CENTRE FOR VETERINARY VACCINE INNOVATION AND MANUFACTURING (CVIM)

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CVIM – Funding partners

- **Biotechnology and Biological Sciences Research Council (BBSRC)**

  Funding the design and construction of the CVIM Building

- **Foreign, Commonwealth and Development Office (FCDO)**

  Funding the science projects

- **Gates Foundation**

  Funding scientific equipment, operational start-up costs and science projects

CVIM – Vision, Mission & Goals

- **Vision:** Working as a global partner to improve animal health and food security through the development of novel, affordable veterinary vaccines targeted at LMICs.

- **Mission:** To accelerate development and manufacturing of vaccines for neglected, zoonotic and emerging infectious diseases of livestock.

- **Goals:** This will be achieved by:

- Partnering with the animal health industry to bridge the gap between upstream R&D and down-stream product development for neglected and tropical livestock/animal diseases.
- Translating innovative science into suitable proof-of-concept for the development of novel vaccine platform technologies.
- Providing specialized expertise and facilities to produce cost-effective vaccines at pilot-scale for transfer to manufacturers.
- Knowledge exchange and know-how with partner LMICs.

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Science focus

- Neglected and emerging diseases of livestock
- Zoonotic diseases
- Low- and middle-income countries (LMIC)
- Viruses, bacteria, parasites
- Also looking at vaccine platforms and modalities

Milestones

- Robust governance structures, independent of Pirbright
- Ongoing recruitment and training of staff
- Setting up GLP facilities, equipment
- Designing the GMP facility
- Initiating key scientific projects
- Initiated key partnerships

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Independent governance

- Joint Oversight Committee
  - Chaired by Prof Helen McShane (University of Oxford)
  - Independent advisor
  - Funders

- Scientific Review Committee
  - Representatives from key areas:
  - Regulatory
  - LMIC (Africa and India)
  - GALVmed

Partnerships

- Technical partners:
  - Quantoom
  - Centre for Process Innovation
  - Institute for Protein Design
  - National Measurement Laboratory
- MCI Morocco
- KEMRI
- GALVmed
- Flexible arrangements with a range of partners

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CVIM - Facilities

Two complementary facilities:

1. Refurbished Good Laboratory Practice (GLP) facility

- Repurposed building (‘A Block’)
- R&D activities: establishing & evaluating vaccine platforms, & developing scalable processes
- CVIM Process Team - 11 staff

2. New Good Manufacturing Practice (GMP) facility

- Building in progress, target completion date: Spring 2026
- Master seed & small-scale vaccine production (for clinical studies)

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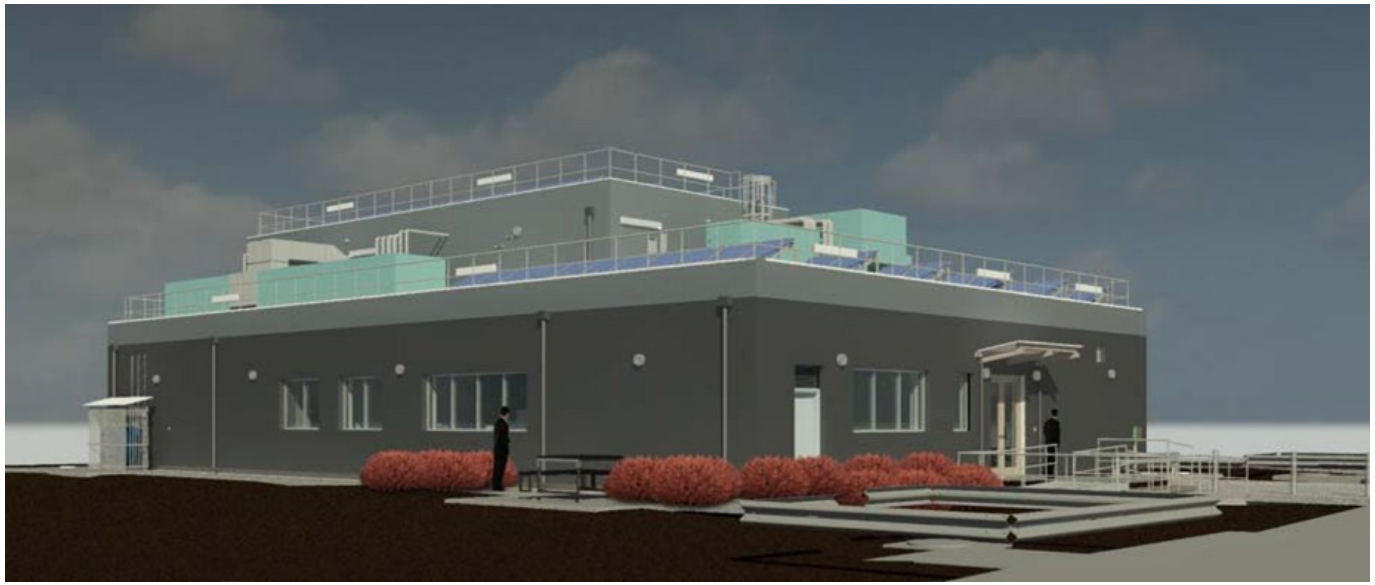
New GMP facility

