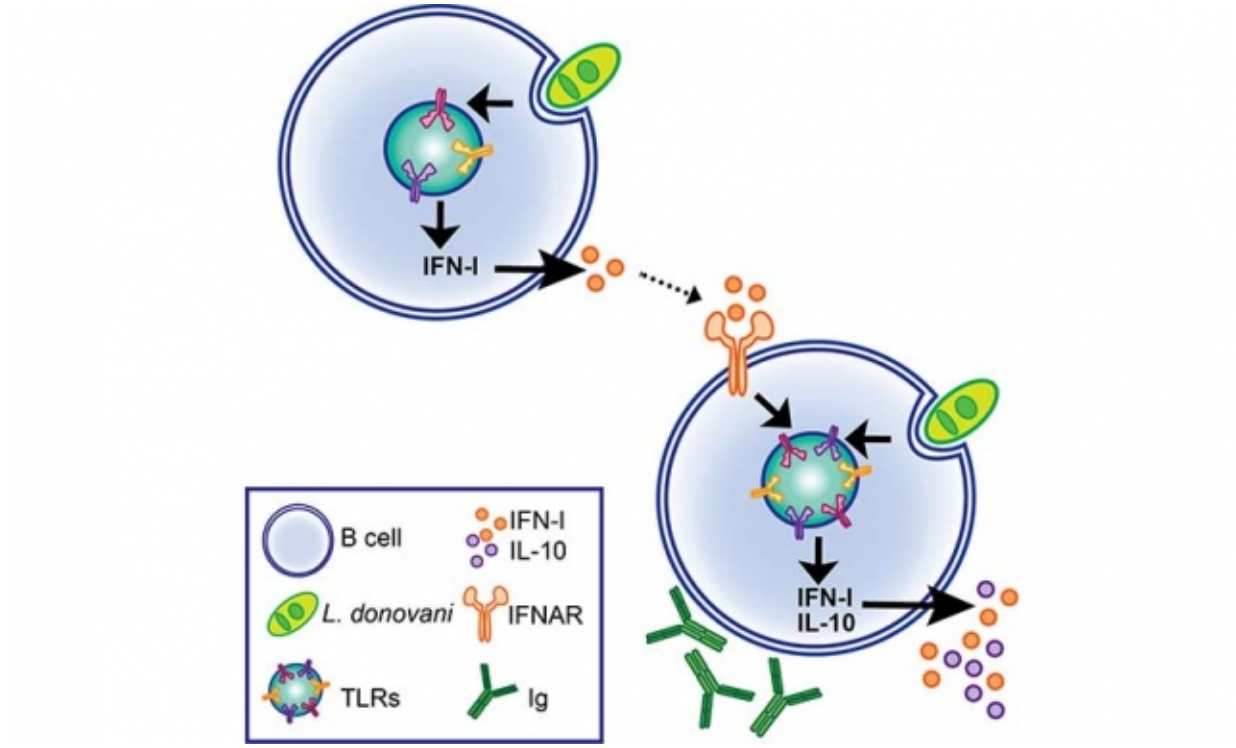
Mechanisms triggering excess antibody production during chronic infection

July 12 2016, by Gisèle Bolduc



Credit: Institut national de la recherche scientifique

Some autoimmune diseases and persistent infections are characterized by high levels of antibodies in the blood. But what are the causes of this hypergammaglobulinemia? A team headed by INRS's Professor Simona Stäger has successfully identified the mechanisms triggering the phenomenon. For the first time ever, she has established a link between

B-cell activation by a protein—type 1 interferon—and unusually high antibody levels.

The team has also discovered that a parasite can directly activate B cells—the cells responsible for producing unusually high antibody levels. Until now, there has been no evidence that B cells can be directly stimulated by the parasite known to cause visceral leishmaniasis, a neglected and often lethal tropical disease also characterized by high levels of antibodies.

How do Leishmania donovani parasites set off this harmful immune reaction? Proteins known as endosomal TLRs (toll-like receptors) recognize the parasites as pathogens, triggering proinflammatory responses.

"In the case at hand, TLRs induce the secretion of interleukin-10 proteins that reduce immune responses and type 1 interferons that increase B-cell antibody production. The fact that type 1 interferons contribute to hypergammaglobulinemia induction was completely unknown," explains Professor Stäger.

Of particular interest is the fact that activation pathways may play a role in other diseases characterized by rising antibody levels that exacerbate conditions. This is a major lead as this poorly understood phenomenon causes immune reactions and other immune pathologies.

More information: Sasha Silva-Barrios et al, Innate Immune B Cell Activation by Leishmania donovani Exacerbates Disease and Mediates Hypergammaglobulinemia, *Cell Reports* (2016). DOI: 10.1016/j.celrep.2016.05.028

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