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Commentary: "Rigidity and Resistance of Larval- and Adult Schistosomes-Medium Interface"

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The article "Rigidity and resistance of larval- and adult schistosomes-medium interface" is devoted to one of the most severe diseases, prevalent in tropical and subtropical areas. Schistosomiasis is a disease related to poverty since the lack of safe drinking water and adequate sanitation are crucial cofactors creating a fertile environment for the development and spread of parasites, especially in agricultural and fishing populations. Due to these conditions, the World Health Organization (WHO) estimated that at least 91.4% of treatment for schistosomiasis is made in Africa[1,2]. However, environmental changes and migrations are increasing the spread of schistosomiasis in the world.

There are two forms in which the disease occurs, i.e., intestinal and urogenital[3], this latter being also related to HIV infection, especially in women[4]; in general, the most vulnerable category are children due to the very frequent contact with infected water; tourists also are affected, showing unforeseen complications as paralysis[5].

The dramatic size of the schistosomiasis spread is demonstrated by the number of people needing preventive treatment which is about 206.4 million in 2016[1].

Our work aims to contribute to the urgent need pointed out by WHO, which includes schistosomiasis within its mission against the neglected tropical diseases, to increase research on schistosomiasis in order to identify effective prevention and treatment protocols[2].

In this framework, our studies have been focused on understanding how larval, developing, and adult blood flukes, *Schistosoma mansoni* and *Schistosoma haematobium* get their nutrients from the host bloodstream while evading attack by immune effectors, and thus, can unscathed live and deposit eggs for years. Immunofluorescence studies, depletion of surface membrane cholesterol by methyl-β-cyclodextrin, and enzymatic inhibition and activation of sphingomyelin (SM) biosynthesis and hydrolysis revealed that SM in the schistosome outer lipid leaflet controls the worm surface membrane permeability[6]. Equilibrium in SM synthesis and hydrolysis allows entry of small nutritive molecules of <400 Da, and prevents access of larger molecules, namely cytotoxic mediators and antibodies. We have surmised that SM protects the worm surface membrane via interacting with surrounding water molecules to form a tight hydrogen bond barrier[7].

We adopted a complementary and unconventional approach in the study reported in the article "Rigidity and resistance of larval- and adult schistosomes-medium interface". From the scientific point of view, these results allowed a comparison among the rigidity of the different investigated Schistosoma. The determination of the strength of the parasite-medium interaction based on a hydrogen-bonded network furnishes a molecular explanation of the different schistosome resistance degree, providing useful information about the mechanisms of defense activated by the parasites against the immune system attacks. The study documents the inability of host antibodies and effectors to access the parasite outer lipid bilayer and challenges entrenched dogmas, namely the importance of schistosome antigens at the host-parasite interface as vaccine candidates, and ADCC (antibody-dependent cell-mediated cytotoxicity) as mechanism of innate and acquired resistance to the parasite.

From the methodological point of view, two main aspects of this article deserve to be highlighted: i) the focus on the molecular mechanisms; ii) the use of neutron scattering.

Biophysics is providing approaches and methods to medicine and immunology, which were not historically used. In the last years, it is now clearer that the conventional methods and techniques used in such domains need to find explanations and support in data obtained at a molecular level. Physics is increasingly involved in medical and immunological research, reflecting the need to use the physical point of view in such investigations. These trends are reflecting a crucial point: a change of spatial and time scale is necessary, and this can be achieved just by transcending the disciplinary boundaries. Sciences advocates interdisciplinarity to which the new generations of scientists need to be directed.

The use of neutron scattering in the biological and biochemical fields has been made possible by the constant improvement of the performances of the neutron spectrometers. Among the peculiarities making neutrons particularly appropriate for such studies, the main ones are[8]: i) they are non-destructive, ii) isotopic substitution; iii) matching between neutron features and typical biomolecular dimensions and times.

A wide range of neutron scattering techniques is at the disposal of biology and biochemistry and then medicine and immunology. For example, membranes and their interactions with proteins and drugs can be investigated by reflectometry[9]; small angle scattering opens the access to structural information of a biosystem by furnishing details about the interacting parts of the same biomolecular complex[10]; crystallography and diffraction allow to determine atomic positions in ordered and disordered systems, binding sites and hydration properties[11,12]. In this framework, elastic neutron scattering has been first successfully and systematically applied by Zaccai[13,14], who demonstrated the versatility of such technique in determining relevant features of increasing complexity systems, from proteins to organisms. Following his approach, we analysed our quasi-elastic neutron scattering data, by selecting the zero exchanged energy region and by characterising the rigidity – or flexibility – degree in relation with the resistance to a thermal stress. Since the quasi-elastic neutron scattering experiments allowed to us to determine the kind and the strength of the schistosome-medium interaction by the characterization of the diffusive dynamics[15], the power of this technique combined with a detailed analysis of the whole energy range is pointed out. It is crucial to remark that the opportunities offered by neutron scattering in medical and immunological domains will be boosted by the powerfully performing spectrometers, which are being built at the European Spallation Source (ESS).

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