New technologies to enhance the immune response in protein subunit vaccines, p67C as a model antigen

- We can improve the immunogenicity of protein antigens using nanoparticle technologies.
- Depending on the nanoparticle used we are enhancing antibody or cellular response (T-CD4$^+$).
- p67C is a good model antigen to test new delivery systems. The combination of SV-p67C + HBcAg-p67C and the two-component p67C-I53-50 are good vaccine candidates with good levels of protection.

Anna Lacasta | Senior Scientist | a.Lacasta@cigar.org

Thanks to all that make this work possible: Karishma T. Mody, Ine de Goyse, Hyung Chan Kim, Elisabeth Kepl, Rachael Gachogo, Naomi Chege, Rose Ojuok, Charity Muriuki, Stephen Mwalimu, Gilad Tauboul, Elisabeth Jane Poole, Nicholas Ndiwa, Brooke Fiala, Lucilla Steinaa, Antonino Cavallaro, Timothy J. Mahony, Neena Mitter, Neil, P. King and Vish Nene.

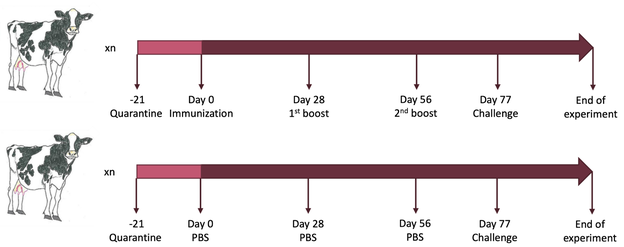
Cattle vaccination against East Coast fever (source: ILRI)

The challenge

- East Coast fever (ECF) is a lethal cattle disease produced by the infection of the apicomplexan parasite *Theileria parva.*
- The existing vaccine (ITM) against ECF has several limitations: difficult to produce, expensive, needs cold chain, expertise for delivery, animals become carriers, risk of introduction of new parasite variants in the field.
- Sub-unit vaccines based on non-infectious parts of the parasite *Theileria parva* can solve all the above problems.
- p67C is a very promising vaccine antigen, but it's weak.

Our innovative approach

- The use of nanoparticle technologies to make p67C a stronger antigen (more immunogenic) and increase protection in cattle.



Holstein Friesian cattle received three doses of p67C antigen subcutaneously 28 days apart, using different formats: soluble p67C (s-p67C), adsorbed on size and pore-controlled silica vesicles (SV-p67C), as VLP fused to the Hepatitis B core antigen (HBcAg-p67C) and as self-assembled two-component protein nanoparticles in three different architectures (p67C-I32-19, p67C-I32-28 and p67C-I53-50). Montanide ISA206VG (w/o/w, Seppic) adjuvant was used at all times. In challenge experiments animals are challenged at day 77 with a leathal dose of T. parva Muguga 3087.

Table 1. Summary of animal experiments and results for the immunogenicity studies in cattle using p67C in different nanoparticle formats.

Immunogen	Num. Animals	Num. doses	p67C (μg)/dose	Total prot. (μg)/dose	Response
s-p67C	x3	X 3	~ 70	100	↓Ab ↓Cells
SV-p67C	x3	X 3	~ 70 in ~500μg silica	100	↓Ab ↑Cells
HBcAg-p67C	x3	X 3	~ 80	300	↑Ab ↓Cells
SV-p67C + HBcAg-p67C	x3	X 3	~ 150	400	↑Ab ↑Cells
p67C-I32-19	x3	x3	~ 70	451	↓Ab ↓Cells
p67C-I32-28	x3	x3	~ 70	366	↑Ab ↓Cells
p67C-I53-50	x3	x3	~ 70	424	↑Ab ↑Cells

Table 2. Summary of challenge experiments with the best candidate nanoparticles: SV-p67C+HBcAg-p67C and p67C-I53-50.

Experim.	Immunogen	nº animals	nº doses	p67C (μg)/dose	Challenge	Immunity
1	SV-p67C + HBcAg-p67C	x15	X 3	~ 150 μg	LD93 (Muguga 3087)	9/15
	Challenge control 1	x15	N/A	N/A	LD93 (Muguga 3087)	1/15
2	p67C-I53-50	x15	x3	~ 140 μg	LD70 (Muguga 3087)	12/15
	Challenge control 2	x15	N/A	N/A	LD70 (Muguga 3087)	5/15

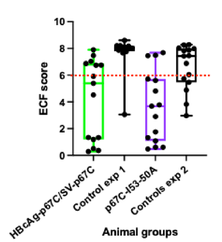


Figure 2. ECF scores for both challenge experiments. Individual animals (black dots), the 25th and 75th percentiles (boxes) and the min and max values (bars) are represented.

If you want to know more

Outcomes

- The immunogenicity of protein antigens using nanoparticle technologies was improved.
- Depending on the nanoparticle used we are enhancing antibody or cellular response (T-CD4$^+$).
- p67C is a good model antigen to test new delivery systems. The combination of SV-p67C + HBcAg-p67C and the two-component p67C-I53-50 are superior to any of the other tested formats.
- We developed several assays to measure cellular and antibody antigen-specific responses (p67C). Especially antibody functional assays (Ag-specific Ab quantification ELISA, seroneutralization assay, etc).

Next steps

- Include other antigen candidates with neutralising capacity to create a cocktail vaccine (ongoing activity funded by the USAID Feed the Future – Animal Health Innovation Lab for the control of ECF)
- Field trial with the cocktail vaccine.
- Engagement with a commercial partner.

Partners

The International Livestock Research Institute thanks all donors & organizations which globally support its work through their contributions to the CGIAR Trust Fund. cgiar.org/funders