

1 *Publishable summary (Coordinator)*

PiroVac is a major international research project designed to develop control measures to combat two major tick-borne diseases of small ruminants, namely theileriosis and babesiosis. This EU-funded research programme aims at improving existing vaccines, designing new vaccines and on capacity building in partner laboratories both in Europe and in endemic areas.



Small ruminant piroplasmiasis is a major threat to livestock production in many areas of the developing world. Theileriosis and babesiosis, caused by the protozoan parasites *Theileria lestoquardi*, *T. uilenbergi* and *Babesia ovis*, infect sheep and goats causing disease, production loss and sometimes death. Consequently, these diseases have a major impact on animal welfare and stock-holder prosperity throughout the world.

By developing effective measures to control these important diseases, the PiroVac project represents a major contribution to achieving the United Nation's Millennium Development Goals of food security, food safety, poverty alleviation, animal welfare and environmental sustainability.

PiroVac is a collaborative effort among a number of established research groups working on theileriosis and babesiosis. The consortium also encompasses laboratories involved in malaria research in order that scientific and technological knowledge in that field can be translated into tools and reagents for small ruminant piroplasms. Industrial expertise in vaccine development and delivery systems has also been incorporated in order to maximise the potential for translational application.

Aim of the project:

The PiroVac project was developed as an integrated approach, encompassing immunology, molecular biology, bioinformatics and genetic engineering together with pathogen genomics and host genetics, which is directed at addressing two broad aims:

- (1) Development of effective and reliable vaccines for use in disease control campaigns for sustainable livestock development.
- (2) Capacity-building for the sustainable implementation of integrated control measures required for disease control and/or eradication through increasing scientific knowledge, training and improvement of infrastructure.

The specific goals of the project are:

- (1) Improvement and development of live attenuated vaccines for the control of small ruminant theileriosis and babesiosis through determining the effectiveness of attenuation using:
 - a) in vivo assessment of attenuation, analysing clinical and immunological criteria (both humoral and cellular responses) of immunised and challenged animals

- b) subtractive libraries and microarray analysis for the identification of attenuation markers
- (2) Sub-unit vaccine design through:
- a) Identification of suitable antigens using a combination of genomics, bioinformatics and gene expression analysis coupled with experimental confirmation of antigen localisation and presentation. To facilitate antigen discovery, parasite molecules involved in host cell invasion, activation of cytokine-producing CD4⁺ T cells and NK cells and activation of cytotoxic T-lymphocytes involved in killing of *T. lestoquardi*-infected leucocytes will be identified.
 - b) Immunological characterisation of the identified antigens as potential vaccine candidates.
- (3) Vaccination trials using:
- a) live attenuated vaccines
 - b) recombinant protein and DNA vaccines

Expected results

The project will contribute to an understanding of the immunological and molecular mechanisms involved in host-pathogen interaction. As important by-products of the project, reagents required for the characterisation of the innate and adaptive immunity of small ruminants will be generated together with the genome sequences of the three pathogens under study.

The PiroVac project is based on the conviction that the interface between genomics, immunology and vaccinology offers the best prospect for major breakthroughs in vaccine discovery and development. Overall, vaccine development will contribute to reducing losses in animal production due to piroplasmiasis of small ruminants and improve the life quality of both farmers and consumers.

Potential applications

- Generation of knowledge and tools required for vaccine production.
- Vaccines useful for upgrading schemes using more susceptible but productive breeds
- Progress into policy innovations and strategies that will meet critical Millennium development goals: food security, food safety, poverty alleviation (eg. improvement of small farmer income), animal welfare and environmental sustainability
- Exploitation of the data for commercial purposes by collaborating with the industry (Arrangements have been done with the industrial participant for commercial exploitation of the products)