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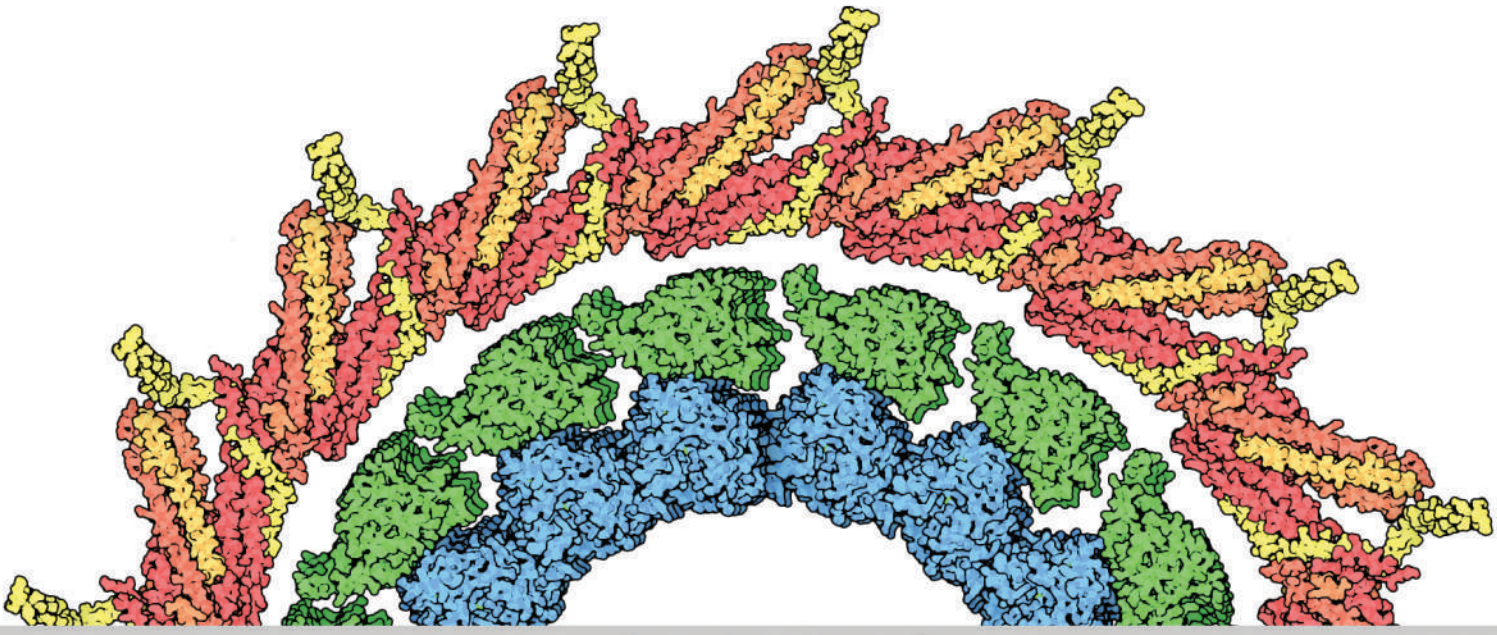

