Title:

Endosymbiotic Bacteria of Shipworms (Bivalvia: Teredinidae) Secrete Compounds with Anti-Parasitic Activity

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Abstract:

Owing to the tremendous biodiversity in the oceans, marine bioprospecting, despite its short history, has already yielded many unique molecules with tremendous therapeutic potential. Shipworms are marine bivalves that survive by borrowing into and consuming wood, a lifestyle entirely enabled by their symbiotic bacteria. In terrestrial xylophagous animals, cellulose-digesting symbiotic bacteria reside in the digestive tract in direct contact with the substrate. In stark contrast, the shipworm digestive tract has few bacteria and the caecum, the primary site of wood digestion, lacks any bacterial community. Since digestion of lignocellulosic substrates provides a nutrient-rich environment, the lack of bacteria in this organ suggests the presence of antibiotic activity as well as celluolytic enzymes. Analysis of the genomes of shipworm symbionts reveals a significant commitment to the production of polyketide and non-ribosomal peptide secondary metabolites. The capacity to produce diverse and unique secondary metabolites combined with the demonstrated ability of shipworm symbionts to produce compounds that move through multiple cellular compartments and effect processes distant from their living quarters suggests a reservoir of unusual anti-microbial compounds worthy of investigation. In preliminary studies, we observed that culture supernatant (SN) from symbiont strain-1 inhibited intracellular growth of the apicomplexan parasites, C. parvum and T. gondii, without toxicity to the host cells. In contrast, SN from a closely related strain (symbiont-2) had no effect on parasite burden. Additionally, strain-1 SN, but not strain-2 SN, exhibited activity against two gram+ bacteria. Comparison of strain-1 and strain-2 genomes identified a non-ribosomal peptide synthase locus absent in the inactive strain. Fractionation of strain 1 SN identified two fractions containing anti-parasitic activity and indicated that the source of the activity is a small molecule. Purification of the compound and identification of its target is ongoing. These studies have tremendous potential to open up a new area of anti-parasitic drug discovery, holding the promise of new molecular targets for drug development, potentially with broad application to many pathogens.