Target completion date: Spring 2026



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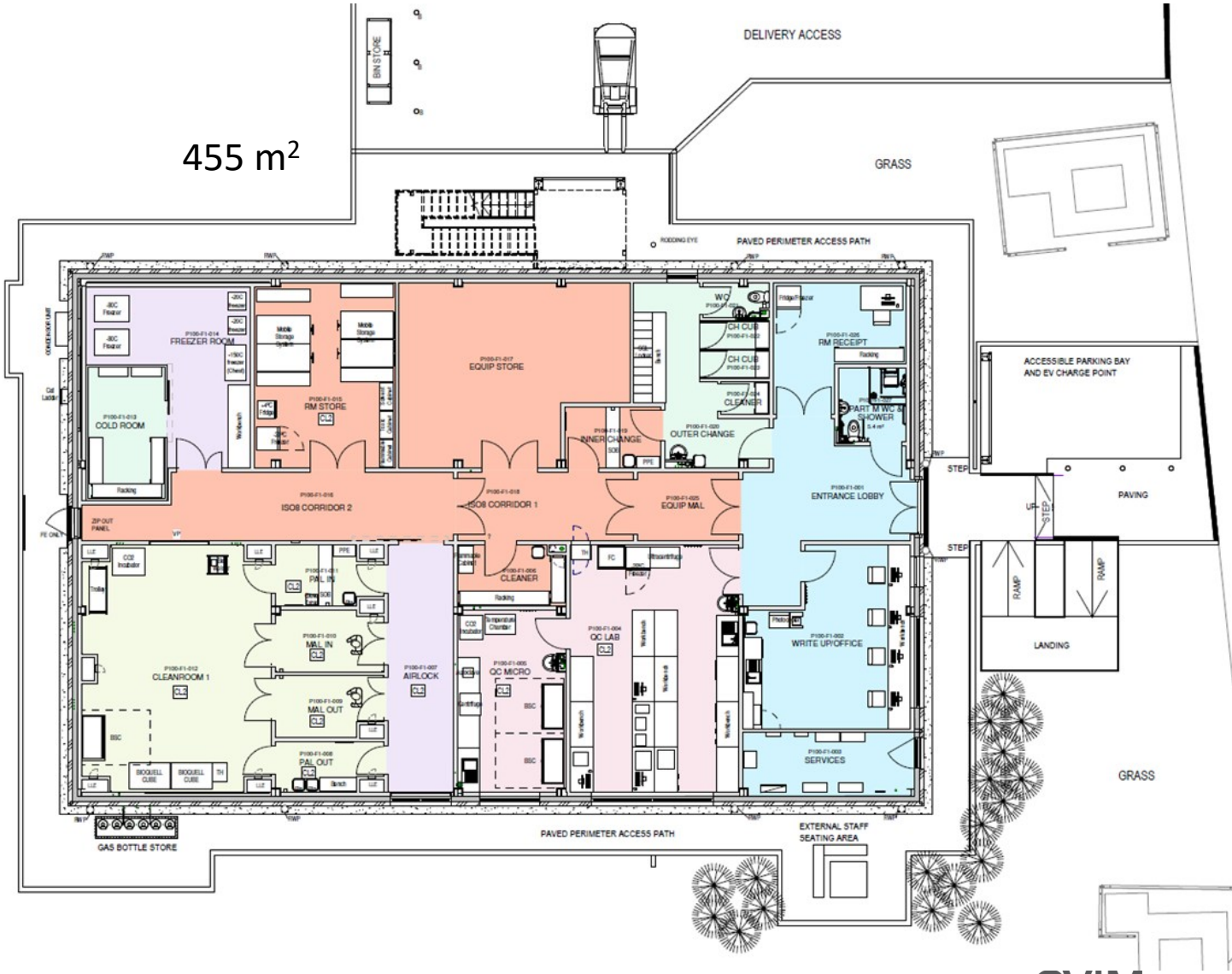
New GMP facility

