Exploring the *Trichuris* peptidome as a source of novel antimicrobials

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Trichuris (whipworm) is a genus of parasitic worms that live in the gastrointestinal tract of mammals. These parasites come into direct contact with the host colonic microbiota and are known to modulate this microbial community to promote their own survival. One way that these worms may perturb the host gut microbiota is through the secretion of antimicrobial peptides (AMPs), which are key, yet somewhat underappreciated, components of the invertebrate immune system. Data from our research team shows that at least four newly discovered whipworm AMPs have efficacy against *Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli* and *Acitenobacter baumannii* (all of which are WHO priority pathogens, posing the biggest threat to human health due to high rates of antimicrobial resistance), while an additional peptide shows broad spectrum efficacy against clinically relevant Gram-negative and positive bacterial pathogens. In addition, all five peptides demonstrate low toxicity against host cells and four of the five are highly stable against host serum proteases. This combination of potent antimicrobial activity, low host toxicity and high serum stability is rare for AMPs, with many drug discovery programs undergoing great efforts to improve the pharmacological profiles of AMP candidates. Given that many parasitic helminths, including *Trichuris* species, have evolved to live in close contact with their host and associated microbial communities, this combination may be a pre-requisite for such AMPs, which must be stable enough to withstand host conditions (e.g. body temperature and proteolysis) whilst causing minimal toxicity. This work may pave the way for the discovery and development of novel antimicrobials from other helminths, which with a few exceptions, are largely underexplored.