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The neural basis of host seeking in skin-penetrating nematodes

Gastrointestinal parasitic nematodes infect over a billion people worldwide and are a major cause of neglected tropical disease. Many of these parasites have an infective third-larval stage that actively searches for hosts using host-emitted sensory cues, and then infects by penetrating through host skin. We are interested in understanding the host-seeking behaviors of infective larvae, as well as the molecular, cellular, and circuit mechanisms that drive host seeking. We use the human-parasitic threadworm Strongyloides stercoralis for these studies because S. stercoralis is unique among parasitic nematodes in its amenability to genetic manipulation. We have shown that S. stercoralis infective larvae are robustly attracted to a diverse array of human-emitted odorants and mammalian body temperature. In this talk, I will focus primarily on our investigations into heat-seeking behavior. Using CRISPR/Cas9 mutagenesis, we identified a cGMP pathway that is required for heat seeking in S. stercoralis. We then identified the primary thermosensory neurons in S. stercoralis, and found that they use a novel temperature-encoding strategy to precisely detect temperatures ranging from ambient to host body heat. We also identified three S. stercoralis thermoreceptor proteins that act in the primary thermosensory neurons, one of which senses temperatures ranging from ambient to host body heat and two of which are tuned specifically to temperatures near host body heat. Our results pinpoint the parasite-specific neural adaptations that enable parasitic nematodes to target humans, and may facilitate the development of novel infection control strategies.