

# Integrated Control of East Coast Fever in cattle of Smallholder Farmers

**Dr Evans Taracha and Dr David Taylor**, International Livestock Research Institute, Kenya and Centre for Veterinary Medicine, University of Edinburgh, UK

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## **Collaborators**

Oxford University, LICR, Brussels, Merial, UK

## **Executive Message**

- East Coast Fever causes high morbidity and mortality in cattle and prevents the introduction of highly productive breeds of cattle that would help small dairy farmers improve their livelihood. ECF is thus a huge economic burden for poor smallholders.
- A new vaccine for ECF will significantly reduce the cost of control and have a major impact on the income of small dairy farmers in Kenya. It will also reduce the impact of toxic chemicals, currently used in control, on the environment and in milk.
- This project aims to achieve this through an integrated approach combining improved vaccine, diagnostics and decision support systems.
- Scientists have used genome sequencing and cloning of selected genes and Random cDNA transfection approach to make dramatic progress in identifying antigens for use in a new vaccine. They have also have focused on two delivery systems; the DNA/MVA prime/boost from the University of Oxford collaborators and the technology developed by Merial, the private sector partner.
- One candidate antigen has been cloned into the Merial delivery system and is ready for testing in cattle. These cattle trials will start in May 2003.



A new vaccine to control ECF will have a major impact on the income of small dairy farmers in Kenya.

## **Background**

Tick-borne diseases (TBDs) are a major constraint to livestock productivity and food security in many developing countries. They cause high morbidity and mortality, prevent the introduction of highly productive breeds of cattle, are expensive to control, and place a huge economic burden on poor smallholder farmers. Theileriosis costs over US\$1 billion annually worldwide. East Coast fever (ECF) caused by the protozoan parasite *Theileria parva* is one of the most serious of the theilerial species that threatens smallholder farmers' livelihoods in eastern, central and southern Africa. There are at least 24 million cattle at risk with over one million dying

each year. The impact of these losses is magnified by the knock on effect of lost opportunities for increasing production through the introduction of improved breeds of cattle, which are particularly susceptible to tick-borne disease, into smallholder production systems.

ECF is thus a major limiting factor working against small farmers climbing out of poverty by moving from subsistence to market oriented enterprises. There is a further urgent need to control ECF given that poor smallholders will play a major role in meeting the increasing demand for meat and milk in developing countries, which is expected to double by 2020.

## Objectives

The purpose of the project is to develop methods for the integrated control of ECF, combining improved vaccine, diagnostics and decision support systems, constraining the livelihoods of poor smallholders in sub-Saharan Africa (SSA).

The short-term scientific objective is to:

- develop an experimental multi-component subunit vaccine against ECF that is shown to be protective to cattle in laboratory trials.

The long-term scientific objective is to:

- generate a safe, efficacious affordable and easily deliverable ECF vaccine in partnership with a commercial company.

ECF has a major impact on livestock production in 11 countries in SSA, including Kenya, Uganda, Tanzania, and Zimbabwe and consequently the demand for a vaccine is considerable. A 60% adoption rate by farmers is projected. Cattle markets in these four countries represent the main targets for a new vaccine. Whilst the size of the small-scale market oriented sector is increasing in all 11 countries the market is largest in Kenya, which has the largest number of smallholder farms.

Kenya, like Uganda and Tanzania ranks ECF in the top two priorities for research. The Kenya Agricultural Research Institute (KARI) has collaborated with ILRI in the development of an improved vaccine, while Uganda and Tanzania support integrated control of ECF.

Impact assessment studies predict significant benefits for farmers using new vaccines to control ECF. Current losses from ECF per animal vary from US\$ 5-14 in indigenous cattle and US\$ 11-105 in exotic and crossbred cattle, depending on the production system. Benefit: cost ratios (BCRs) for a vaccine-based control strategy are predicted to range from 2:1 to 7:1. Whole farm simulation modelling predicted BCRs of 2:1 at the Kenya coast and 5:1 in the Kenya highlands.

## Highlights

The aim of this project is to find antigenic components of the schizont that are recognised by protective CTLs and thus trigger protection of an experimental vaccine would then be developed based on these components.

The bulk of this research project has been laboratory based using the well-equipped facilities in Brussels, the UK and at ILRI in Nairobi. Progress has been good.

