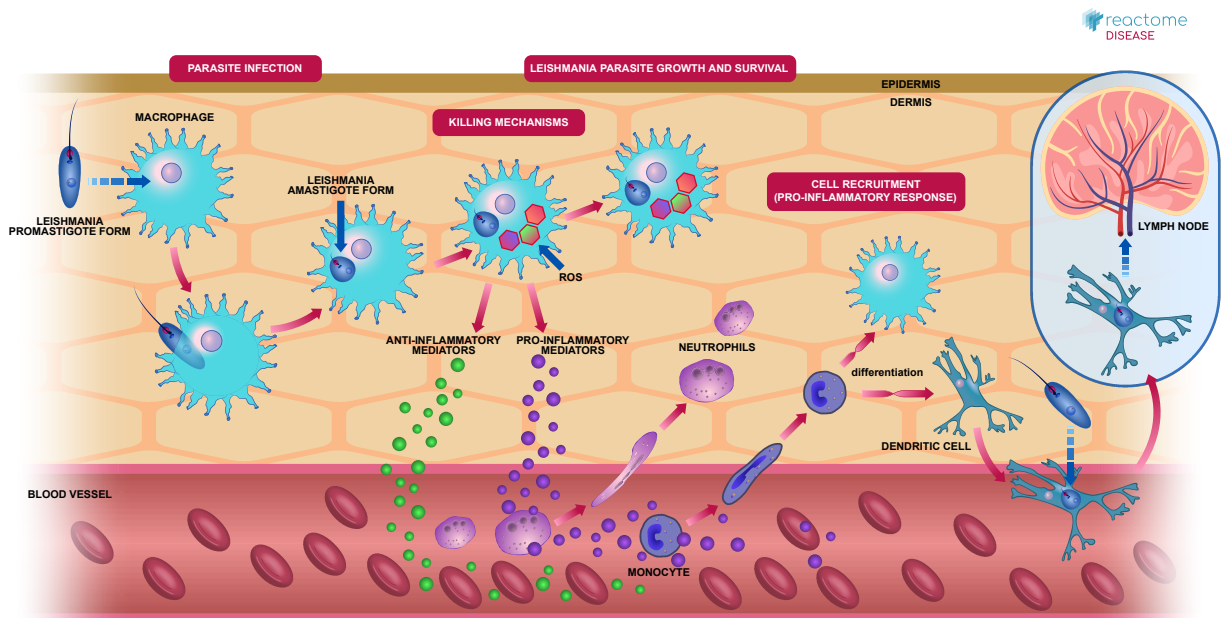


# Leishmania infection



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/textbook/).

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## Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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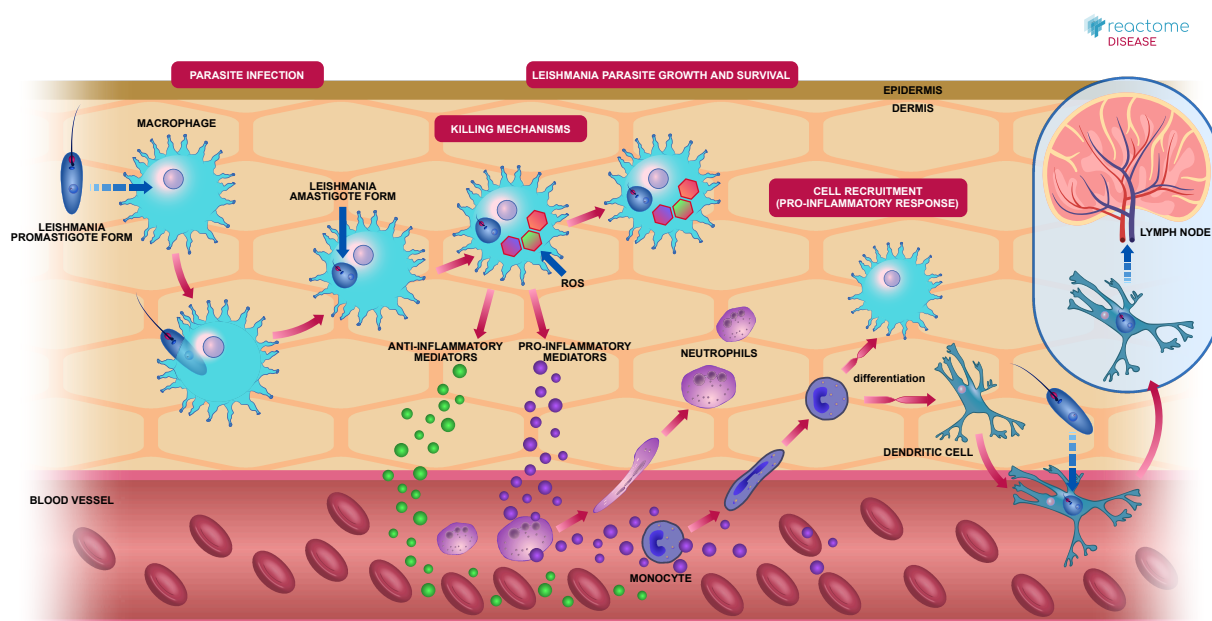
Reactome database release: 88

