Novel bacterial communication system to combat antimicrobial resistance

All living cells have sensors that detect environmental changes – such as reactive oxygen species (ROS) or free radicals – caused by cell stress or metabolism.

Researchers from SMART's Antimicrobial Resistance (AMR) interdisciplinary research group, alongside their collaborators, have discovered a new stress signalling system that enables bacteria cells to adapt and protect themselves against the immune system and certain antimicrobial agents.

An enzyme, RlmN, was observed to directly sense chemical and environmental stresses, and rapidly signal for the production of other proteins that allow the bacteria cell to adapt and survive. This breakthrough discovery of RlmN as a stress sensor has revealed a new mechanism of antimicrobial resistance that can be targeted for drug development.

BACKGROUND

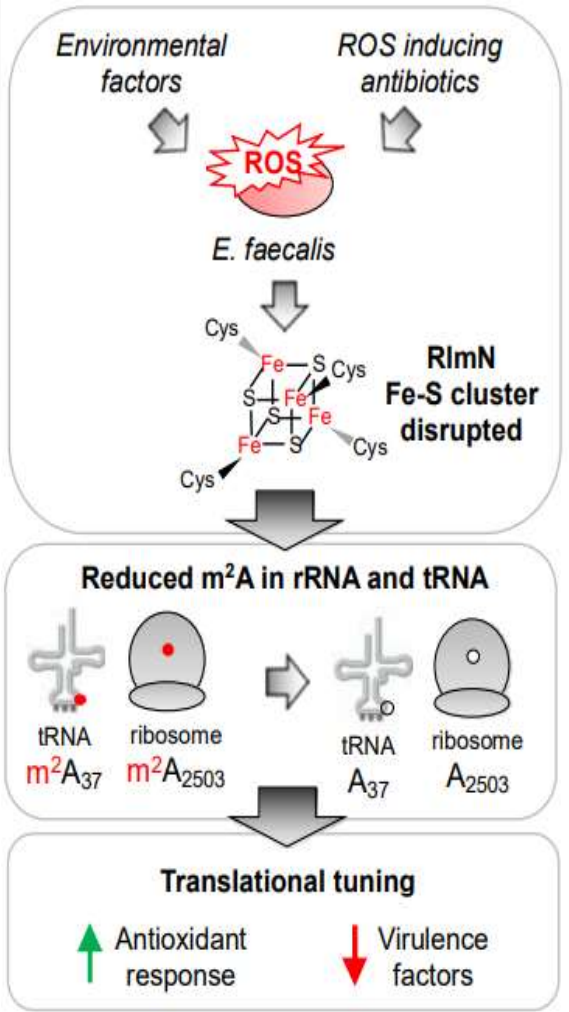
The increasing resistance of bacteria against antimicrobials is a silent global pandemic that endangers public health, as it diminishes the effectiveness of current antibiotics and raises mortality rates.

Understanding the mechanisms bacteria utilise to adapt and evolve against stressors can help researchers develop new and novel therapies to combat AMR.

METHODOLOGY

Researchers exposed Enterococcus faecalis (E. faecalis) cells to low, non-toxic doses of various antibiotics and toxic chemicals made by the immune system.

Using a sophisticated mass spectrometry technology developed at SMART and MIT, researchers simultaneously identified 50 different Ribonucleic acids (RNA) modifications when E. faecalis bacterial cells were exposed to very low, non-toxic doses of a wide variety of antibiotics and toxic chemicals made by the immune system.



Working model of RlmN as a sensor for oxidative stress

RESULTS

Researchers found that only one of the 50 modifications changed – a chemical called 2-methyladenosine (m2A) decreased, and proved that this modification was made by RlmN in E. faecalis and went on to show how it is inactivated by ROS.

The discovery of the RlmN system illustrates that cells possess a much quicker mechanism for cell responses.

CONCLUSION

The researchers concluded that RlmN inhibition represents a signalling mechanism for bacterial drug resistance and immune evasion, as ROS is induced by certain antibiotics and human immune cells. This discovery is the first example of a direct connection between a sensor system and translation machinery to generate proteins to combat ROS.

Moving forward, SMART AMR will work on gaining a comprehensive understanding of this new signalling mechanism, enabling the development of new and improved drugs.

In collaboration with: Massachusetts Institute of Technology, Nanyang Technological University Singapore, SCELSE