Yepes, E., Varela-M, R.E., López-Abán, J., Rojas-Caraballo, J., Muro, A., and Mollinedo, F. (2015). Inhibition of granulomatous inflammation and prophylactic treatment of schistosomiasis with a combination of edelfosine and praziquantel. *PloS Neglected Tropical Diseases* 9(7):e0003893.

BACKGROUND:
Schistosomiasis is the third most devastating tropical disease worldwide caused by blood flukes of the genus Schistosoma. This parasitic disease is due to immunologic reactions to Schistosoma eggs trapped in tissues. Egg-released antigens stimulate tissue-destructive inflammatory and granulomatous reactions, involving different immune cell populations, including T cells and granulocytes. Granulomas lead to collagen fibers deposition and fibrosis, resulting in organ damage. Praziquantel (PZQ) is the drug of choice for treating all species of schistosomes. However, PZQ kills only adult Schistosoma worms, not immature stages. The inability of PZQ to abort early infection or prevent re-infection, and the lack of prophylactic effect prompt the need for novel drugs and strategies for the prevention of schistosomiasis.
METHODOLOGY/PRINCIPAL FINDINGS:
Using in vitro and in vivo approaches, we have found that the alkylphospholipid analog edelfosine kills schistosomula, and displays anti-inflammatory activity. The combined treatment of PZQ and edelfosine during a few days before and after cercariae infection in a schistosomiasis mouse model, simulating a prophylactic treatment, led to seven major effects: a) killing of Schistosoma parasites at early and late development stages; b) reduction of hepatomegaly; c) granuloma size reduction; d) down-regulation of Th1, Th2 and Th17 responses at late post-infection times, thus inhibiting granuloma formation; e) upregulation of IL-10 at early post-infection times, thus potentiating anti-inflammatory actions; f) down-regulation of IL-10 at late post-infection times, thus favoring resistance to re-infection; g) reduction in the number of blood granulocytes in late post-infection times as compared to infected untreated animals.
CONCLUSIONS/SIGNIFICANCE:
Taken together, these data suggest that the combined treatment of PZQ and edelfosine promotes a high decrease in granuloma formation, as well as in the cellular immune response that underlies granuloma development, with changes in the cytokine patterns, and may provide a promising and effective strategy for a prophylactic treatment of schistosomiasis.