Inside GMP containment area:

- Single GMP cleanroom (Grade C, ISO7) with isolator (Grade A)
- Cold room (+4℃; CNC) freezer room (-20,-80,-150℃)
- Storage room for consumables & spares (Grade D)
- Equipment storage for handling different platforms (Grade D)
- ≤200L single-use bioreactors

Outside GMP containment area:

- Receipt room, QC labs (micro & non-micro), office area



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GLP Facility

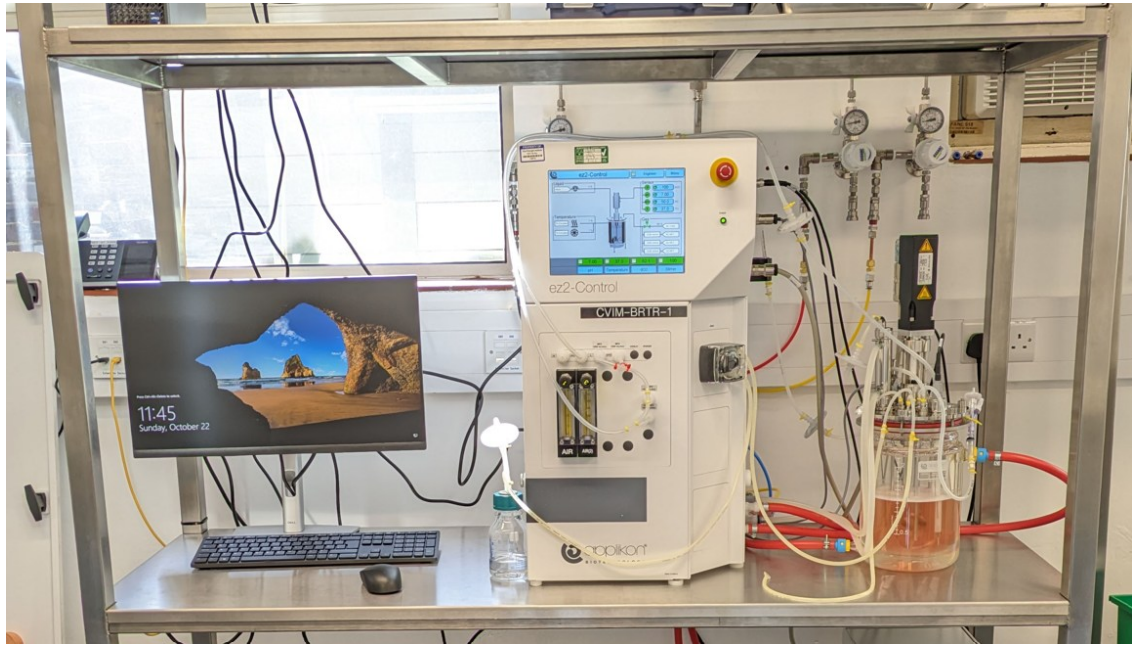
- Refurbished to accommodate process scale up across different platforms
  - Installed specialist equipment & gas lines for bioreactor-based scale up.
- Spatially segregated projects by room to prevent contamination.
- Working to GLP to facilitate transition of documentation & processes to industrial partners &/or CVIM GMP facility
- Align consumables with regulatory requirements
  - Non-animal origin, GMP compliant

