PRe-clinicAl studies of a PSA-based human vaccine candidate targeting visceral, cutaneOus and mucocutaneous Leishmaniasis and Development of the associated procedures for further clinIcal trials.

Coordination: G.M. PAPIEROK

Institut Pasteur Paris – 23rd Sept., 2010

A European Project supported within the Seventh Framework Programme for Research and Technological Development

LIST OF BENEFICIARIES (8 partners)

Beneficiary Organization Name	Beneficiary Short Name	Specialisation	Country
Virbac SA	VIRBAC	Veterinary pharmaceutical industry	FRANCE
Consulting Group	ALMA	Consulting company	FRANCE
Syncrosome	SYNCROSOME	Preclinical studies	FRANCE
Indian Council of Medical Research – Institute of pathology	ICMR	Visceral leishmaniasis	INDIA
Universidad Peruana Cayetano Heredia	UPCH	Tegumentary leishmaniasis	PERU
Institut Pasteur de Tunis	IPT	Clinical research	TUNISIA
Institut de Recherche pour le Développement – UMR177	IRD	Parasitic immunobiology	FRANCE
Instituto de Salud Carlos III	ISCIII	Diagnosis and immunology	SPAIN

WHY THIS CONSORTIUM COMPOSITION?

- An **historical private-public partnership:** VIRBAC + IRD

- **Other labs and clinics** covering a broad panel of:
  - Leish species
  - clinical forms of Leish human infections
  - technical specificities

for A SIGNIFICANT COMPLEMENTARITY

rapsodi
Against Leishmaniasis

OUR PARTNERS IN THE WORLD

Création :: Comète :: www.comete.com

STORY OF THE LEISHMANIA VACCINES DEVELOPMENT

Phase 1: 1995 / 2003 → Bio Veto Test (BVT)
→ IRD

Development of **Canileish®** vaccine (5 patents, 10 publications)

Phase 2: 2003 / 2009 → VIRBAC (acquisition of BVT)

→ IRD

End of development, launch of **Canileish®** in 2011 in Europe

Phases 1 & 2 obtained several grants (from French government…), establishment of several consortiums and international specific relations.

FROM A LEISH VACCINE FOR THE DOG RESERVOIR TO A HUMAN VACCINE

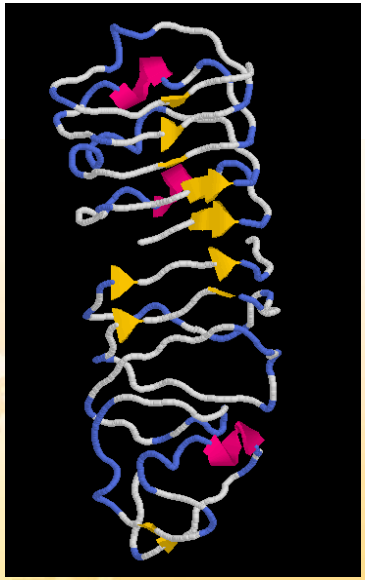
Phase 3: 2009 / 2012 → **RAPSODI Program**
→ **Extension to human vaccine**

BASIS OF THESE DEVELOPMENTS
PSA: Protein Surface Antigen

- ESP: Excreted Secreted Proteins of *Leishmania infantum* . ESP is the active principle of the dog vaccine Canileish®

- PSA is the **major immunodominant active constituent** of these ESP

- Remarkable PSA properties on different animal species



MAIN GOAL OF THE RAPSODI PROJECT

The main goal of the project is to develop:

- a **human vaccine** candidate targeting most, if not all, *Leishmania* species,

- and all the **associated procedures and methods** required for the subsequent clinical trials (i.e. selection of the appropriate population, assessment and follow up of vaccine efficacy and evaluation of the impact of future human vaccination trials on disease's prevalence).

REQUIREMENTS FOR THE HUMAN VACCINE CANDIDATE

- Req 1: **Synthetic Leish vaccine**: peptide or recombinant prot. (affordable to the population in need, stable, easy to produce…) (WP1)

- Req 2: A vaccine **for all Leish species** (WP1, WP5)

- Req 3: A vaccine taking into account the **high polymorphism of HLA molecules** (WP1, WP5)

REQUIREMENTS FOR THE HUMAN VACCINE CANDIDATE

- Req 4: **Establishment and standardization** of all associated procedures and methods required for efficient vaccination trials (WP1, WP3, 4, 5)
  - → selection of appropriate population
  - → assessment and follow up of the vaccine efficiency
  - → evaluation of the impact of future human vaccination trials on the disease's prevalence

- Req 5: Specific biological samples from different individual groups **(recruitment strategy)** (WP2)

- Req 6: **Training partners** on common standardized protocols and **dissemination** to scientific community (WP6)

RESULTS FOR PERIOD 1: Req 1

Comparative industrial trials (production & formulation):

peptides (sp PSA) / recombinant prot. (nsLaPSA)

Peptides >> recombinant proteins (price x 100)

for the development of an affordable synthetic vaccine.

Recombinant prot. nsLaPSA is used as a **reference**.

RESULTS IN SEPTEMBER, 2010: Req 2 & Req 3

The 3 peptides A17E, A17G and E34Pc were found to be efficient in dogs. But preliminary results on human cells (WP5) revealed that these 3 peptides are not sufficient, to cover:

→ all Leish species, specifically with new world Leishmania

→ all HLA classes groups

↳ **Early 2010:** modification of the workplan, with a requirement for additional peptides.