This document contains 5 pathways ([see Table of Contents](#))

## Leishmania infection ↗

**Stable identifier:** R-HSA-9658195

**Diseases:** cutaneous leishmaniasis



Intracellular parasites of the genus *Leishmania* constitute the etiologic agent of a disease complex called Leishmaniasis. *Leishmania* parasites alternate between two distinct developmental stages: the insect-adapted, flagellated, extracellular “promastigote” and the mammal-adapted, non flagellated, intracellular “amastigote” form, where the later resides within phagolysosomal vesicles of the phagocytic cell (Liu et al. 2012a). Paradoxically, the macrophage, which is the main host cell where the parasite replicates and grows, is at the same time the main cell responsible for its elimination.

The uptake of *Leishmania* promastigotes by host cells is a receptor mediated process that initiates phagocytosis (Ueno et al. 2012). Some parasites differentiate and survive within the macrophage phagolysosomes; others are killed by the acidic and higher temperature environment (Rossi et al. 2018). In the end, it is the balance between the host and parasitic factors that control the activation/deactivation of macrophages that determines the fate of the parasites as well as the infection outcome (Liu et al. 2012b).

The pathways curated here summarize the major steps of parasite internalization by the macrophage, the defence mechanisms that are turned on and the mechanisms of evasion of the parasite to counteract them.

## Literature references

- Rossi, M., Fasel, N. (2018). How to master the host immune system? *Leishmania* parasites have the solutions!. *Int. Immunol.*, 30, 103-111. ↗
- Ueno, N., Wilson, ME. (2012). Receptor-mediated phagocytosis of *Leishmania*: implications for intracellular survival. *Trends Parasitol.*, 28, 335-44. ↗
- Liu, D., Uzonna, JE. (2012). The early interaction of *Leishmania* with macrophages and dendritic cells and its influence on the host immune response. *Front Cell Infect Microbiol*, 2, 83. ↗

## Editions

2020-02-04	Reviewed	Gregory, DJ.
2020-02-05	Authored, Edited	Jassal, B.
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## Parasite infection ↗

**Location:** [Leishmania infection](#)

**Stable identifier:** R-HSA-9664407

**Diseases:** cutaneous leishmaniasis

# Leishmania phagocytosis



Leishmania parasites are dimorphic protozoa, being extracellular and flagellated (promastigotes) in the vector insect, and intracellular and aflagellated (amastigotes) in the host. While the vector fly feeds on the blood of the host, it transmits the promastigotes which are subsequently phagocytosed. The transition to the non motile form occurs within the phagosomal pathway; this process requires the delay of the maturation of the phagosome in such a way that the pH conditions are not harmful to the promastigote. Once it is in the amastigote form, maturation of the parasitophorous vacuole continues (Martínez López et al. 2018).

## Literature references

Martínez-López, M., Sancho, D., Iborra, S., Soto, M. (2018). *Leishmania* Hijacks Myeloid Cells for Immune Escape. *Front Microbiol*, 9, 883. ↗

## Editions

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## Killing mechanisms ↗

**Location:** [Leishmania infection](#)

**Stable identifier:** R-HSA-9664420

**Diseases:** cutaneous leishmaniasis

# WNT5:FZD7-mediated leishmania damping



The long-lasting *Leishmania* infection is established within macrophages in which the most effective killing response is the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS). (Rossi and Fasel 2018). Additionally, autophagy has been described as an innate immune mechanism for eliminating intracellular pathogens, although its role in restricting *Leishmania* replication is unclear (Veras et al. 2019)

## Literature references

Rossi, M., Fasel, N. (2018). How to master the host immune system? *Leishmania* parasites have the solutions!. *Int. Immunol.*, 30, 103-111. ↗

Frank, B., de Oliveira Almeida Petersen, AL., Weber, H., Scholz, CJ., Stigloher, C., Mottram, JC. et al. (2015). Autophagic digestion of *Leishmania major* by host macrophages is associated with differential expression of BNIP3, CTSE, and the miRNAs miR-101c, miR-129, and miR-210. *Parasit Vectors*, 8, 404. ↗

