rapsodi

Against Leishmaniasis

A European Small-Scale Project supported through the Seventh Framework Programme
for Research and Technological Development.

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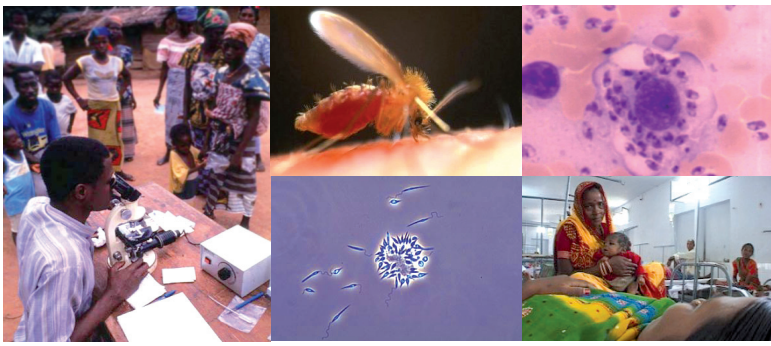
What is Leishmaniasis?

Leishmaniasis is a disease caused by protozoan parasites that belong to the genus *Leishmania* and is transmitted by the bite of certain species of sand fly (subfamily *Phlebotominae*). Human infection is caused by about 21 of the 30 known species of *Leishmania*, and **clinical syndromes varies from cutaneous (CL),** ranging from self-healing lesions to diffuse or recidivist to disfiguring **muco-cutaneous (ML)** or usually **fatal and more progressive visceral leishmaniasis (VL),** also known as kala-azar, the most severe and chronic form of leishmaniasis.

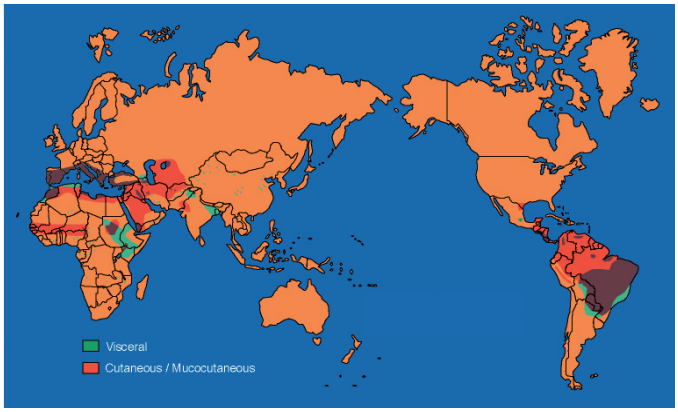
The *Leishmania* parasite infects humans through the bite of phlebotomine and can be life-threatening



Context

Leishmaniasis has been categorized by the World Health Organization as a «re-emerging and uncontrolled disease». This re-emergence, which may be linked to climate change, has detrimental effect on the development of endemic countries. Current treatment strategies involve various drugs, the use of which is (or will be) associated to the development of resistance. Moreover, such treatments are usually quite expensive compared to the actual wealth of the affected nations. Indeed, as leishmaniasis is principally affecting developing countries, strategies aiming at controlling the disease will need to be affordable.

Since vaccination is expected to be the most cost-effective mean of control, it appears as the solution of choice for a global control and/or eradication of the parasite infection.

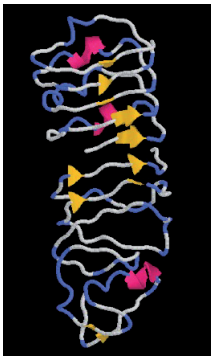


adapted from www.wehi.edu.au

The geographical distribution of leishmaniasis is restricted to tropical and temperate regions

Key figures:	88 endemic countries 360 Mo individuals at risk	Prevalence: 14 Mo individuals	Incidence: 2Mo individuals	Mortality rate: 59 000 / year

A prophylactic vaccine is a realistic goal



PSA-like proteins represent the active principle of the vaccine candidate

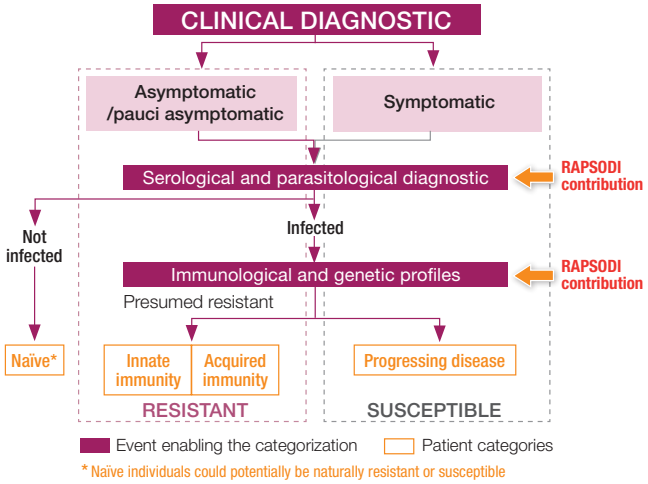
In endemic areas, most of the infected people do not develop clinical symptoms and past episode of leishmaniasis leads to lifelong immunity against re-infection with the same subspecies, once the infection is healed. **This leads to the assumption that the development of a vaccine is feasible.** Even so, no such vaccine is available today.

