

A protein has been identified as a potential therapeutic target for leishmaniasis vaccines

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According to the results of research led by the Complutense University of Madrid (UCM), one of the various strategies deployed by the Leishmania parasite to avoid triggering the human immune system is to activate the SHP-1 protein.

The parasite does this by secreting a molecule capable of interacting with the Mincle receptor expressed by antigen-presenting dendritic cells that help induce T-lymphocytes to trigger an immune response.

"For dendritic cells to be able to present antigens to T-lymphocytes, they must also have been infected by the pathogen, or must acquire 'remains' from another [infected cell](#). This latter process is called 'cross-antigen presentation' and requires specialized enzymatic machinery," explained Salvador Iborra, a researcher in the Department of Immunology, Ophthalmology and ENT at the UCM.

Besides helping to control physiological cell processes such as growth and proliferation, the newly discovered function of SHP-1 presented in

Cell Reports is to limit the capacity of dendritic cells to cross-present antigens in order to prevent autoimmune disorders, i.e. to prevent lymphocytes from attacking healthy body tissue. The parasite masks its presence by activating this aspect of [immune response](#) control.

SHP-1 inhibitors, key to vaccination

This study, conducted jointly with the Spanish National Centre for Cardiovascular Research (Spanish initials: CNIC) and the Champalimaud Centre for the Unknown in Lisbon, was conducted using genetically modified mice as an experimental model that lacks the Mincle receptor or the SHP-1 enzyme in dendritic cells.

"In addition, we have been able to test the usefulness of chemical compounds that block SHP-1 activation, such as NSC-87877. Among our results, we have shown that vaccination with [dendritic cells](#) treated with this inhibitor and loaded with parasite lysates induced a response in cytotoxic lymphocytes that protected the mice against infection," Iborra reported.

The UCM researcher added that SHP-1 not only inhibits cross-presentation of Leishmania antigens, but also of virus-infected and irradiated [cells](#); consequently, "SHP-1 is a potential target that could limit the effectiveness of a vaccine based on inactivated viruses or [parasites](#) and intended to induce a cellular response mediated by cytotoxic lymphocytes."

Although vaccines against canine leishmaniasis exist for dogs, which act as reservoirs of the disease, there are still no vaccines against the disease in humans, so "any advance in our knowledge of immunity to the parasite is useful for the development of an effective vaccine," Iborra

concluded.

More information: Sofía C. Khouili et al, SHP-1 Regulates Antigen Cross-Presentation and Is Exploited by Leishmania to Evade Immunity, *Cell Reports* (2020). DOI: [10.1016/j.celrep.2020.108468](https://doi.org/10.1016/j.celrep.2020.108468)

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