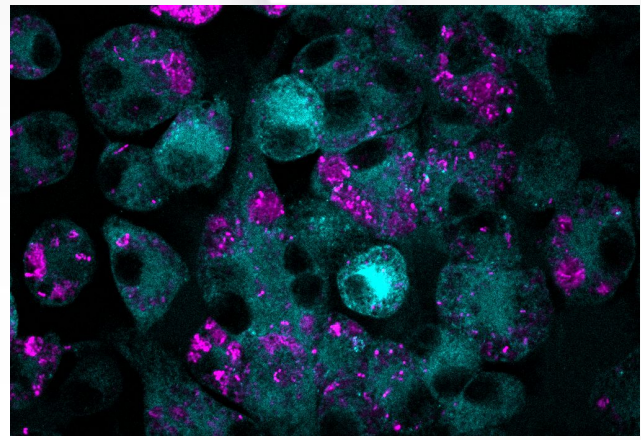


SMART OVERCOMING VANCOMYCIN RESISTANCE WITH NOVEL COMBINATION THERAPY

Singapore-MIT Alliance for Research and Technology

Vancomycin-resistant *Enterococcus faecalis* (VRE) is a 'hard-to-kill' bacteria due to its increasing antimicrobial resistance and can cause serious infections such as urinary tract, wound, and bloodstream infections. Current treatment options for VRE infections are limited due to its intrinsic and acquired resistance to the antibiotic, vancomycin, and other commonly used antibiotics.

Developed by SMART AMR researchers and their collaborators, the novel combination therapy using mitoxantrone (MTX) and vancomycin fights VRE and accelerates wound healing. With this breakthrough and research foundation, researchers can potentially innovate new therapies to overcome vancomycin resistance in the future.

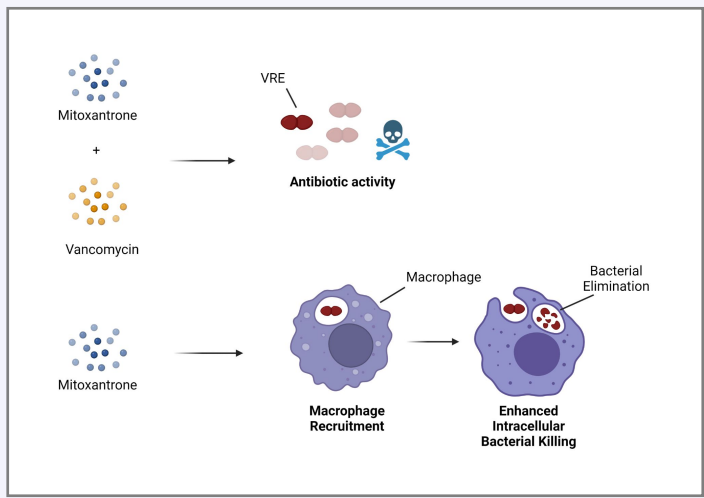


A confocal microscopy image of macrophages treated with MTX (cyan) that have eaten bacteria (magenta).

BACKGROUND

Why is this important?
Facing the growing threat of antimicrobial resistance, new and innovative approaches to treating bacterial infections are being developed, including the use of antimicrobials and host-targeted therapies. The novel combination therapy using MTX and vancomycin presents a highly effective treatment for VRE infections.

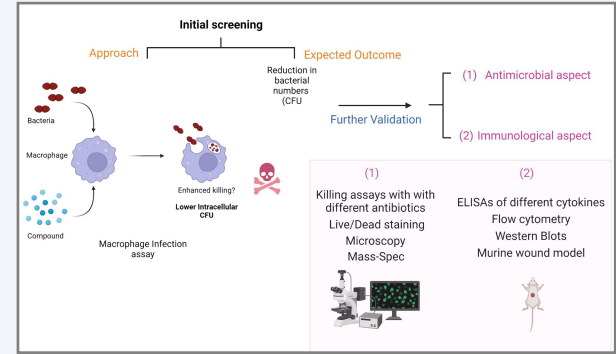
RESULTS



MTX was found to have potent antimicrobial activity against gram-positive bacteria and synergises well with vancomycin against VRE. MTX was also discovered to promote the recruitment of immune cells to the wound site and enhance the killing of bacteria.

Image created with BioRender.com

METHODOLOGY



The initial screening evaluated macrophages for their ability to kill bacteria in the presence of the compounds. MTX was further validated and evaluated for its antimicrobial and immunological activity, in combination with other antibiotics or alone, through in vitro killing assay experiments and using an in vivo mouse wound infection model. Image created with BioRender.com

CONCLUSION

The researchers discovered the synergy between MTX and vancomycin to create a highly effective dual bacterium- and host-targeted therapy against VRE infections.

The novel combination therapy targets both VRE and the host, which stops the growth of VRE and stimulates the host immune system. By enhancing the host immune system, it improves bacterial killing and wound healing by bringing more immune cells to the site of infection and by making the immune cells better at killing bacteria.

The researchers are also furthering their research to focus on the development of topical treatments for chronic diabetic wound infections.