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Resistance to visceral leishmaniasis: new mechanisms involved

Researchers from CNRS, Université Toulouse III - Paul Sabatier and IRD have elucidated new molecular mechanisms involved in resistance to visceral leishmaniasis, a serious parasitic infection. They have shown that dectin-1 and mannose receptors participate in the protection against the parasite responsible for this infection, by triggering an inflammatory response, while the DC-SIGN receptor facilitates the penetration of the pathogen and its proliferation in macrophages[1]. This work, conducted on both mice and humans and published on 16 May 2013 in the journal *Immunity*, opens new perspectives for the prevention and treatment of this disease.

Leishmaniasis is one of the most serious fatal parasitic infections in the world: 1.5 to 2 million infected individuals are recorded every year, of which 500,000 involve cases of visceral leishmaniasis. This chronic disease is a public health problem in Latin America, Asia, Africa, and more recently, southern Europe.

Leishmania, the parasite responsible for the infection, colonizes the macrophages where it proliferates. Dectin-1, mannose and DC-SIGN are three receptors of the C-type lectin family, present on the surface of macrophages. Depending on their state of differentiation, they can either contribute to eliminating the parasite or instead facilitate its proliferation by hijacking the defence mechanisms of the macrophage to the parasite's advantage and thus bring about infection. These cells therefore represent a major target in the defence of the host against the pathogen.

This work, conducted by research teams from the Laboratoire Pharmacochimie et Pharmacologie pour le Développement (Université Toulouse III - Paul Sabatier/IRD) and the Institut de Pharmacologie et de Biologie Structurale (CNRS/Université Toulouse III - Paul Sabatier), was initially carried out on mice then on human cells. It shows that dectin-1 and mannose receptors have an inhibiting effect on the parasite. In fact, they trigger the production of oxygenated free radicals[2] and inflammatory mediators, thereby helping to eliminate the parasite. The researchers also highlighted the opposite role of the DC-SIGN receptor, which participates in the phagocytosis of *Leishmania* and favors its proliferation by inhibiting macrophage microbicidal activity.

[1] A macrophage is a cell of the immune system, located in tissues that can be subject to infection or an accumulation of debris that needs to be eliminated (liver, lungs, lymphatic ganglions, spleen, etc.), and which has in particular a phagocytosis function, in other words the ability to ingest and destroy parasites, bacteria, yeasts, cell debris, etc.

[2] Oxygenated free radicals are chemical species produced by macrophages that have the property of destroying pathogens.

Confirmed in humans, these results also show for the first time that C-type lectins control the balance between pro-inflammatory and anti-inflammatory lipid mediators, contributing to the orientation of the anti-parasitic defence.

This discovery represents a breakthrough in infectious diseases and could pave the way for the development of new medicines.

Bibliography

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