Spider peptides battle superbugs and cancer

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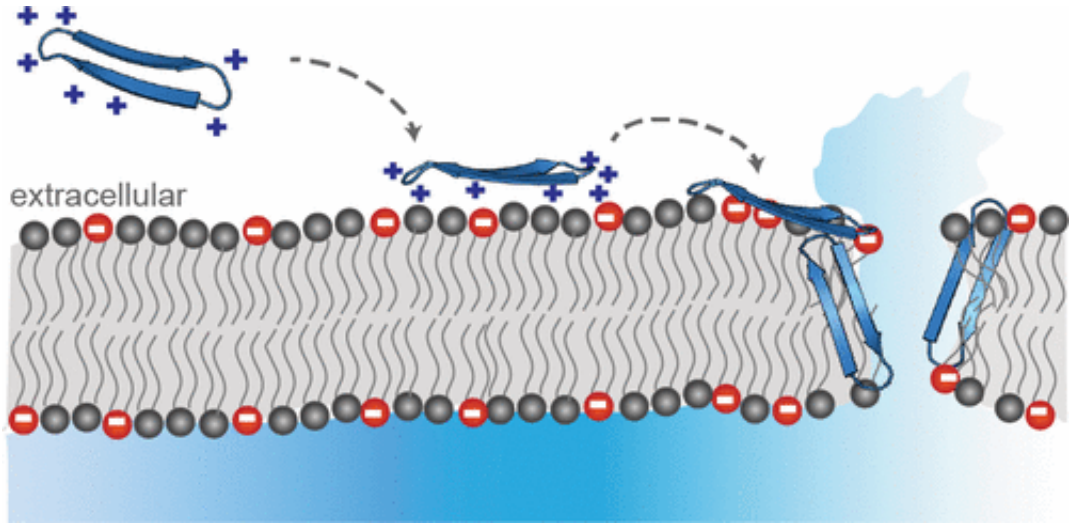

Credit: American Chemical Society

As antibiotic resistance rises and fears over superbugs grow, scientists are looking for new treatment options. One area of focus is antimicrobial peptides (AMPs), which could someday be an alternative to currently prescribed antibiotics, many of which are becoming increasingly useless against some bacteria. Now, a team reports in *ACS Chemical Biology* that they have improved the antimicrobial—and anticancer—properties of an AMP from a spider.

According to the U.S. Centers for Disease Control and Prevention, 2 million people become infected with antibiotic-resistant bacteria in the U.S. each year. Because no known antibiotics work against these

bacteria, patients simply have to hope that their natural defenses eventually overcome the infection. But some patients experience severe symptoms, landing them in a hospital, and in extreme cases, they could die. Researchers are trying to find alternatives to traditional antibiotics, and one such possibility is a group of peptides called AMPs. These peptides are found in all plants and animals as a type of immune response and have been shown to be potent antibiotics in the laboratory. Gomesin, an AMP from the Brazilian spider *Acanthoscurria gomesiana* can function as an antibiotic, but it also has anticancer activity. When gomesin was synthesized as a circle instead of as a linear structure, these characteristics were enhanced. Sónia Troeira Henriques and colleagues wanted to further boost the peptide's traits.

The team made several variations of the cyclic gomesin peptide and found that some of these were 10 times better at killing most bacteria than the previously reported cyclic form. In other experiments, the new AMPs specifically killed melanoma and leukemia cells, but not breast, gastric, cervical or epithelial cancer cells. The researchers determined that the modified peptides killed bacteria and cancer cells in a similar way—by disrupting the cells' membranes. The group also notes that the modified AMPs were non-toxic to healthy blood cells.

More information: Sónia Troeira Henriques et al. Redesigned Spider Peptide with Improved Antimicrobial and Anticancer Properties, *ACS Chemical Biology* (2017). DOI: 10.1021/acschembio.7b00459

Abstract
Gomesin, a disulfide-rich antimicrobial peptide produced by the Brazilian spider Acanthoscurria gomesiana, has been shown to be potent against Gram-negative bacteria and to possess selective anticancer properties against melanoma cells. In a recent study, a backbone cyclized analogue of gomesin was shown to be as active but more stable than its native form. In the current study, we were interested in improving the

antimicrobial properties of the cyclic gomesin, understanding its selectivity toward melanoma cells and elucidating its antimicrobial and anticancer mode of action. Rationally designed analogues of cyclic gomesin were examined for their antimicrobial potency, selectivity toward cancer cells, membrane-binding affinity, and ability to disrupt cell and model membranes. We improved the activity of cyclic gomesin by ~10-fold against tested Gram-negative and Gram-positive bacteria without increasing toxicity to human red blood cells. In addition, we showed that gomesin and its analogues are more toxic toward melanoma and leukemia cells than toward red blood cells and act by selectively targeting and disrupting cancer cell membranes. Preference toward some cancer types is likely dependent on their different cell membrane properties. Our findings highlight the potential of peptides as antimicrobial and anticancer leads and the importance of selectively targeting cancer cell membranes for drug development.

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