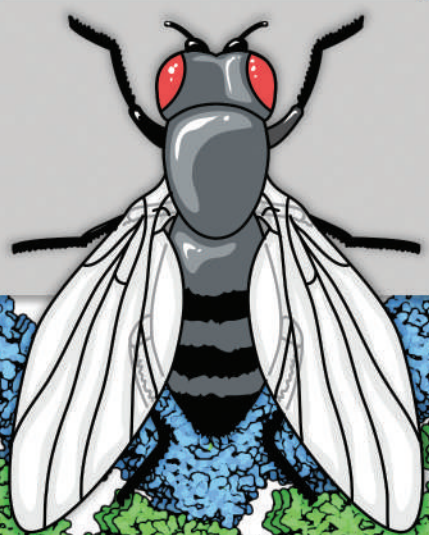

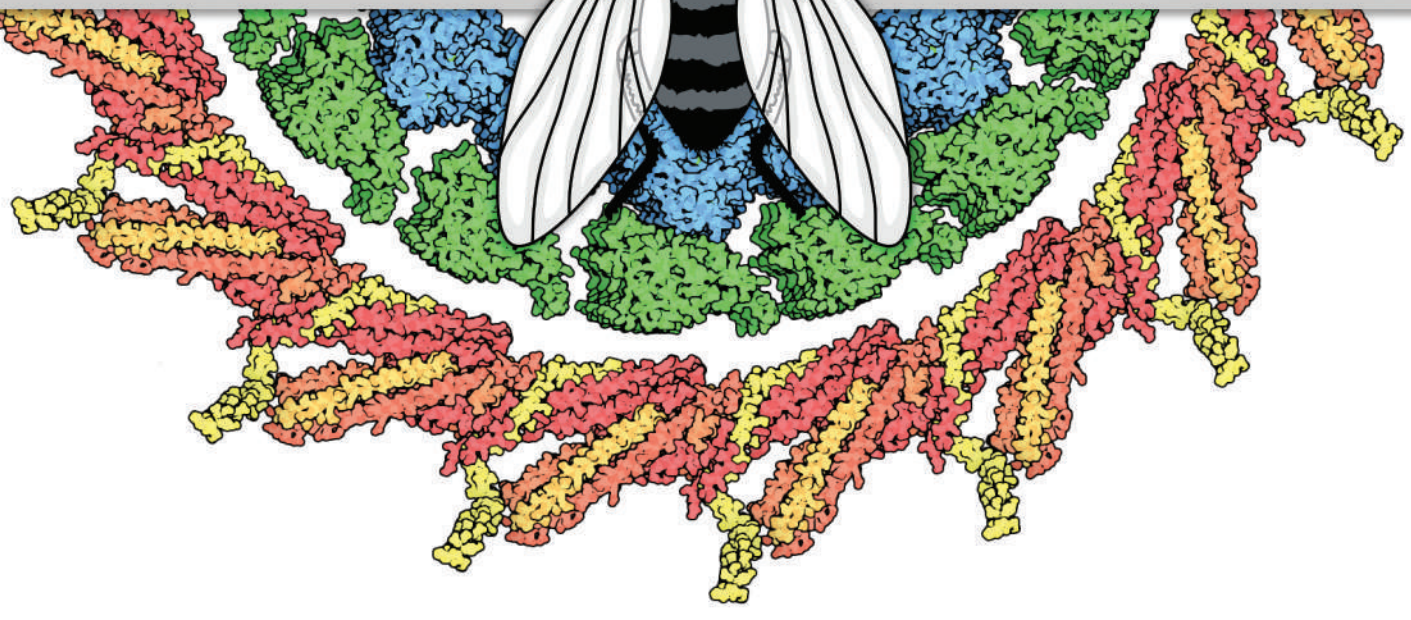

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Resisting Antimicrobial Resistance: Flavodoxin Inhibitors to Combat *Helicobacter pylori* Infection

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In 2017, the World Health Organization included Helicobacter pylori in the first ever priority list of antibiotic-resistant bacteria. These microorganisms represent a huge threat to human health, so the development of novel and effective treatments against them is urgently needed. Regarding Helicobacter pylori, several compounds have been identified acting on specific therapeutic targets such as its flavodoxin, a small redox protein which takes part in an essential pathway for the bacterium´s survival. Following several rounds of rational redesign, the in vitro therapeutic indexes of these compounds against reference stains and drug-resistant clinical isolates have been raised. Furthermore, these inhibitors are able to significantly reduce the gastric bacterial load and eradicate the infection in up to 60% of the treated mice when used as sole agents. After increasing their aqueous solubility by incorporation of polar groups, the metabolic stability of some of these new variants is improved. On the other hand, the efficacy of these derivatives against a variety of bacteria from different phyla reveals that they seem to be selective for Helicobacter pylori and thus less damaging to the human gastrointestinal microbiota than broad-spectrum antibiotics. Therefore, after unraveling its mechanism of action and optimizing its pharmacokinetic properties, this new family of antimicrobials could constitute a good alternative to fight *Helicobacter pylori* resistant strains.

Keywords

Medicinal Chemistry | Drug Discovery | Antimicrobial Resistance | Flavodoxin