Among the different *Leishmania* antigen preparations that have been investigated so far, **a crude excreted-secreted antigen obtained from promastigote culture supernatant of *Leishmania infantum* gave highly promising results on dogs** (dogs and humans being the main reservoirs of *Leishmania*). It induces a long lasting Th1-mediated protection against experimental and natural canine visceral leishmaniasis. The Promastigote Surface Antigen (PSA) protein was identified as the active constituent eliciting protective immunity. Research work is on-going to define the smallest peptide sequence from PSA bearing immunodominant properties.

As the PSA is present in all *Leishmania* species, **the resulting vaccine could potentially protect population from the visceral and tegumentary leishmaniases forms caused by all *Leishmania* species. RAPSODI aims at turning such results into a human vaccine candidate ready for clinical trials.**

Vaccine alone is not enough

The wide status diversity toward the infection among individuals renders the evaluation of a vaccination campaign rather difficult. For instance, the inclusion of different proportions of resistant and susceptible subjects in the vaccinated and placebo groups could seriously impair the result of a clinical trial. But tools enabling the precise categorization of the target population are still missing. **RAPSODI aims at developing the necessary tests** (based on host parasitological, immunological and genetic parameters) **to select the individuals for vaccination and follows its efficacy.**



Objectives

The objectives of RAPSODI can be categorized into 3 complementary axes:

1 A good vaccine candidate

- To identify the best active principle (PSA or smallest peptide sequence)
- To design a human compatible, affordable, thermally stable and safe formulation
- To validate the immune cross-protection properties of the vaccine

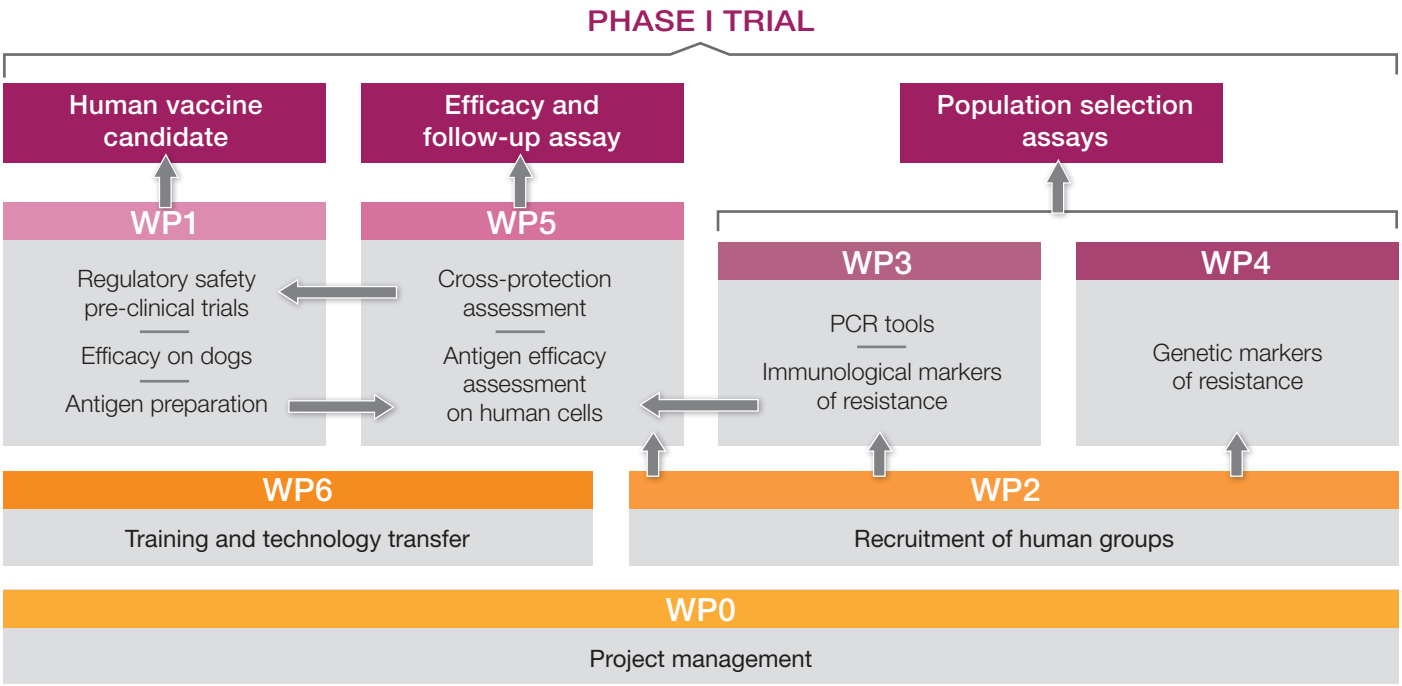
2 Population selection tools

- To design predictive immunoassays for the identification of susceptible or vaccinated individuals
- To design a marker signature for genetic susceptibility assessment

3 Vaccination assessment tool

- To design the immunoassay for vaccination follow-up.

Methodology

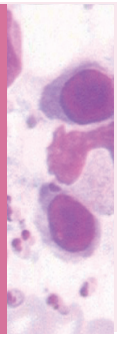


Consortium

The RAPSODI consortium is based on a long-lasting public-private partnership and includes research teams from endemic areas throughout the world.

Acknowledgement

The RAPSODI project is supported by the European Commission through the Seventh Framework Programme for Research and Development and has been running since January 1st 2009 (duration 36 months).



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