses.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.