Upstream processing capability

Suspension cell culture of mammalian, insect & yeast cells

- Scalable process - 1L, 3L & 15L glass autoclavable bioreactors

- Installed gas lines (O_2, N_2, CO_2 & compressed air)
- Operate bioreactors as a closed system using tube biowelder & biosealer



- Metabolite analyser – inform feeding strategy
- Evaluating single-use bioreactor options

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Downstream processing capability

Reduce costs by streamlining downstream processes

- Depth filtration to clarify crude lysates
- Tangential flow filtration (TFF) system - diafiltration & concentration
  - Can be operated as a closed system with single-use options
  - Scalable
- End point filtration for sterility

- Sourcing chromatography system

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RNA Capability

To support evaluation of RNA as a veterinary vaccine platform

Equipment

- Ntensify mini system - IVT & single-step bead-based purification
- Up to 48 mRNA constructs at a 2mg scale, or a single at 100mg scale.

- Supported by Ignite+ encapsulation & QC equipment (DLS, Tapestation, Qubit, Nanodrop)

Platforms

- mRNA & saRNA platforms

Established vaccine platforms

Multiple platforms over different LMIC disease areas:

- **ChAdOx/hAd5** (replication incompetent viral vector) – RVF
- **Yeast** (*Pichia pastoris*) – IBV
- **Baculovirus** (Tnao38 insect cells) – FMDV Virus-like particles
- **mRNA** – PPR (model system), Marek's disease, FMDV, ASFV

Adenovirus vaccine platform

Aims: To support the development of a Rift Valley Fever (RVF) vaccine for use in livestock

Objectives:

1. To develop a scalable, cost-effective process for RVF vaccine production using the adenovirus platform
2. To evaluate the vaccine in target host species
3. To support process transfer to industry

Evaluating two adenovirus systems:

- ChAdOx RVF - Collaboration with University of Oxford
- hAd5 RVF – Collaboration with GALVmed

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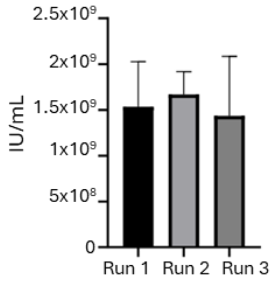
Adenovirus vaccine platform

Cell selection

- Cell growth
- Cell infection
- Virus production
- QC assays

USP optimisation

- Gassing/impeller
- Seeding & infection density
- MOI & DOI
- Feeding strategy
- Harvest method



DSP optimisation

- Clarification
- Buffer exchange
- Concentration
- End-point filtration

Product evaluation

- Antigen expression
- Yield IU/mL
- P/IU ratio
- RCA assay
- Storage
- Genetic stability
- In vivo: Immunogenicity & dose escalation study
- VNT

