Parasite that causes lymphatic filariasis releases vesicles containing microRNA that may control host

September 24 2015

Lymphatic Filariasis is a neglected tropical disease caused by three different species of parasitic worm, which are spread between human hosts by mosquitos. The molecular interactions between the worm, mosquito and human are dynamic and delicately balanced, meaning that disrupting these interactions might be an avenue for the development new therapeutic treatments.

The worm *Brugia malayi*, one of the parasites which causes elephantiasis, develops as larvae inside the mosquito vector until it reaches the infective L3 stage where it is transmitted back into the human host when the mosquito drinks blood. The adults live and mate within the human lymphatic system while offspring are shed into the bloodstream to be picked up again by mosquitoes. While the life-cycle is well documented it has been harder to define the exact molecules that the parasite uses to control its hosts. Research has traditionally searched for secreted proteins and while there are several candidates, along with proteins expressed on the surface of the parasite that may play a part, recent research has revealed that small non-coding RNAs may also be involved in controlling the host's response to the parasite.

Researchers examined both infective L3 stage larvae and adult worms to see if they produced any exosome-like extracellular vesicles; small bioactive vesicles with a homologous size and shape. They found that the infective larvae released small microvesicles abundant in microRNAs -

small non-coding RNAs used to control gene expression. Some of these miroRNAs are identical to those used by the human host, suggesting that L3 stage larvae may produce these vesicles specifically to aid with host infection.

Analysis of the contents of the larval vesicles also revealed proteins characteristically found in exosomes as well as proteins able to bind to bioactive molecules such as host proteins and DNA. Several microRNAs were found to share sequence conservation with human microRNAs including perfectly conserved seed sites (the area which recognizes and binds to the regulatory target). Using florescent dyes, the researchers also showed that the vesicles were internalized by human macrophages where they activated a pro-inflammatory response pathway.

This research points to an exciting new mechanism for host-pathogen interaction in the parasites that cause Lymphatic Filariasis. Further study of these vesicles and the way they interact with host tissues may reveal new opportunities for therapeutic targets or treatment strategies to prevent infection.

More information: *PLOS Neglected Tropical Diseases*, dx.plos.org/10.1371/journal.pntd.0004069

Provided by Public Library of Science