In order to find suitable antigens to form the basis of an effective vaccine the researchers have adopted a twin track approach to identify potential vaccine targets as well as investigating two delivery systems. Major achievements include:

### Antigen identification

#### 1. Genome sequencing and cloning of selected genes

The sequencing of the genome has been completed except for one component of Chromosome 3 and will be published shortly. Some 88 target genes have been selected for cloning from the top 100 and tested in *in vitro* assays to identify vaccine candidate antigens. To-date 60 have been cloned and are being evaluated *in vitro* at ILRI. So far, 3 candidate antigens have been identified through this screening and will be evaluated for vaccine potential.

Annotation of chromosomes 1 and 2 is complete and that of chromosome 4 nearly complete. This will provide a basis for selecting more target antigens for testing.

#### 2. Random cDNA transfection approach

A library of 1000 pools of 50 cDNAs has been screened using two interferon gamma (IFN- $\gamma$ ) release assays: an ELISPOT assay and a bioassay.

The screening of the cDNA library was initiated the collaborator's (LICR) laboratory in Brussels and has continued at ILRI.

To-date, 4 candidate antigens have been identified and are being formulated into the appropriate delivery systems for evaluation in cattle. The screening is on going and targeted to obtain 15 vaccine candidates.

## Antigen delivery

Researchers initially tried out the antigen delivery strategies in cattle using a model antigen but quickly moved on to using the vaccine candidate antigens identified through the project.

Activities have focused on two delivery systems namely the DNA/MVA prime/boost in use by the University of Oxford collaborators and the technology developed by Merial, the private sector partner. One candidate antigen has been cloned into the Merial delivery system and is ready for testing in cattle. Merial have sent an animal experimental protocol for evaluating this vaccine in cattle. DNA and MVA of one candidate antigen are well underway to allow evaluation by the prime/boost method. These cattle trials will start in May 2003.

## Laboratory trials

Significant progress has been made taken towards initiating vaccine trials in cattle under laboratory conditions. These have involved a successful breeding programme to generate cattle of desired genetic backgrounds. Experimental designs for testing the vaccines using the prime/boost method and the Merial technology have also been worked out.

## Optimisation of high throughput assays

Two high throughput *in vitro* assays that have been used to screen the genes selected from the genome sequence database and pools of cDNA from the random schizont cDNA library are major new techniques developed by the project. These assays are both based on the detection of interferon- $\gamma$  release by T cells from *Theileria*-immunised cattle in the presence of cells transfected with test genes. One of the assays is an immuno-assay and the other a bioassay, both with comparable sensitivity. Further assays are under development and will be deployed in the monitoring of immune responses in cattle vaccinated with candidate antigens. This work has further strengthened the expertise of scientists in Nairobi.

## Impact

The major outcome of the research will be a robust, cheap and easy to deliver subunit vaccine against ECF. Such a vaccine will improve the livelihoods of resource poor smallholder farmers by reducing mortality of animals and increasing milk production. More milk for sale will enable farmers to raise their income.

The availability of an effective vaccine will also have a positive environmental effect by reducing

the current reliance on toxic chemicals for the control of ECF. This will reduce contamination of milk and the wider environment. The technologies generated from this research will have application in development of vaccines against other livestock diseases in poor countries.

## Dissemination

The project underwent a second annual review in March 2003 by External Reviewers. All collaborators, except Merial, attended. The review panel rated progress of the project in terms of antigen identification as outstanding. The panel also acknowledged the significant steps that have been made towards initiating cattle trials.

To enhance the free flow of information, an inter-institutional agreement was proposed. It was also agreed that a holding patent to protect the vaccine candidates and the process of identification be filed soon.

BBC Science in Action January 2003, An interview on the project activities was broadcast on the BBC's World Service weekly science magazine programme.

## Next Steps

The main targets for the next period of the project will include:

- Further antigen identification following the identification of 7 targeted candidates.
- Evaluation of the 7 vaccine candidates before comprehensive laboratory trials to develop an experimental vaccine and subsequent field-testing.

Laboratory trials starting in May 2003 will provide proof-of-concept and lead to the availability of an experimental vaccine against ECF. This will represent a major milestone in the efforts to develop an efficacious, cheap, and easy-to-deliver subunit vaccine, which will constitute a sustainable control regimen for ECF. Such a vaccine will predominantly benefit smallholder dairy farmers and their families who will be able to generate more incomes from their cattle.

## Links and further information

This project is part of the series:  
R7358 Development of s subunit vaccine against ECF.  
R7365 Identifying antigens of *T.parva* that might be used in a vaccine for ECF.