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Commentary

Understanding Hidden Antigens and Targeting Parasitic Nematodes

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Nematodes can be free-living or parasitic in nature. Infections with parasitic nematodes that directly or indirectly affect the health and productivity of humans and livestock have been the subject of scientific studies for decades. Overall, the treatment and control of nematode parasites are limited and dependent on single or repeated administration of anthelmintics, a strategy that has led to true anthelmintic resistance in animals and the concern for resistance in mass drug administration programs for humans. Efforts to discover new agents that offer improved performance in efficacy, safety and convenience are complicated with many challenges (Geary et al., 2015). An alternative strategy to worm control has been vaccination, where the concept of targeting intestinal proteins as 'hidden antigens' (Munn, 1997) has been explored for several helminth parasites with mixed results (Bassetto et al., 2011; Morris et al., 2013; Pearson et al., 2010). Global 'omic' approaches are now paving the way to better understand the biology of many organisms and to help identify and/or infer functional attributes of various genes and proteins (Rosa et al., 2015; Taylor et al., 2013) that might identify "soft spots" in the organism(s) that in turn greatly narrows the large numbers of targets that could be exploited for therapeutic or prophylactic approaches.

In this issue of *Ebiomedicine*, Wang et al. (2015) describe the establishment of a comprehensive functional database for nematode intestinal proteins. Using transcriptional and proteomic complements of representative nematodes, a selection of protein families that are universal or restricted to intestinal regions (IntFams) forms the basis of the study. While *Haemonchus contortus*, *Ascaris suum* and *Trichuris suis* are used as surrogates for similar niche specific human-gastrointestinal infections of *Necator americanus*, *Ascaris lumbricoides* and *Trichuris trichiura*, inferences for clade-specific representative parasitic filarial nematodes (*Brugia malayi* and *Loa loa*) have also been derived. The study is centered on the identification of conserved IntFams (cIntFams) across all nematodes that have the potential for broad-spectrum pan-nematoda control, while species or clade-specific divergent IntFams (ncIntfams) represent novel functions. There are a number of reasons that make this study interesting. Firstly, this knowledgebase provides a launchpad not only for directed research to understand inherent biological functions and pathways, but also as a gateway for the rapid identification of potential therapeutic targets. Secondly, if we consider the time and effort required for traditional drug screening in experimentally-infected animals or *in-vitro* screens, fusion of molecular techniques with evolutionary informatics presents a fertile ground for more effective drug discovery efforts (Geary et al., 2015). As a proof of principle, Wang, Q. et al., describe the identification of IntFam proteins that are homologous to host proteins but are sufficiently different to allow for distinct ligand binding, a concept that, certainly warrants further drug-targeting studies. Further, not all parasitic nematodes can be maintained *in-vitro* or in animal models, and hence there is limited availability of biological material available to the scientific community. Though drawing parallels from the database can be very helpful in such cases, one needs to be cautious extrapolating across an entire phylum given the variability among the nematode genomes. Understanding the functional implications of these species specific IntFams would enable selective strategies to target intestinal parasitic nematodes, filarial parasites, and other veterinary important nematode parasites.

From the therapeutic viewpoint, the best and quick way to address the hurdles of controlling parasitic nematodes lies in the solid understanding of the basic biology of the organism and drawing parallels to targets of approved drugs that already have established safety profiles. This approach of repurposing FDA approved drugs (O'Connell et al., 2015) greatly cuts down the huge lag-time in identifying lead-compound(s) for testing and is gaining momentum in the global efforts to control helminth infections. This study by Wang et al., hopefully will be a beneficial tool for narrowing down such targetable pan-nematoda or tissue-specific or species specific 'spot spots' that can possibly address potential problems of drug resistance as well.

Conflict of Interest

I declare no competing interests.

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