Process transfer

- Data portfolio
- Cell & virus seeds
- CPP & CQA
- QC assays

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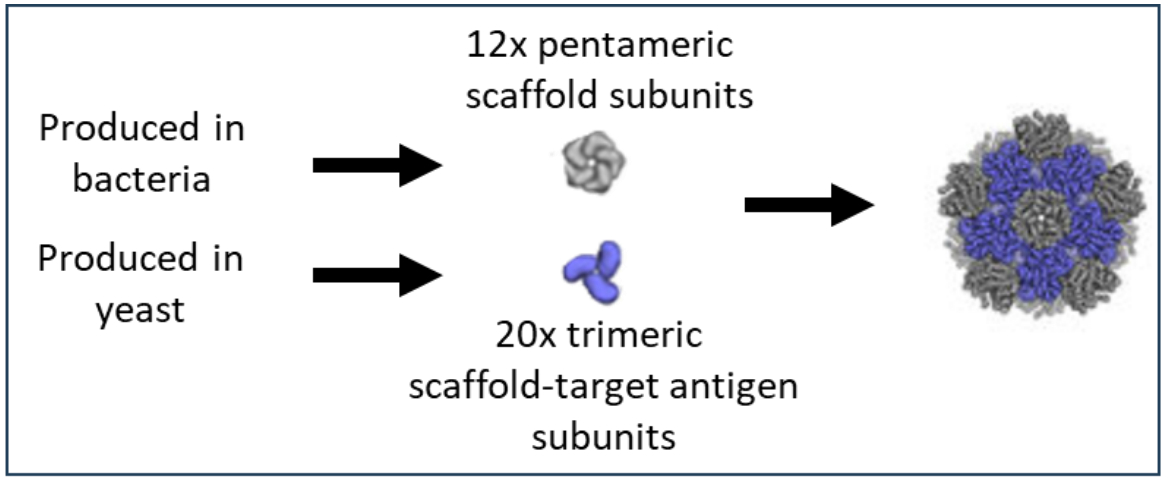
Nanoparticle vaccine platform

Aims: To evaluate the application of a two-component, self-assembling nanoparticle vaccine platform for use in livestock.



Adated from Bale *et al Science* 2016

Objectives:

1. To develop a scalable, cost-effective process for producing target antigens fused to a nanoparticle scaffold subunit using the yeast (Pichia pastoris) platform. Target antigens: (1). Spike RBD of infectious bronchitis virus (IBV) of chickens and (2). H protein of peste des petits ruminants (PPR).
2. To evaluate nanoparticle vaccines in target host species.

- Collaboration with IPD, University of Washington.

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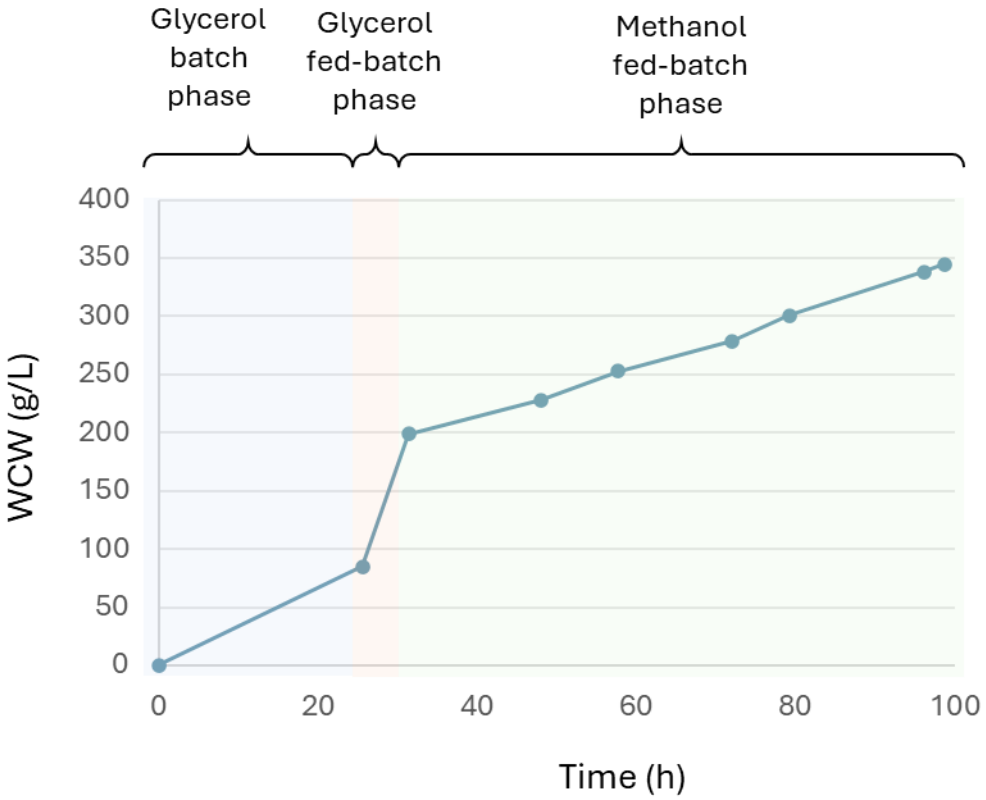
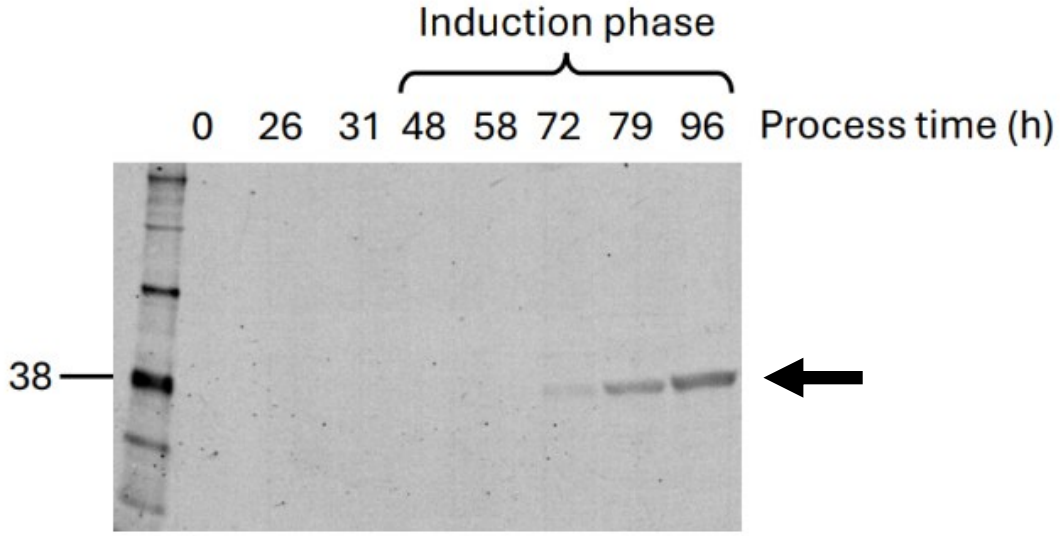
Nanoparticle vaccine platform