RESULTS IN SEPTEMBER, 2010: Req 2 & Req 3

→ For the detection of these additional peptides of PSA

A full investigation of peptides was performed by the partners with specific focus on both the genetic diversity among Leish species, and the need to take into account the high polymorphism of HLA class I and class II molecules.

→ Results in June, 2010:

5 new detected peptides (3 class I and 2 class II)

→ **Production and formulation** in progress, trials on human cells in progress, **trials on dogs** planed in September / December, 2010

RESULTS IN SEPTEMBER, 2010: Req 4

Establishment and standardization
of all associated procedures and methods required
for efficient vaccination trials

- common PCR methods to detect and quantify low levels of all Leishmania

- a general ELISA protocol measuring the qualitative humoral responses in seropositive individuals (in progress)

- common tools measuring cellular mediated immunity to discriminate between presumed resistant and susceptible individuals (to be confirmed on larger groups)

- Proof of concept and feasibility in the field of a new experimental approach of host inter individual macrophage phenotypic variability associated with patterns of gene expression

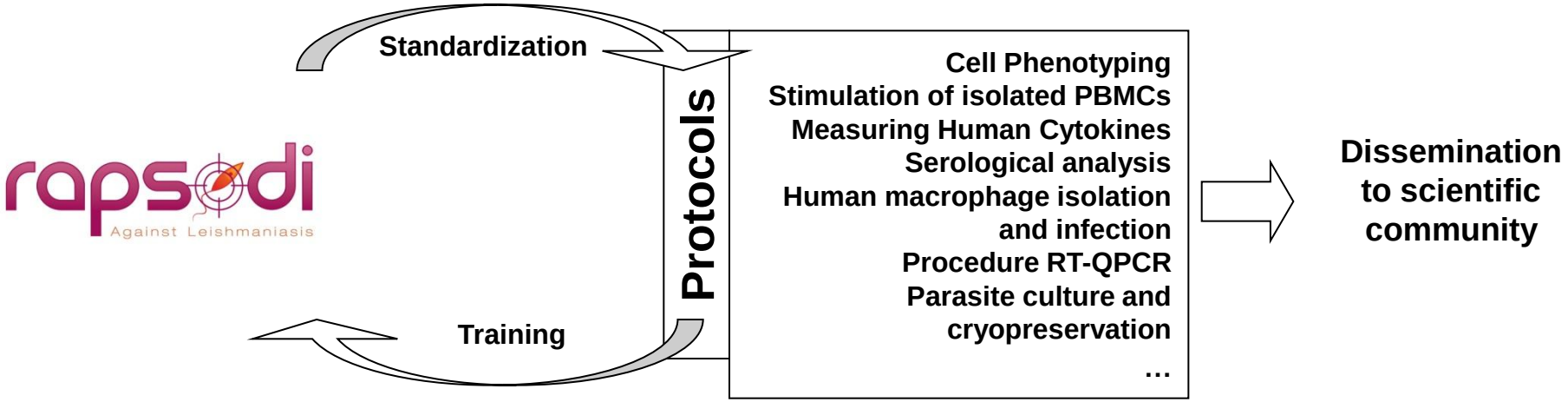
RESULTS IN SEPTEMBER, 2010: Req 5

Recruitment, biological samples

	Naïve	Asymptomatic	Active patients	Healed
Spain	20	7	-	-
France	41	1	-	-
Tunisia	3	15	2	21
Peru	24	23	68	14
India	7	6	26	6

Total of recruited human sample in September, 2010: **284**

RESULTS IN SEPTEMBER, 2010: Req 6

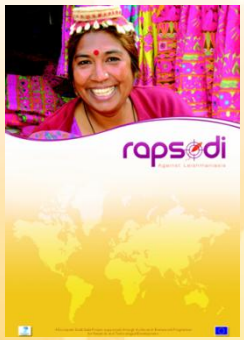


→ **Training**: 6 trainees on 3 missions + mission of IRD at IOP lab

→ **Dissemination**:

Presentations

Booklet



Website

GENERAL IMPACTS OF RAPSODI (Long-term objectives)

- Impact on **health and quality of life** (problem of treatment)
- Contribution to **standards** (tools for epidemiological studies,…)
- Impact on European and endemic area **research**

Dissemination and/or exploitation of project results:

- **Patents** (according to the rules of Rapsodi consortium)
- International **publications**
- **Agreements** with external laboratories and universities, and diverse **presentations** at congresses

ECONOMIC IMPACTS OF RAPSODI (Rough estimate)

- In the **animal** field:
  - Vaccine market: …… **25 M€/year**
  - Diagnostic tests market: .. **0.5 M€/year**

- In the **human** field:
  - Vaccine market: …… **300 M€/year**
  - Diagnostic tests market: … **20 M€/year**

SHORT-TERM OBJECTIVES

- **Exact definition** of the synthetic Leish vaccine for 2011:
  - for **humans** (after trials on human cells with diverse peptides)
  - possible transfer to **dogs**

- **Establishment of standardized methods**:
  - **ELISA** and **PCR** (end 2010)
  - **new methods**: for resistance detection, for vaccination follow up (end 2011)

- **Establishment of relations** with:
  - **human pharmaceutical industries**
  - **organizations** like WHO…
  - and **specific research labs** for forecast phases 1 & 2 of human Leish vaccine development


They'll have my skin soon……!!!!!
Researcher
Leishmania
PRIHS