## Editions

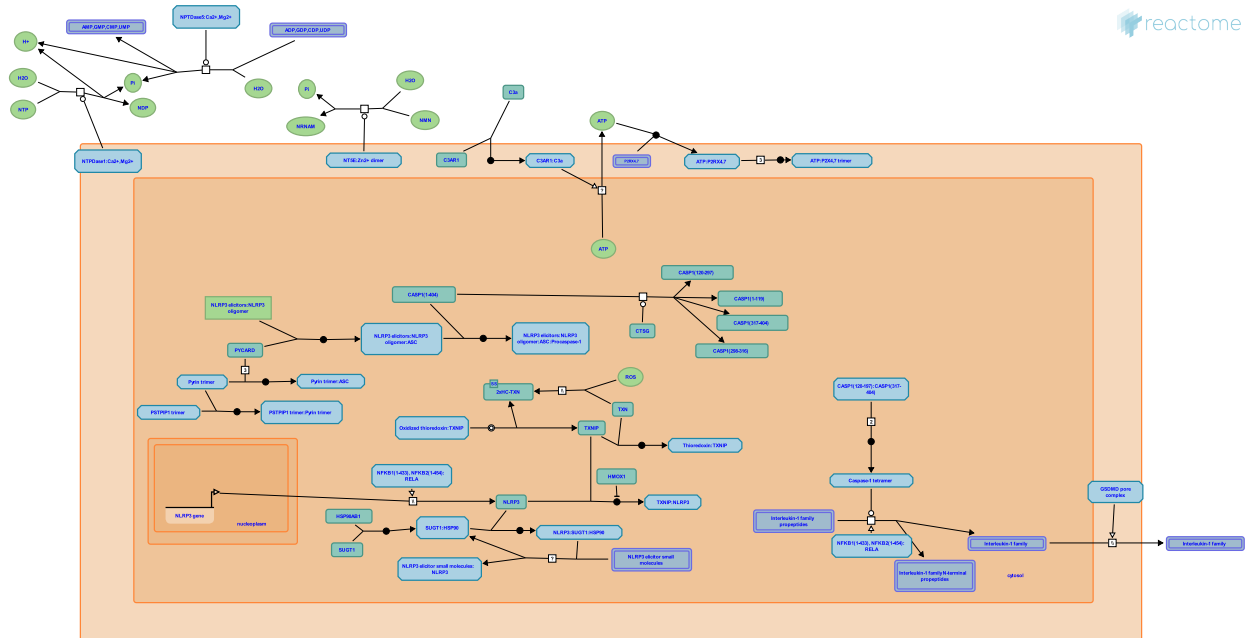
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# Cell recruitment (pro-inflammatory response) ↗

**Location:** Leishmania infection

**Stable identifier:** R-HSA-9664424

**Diseases:** cutaneous leishmaniasis



Migration of immune cells is orchestrated by a fine balance of cytokine and chemokine responses. During Leishmania macrophage interaction, either pro inflammatory or anti-inflammatory cytokines are produced, having an impact in the establishment of infection and further clinical outcome (Navas et al. 2014). Toll like receptors, GPCRs such as the purinergic receptors P2YRs, complement receptor 3A and interleukin receptor 15 amongst others, have been associated with the production of pro inflammatory cytokines (Lai and Gallo 2012 & Cekic et al. 2016). A strong pro inflammatory response in the acute phase of the infection helps to control the parasite load when the recruited cells enhance microbiocidal mechanisms. However, alterations in the chemokine network may contribute to uncontrolled immune responses that can modulate parasite survival and promote or mitigate the associated immunopathology, thereby influencing the outcome of infection (Navas et al. 2014).

## Literature references

Saravia, NG., McMahon-Pratt, D., Gómez, MA., Freudzon, M., Vargas, DA., Navas, A. (2014). Chronicity of dermal leishmaniasis caused by Leishmania panamensis is associated with parasite-mediated induction of chemokine gene expression. *Infect. Immun.*, 82, 2872-80. ↗

Gallo, RL., Lai, Y. (2008). Toll-like receptors in skin infections and inflammatory diseases. *Infect Disord Drug Targets*, 8, 144-55. ↗

Cekic, C., Linden, J. (2016). Purinergic regulation of the immune system. *Nat. Rev. Immunol.*, 16, 177-92. ↗

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## Leishmania parasite growth and survival ↗

**Location:** [Leishmania infection](#)

**Stable identifier:** R-HSA-9664433

**Diseases:** cutaneous leishmaniasis

**Anti-inflammatory response favouring Leishmania parasite infection**



Leishmania parasites infecting macrophages are considered a good model to study successful evolutionary mechanisms of evasion of the macrophage mediated immune response (Olivier et al. 2005). To evade killing by the host, Leishmania parasites manipulate the host's cellular signaling mechanisms, to prevent the production of microbicidal molecules and stimulating the activation of protective signaling pathways or to interfere with effective antigen presentation (Liu et al. 2012a). In most natural infections or after the resolution of the disease, a few Leishmania parasites remain in the host, perhaps as a product of a balance between forces favouring parasite persistence and those favouring destruction (Mandell et al. 2017).

### Literature references

Mandell, MA., Beverley, SM. (2017). Continual renewal and replication of persistent Leishmania major parasites in concomitantly immune hosts. *Proc. Natl. Acad. Sci. U.S.A.*, 114, E801-E810. ↗

Liu, D., Uzonna, JE. (2012). The early interaction of Leishmania with macrophages and dendritic cells and its influence on the host immune response. *Front Cell Infect Microbiol*, 2, 83. ↗

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