Yeast expression of scaffold-IBV Spike RBD

Growth of yeast in bioreactor





Anti-His western blot

- **Glycerol → methanol** initiates target protein expression
- Scaffold-Spike Ag subunits secreted into medium

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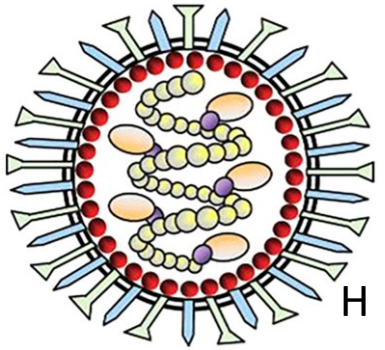
RNA vaccine platform



Proof-of-concept project

- Selected peste des petits ruminants (PPR) as the target disease to initially evaluate the application of RNA vaccines for use in livestock

  - Single immunologically relevant target antigen: Hemaglutinin (H) glycoprotein
  - Available reagents to assess expression of target antigen.
  - Archived records of PPR studies.
  - Robust challenge model in target species.
  - Correlation of efficacy based on neutralising Ab titre.

- Collaboration with Quantoom Biosciences.

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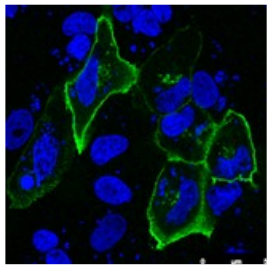
In vitro work– assessment of antigen expression

mRNA/saRNA panel with different:

- Cap structures
- 5’ & 3’ UTRs
- Base analogues
- Localisation & secretion signals

