

Can parasites and their products provide therapeutic leads?

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When we think of parasites be they endoparasites like protozoans or helminths, or ectoparasites like ticks and mites, we inadvertently think of the negative impact they have on human and animal health. This is because these parasites cause diseases which affect a large segment of the world's population. For instance, more than 1.5 billion people, or 24% of the world's population, are infected with soil-transmitted helminth infections worldwide, mainly in tropical and subtropical areas, with the greatest numbers occurring in sub-Saharan Africa, the Americas, China and East Asia. Over 267 million preschool-age children and over 568 million school-age children live in areas where these parasites are intensively transmitted, and are in need of treatment and preventive interventions.¹

A successful parasite will need to evolve to better counter or hide from the host's immune system and thus immunomodulation of the host's immune response is an important goal of a successful parasite.² In addition, individuals with a specific parasitic infection may actually be protected from other disease conditions.³ A review by Hunter and McCay (2004)⁴ provided an impetus for researchers to explore the potential of helminth therapy on enteric inflammation as it was postulated that immune deviation whereby Th-2 cytokines were mobilised in response to helminth infections will prevent or antagonise disease-promoting Th-1 events in the gut e.g. inflammatory bowel disease (IBD).

Autoimmune diseases are now estimated to affect almost 10% of the world's population.⁵ With the accruing global burden of autoimmune diseases, there is increased interest in harnessing the ability of helminths to activate immunoregulatory circuits and control immunity. Immunologists have also focussed on the excretory and secretory products released by helminths that can immune-modulate the host's responses to serve as potential therapeutic proteins in the treatment of allergic and autoimmune inflammatory disease. Helminth secretomes are a rich source of novel drug and vaccine targets and a number of potential secretomes have been identified such as protease inhibitors with immunomodulatory properties, for example cystatins

and serpins.⁶ Mouse models have provided strong evidence that helminthic therapy, ES components and helminthic-derived synthetic molecules can treat or prevent inflammatory diseases such as IBD, type 1 diabetes, multiple sclerosis (MS), rheumatoid arthritis (RA) and asthma.⁷ While results of human trials in celiac disease, ulcerative colitis, MS, RA and psoriasis have established that therapy is safe with some evidence of therapeutic effect, the results with these human trials are not as striking as those using the mouse models.⁷ Further studies are necessary to characterise and mimic the full immunomodulating abilities of helminths to capitalise on their potential as therapeutic agents of autoimmune diseases.

Another approach to helminth therapy would be to develop biotherapeutics from helminths. A recent study identified two molecules (cystatin and MIF-2) from filarial parasites which showed potential as small molecules for the treatment of colitis as administration of these molecules significantly reduced inflammation and reversed clinical symptoms.⁸ Another study by Li et al (2014) demonstrated that a recombinant *Schistosoma japonicum* cystatin (rSJ-Cys), a cysteine protease inhibitor that induces regulatory T-cells, was able to provide significant therapeutic effects on caecal ligation and puncture- induced sepsis in mice with increased survival rates, suggesting that rSJ-Cys is a promising therapeutic agent on sepsis.⁹

Therefore parasites do have a potential in therapy of diseases. More in-depth studies are needed on parasites particularly helminths, to explore their potential as immunoregulators / therapeutic agents for treatment of both inflammatory diseases as well as other diseases. Research on protozoan parasites as potential therapeutic agents is yet another new area that can be considered.

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