LFT



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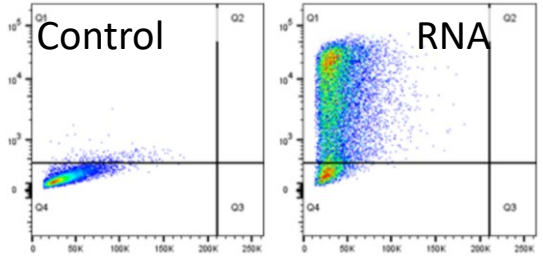

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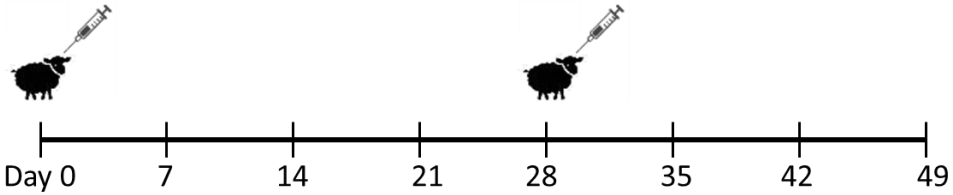

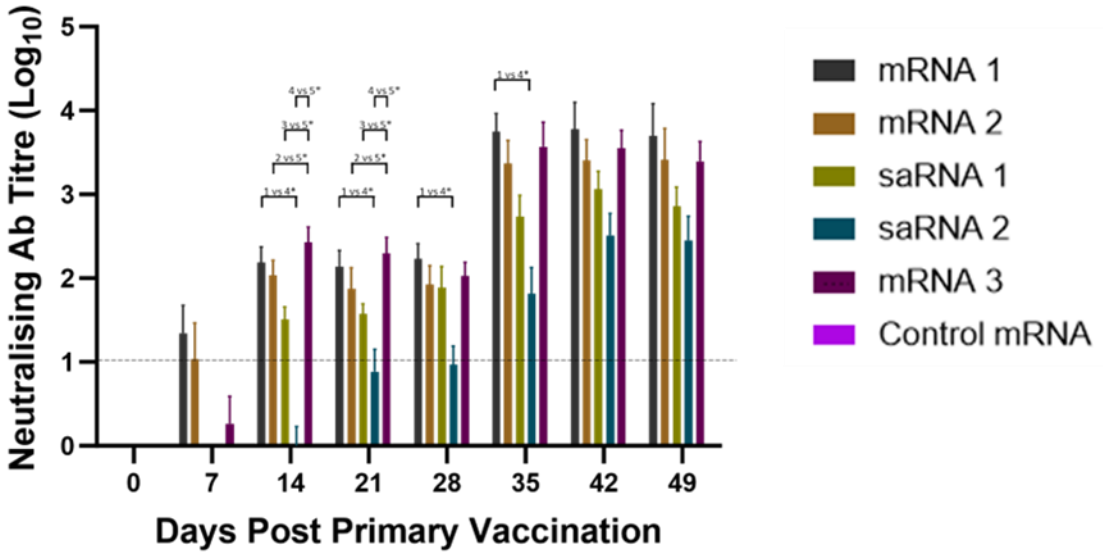

- Protective(>10) nAb titres by 4 out of the 5 RNA vaccines on day 14 (pre-boost) and by all five on day 35 (post-boost)

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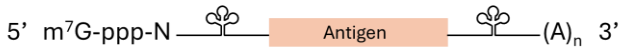
RNA vaccine platform

Ambitious plans to evaluate:



- Antigen complexity
- Antigen expression
- Innate response
- Immunogenicity, dose, onset & duration of immunity
- Test different LNPs & alternative encapsidation/carrier strategies
- Safety/toxicity
- Compare with other vaccine platforms

Lessons learnt

- Intellectual property landscape / freedom to operate
- Provenance of material
- Contracts take a long time
- Importance of the Target Product Profile
- Clear go/no go decision points
- Industrial partner identified

Summary of CVIM capabilities

- Assessment of multiple novel vaccine technologies
- Development of livestock vaccines for LMICs
- GMP Manufacturing scale-up
- Novel vaccine formulation
- Master Seed production
- Technology transfer
- Coaching and training opportunities

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