

## Foot-and-mouth disease virus (FMDV) vaccines

Bryan Charleston  
Institute of Animal Health

Foot-and-mouth is a disease of global socioeconomic importance, with vaccination the principle tool for control in endemic countries. Improvements in vaccines require advances in our understanding of the host immune response, one aspect of which the study group is asked to consider. Major problems limit the capacity of FMDV vaccines to control infections in developing countries. The virus is notoriously unstable which reduces the yield and effectiveness of the vaccine. A FMDV-specific difficulty is that effective vaccination requires the presence of intact inactivated virus or virus-like particles. Individual proteins or peptides have proven to be insufficiently immunogenic for use as vaccine antigen.

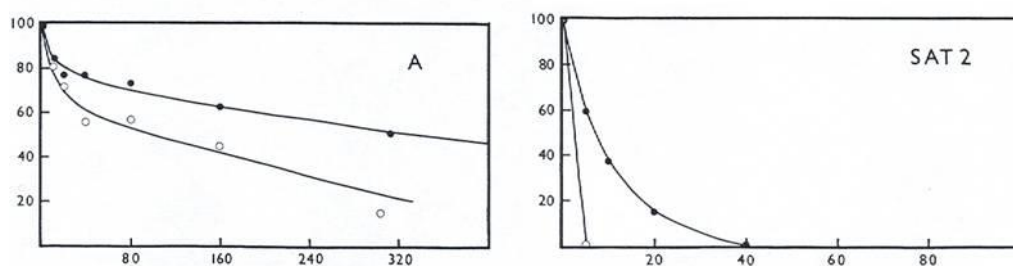
To be recognised by T lymphocytes, viral protein must first be converted into short peptide pieces by antigen presenting cells such as dendritic cells (DC), which thereby control the magnitude and character of the immune response. We have evidence to show vaccine produced from viruses of different serotypes can differentially stimulate T cell responses. The principle difference between these virus strains is their capsid stability (see below), which may influence both the uptake of virus capsid by DCs and the subsequent controlled processing of the capsids to produce peptides for presentation to stimulate T-cells (responsible for helping B cells to produce antibodies and clear the virus).

We would like a model of this process to be developed to explore the interplay of uptake and processing of viral capsids and the impact of capsid stability on gross dynamics of the system. If possible, we would like the group to address the specific question of whether it is the virus strains' different stability properties that are responsible for the observed differences in system behaviour. We assume this would either be driven by the characteristics that capsid stability (or instability) imparts to an individual virus particle or how the DCs handle virus fragments as opposed to whole virions.

Specifically,

- 1) Is the efficiency of capsid uptake from the extracellular environment by specialised antigen presenting cells (dendritic cells), influenced by the stability of the capsids?
- 2) Is the processing of the capsid proteins into short peptides influenced by the stability of the capsids?
- 3) Is the magnitude of the T cell response influenced by the period of time antigen is retained in dendritic cells?
- 4) Overall, does capsid stability result in an increased specific T cell proliferative response in antigen presentation assays?

**Comparison of the thermal stability of A and SAT2 capsids.** In the below figures the y-axis shows the percentage of intact capsids remaining after incubation at 49°C. The x-axis shows the incubation time in minutes. Closed circles represent live virus and open circles represent inactivated virus (vaccine antigen). Using this assay, A capsids (left) are approximately 50 fold more stable than SAT2 (right) capsids.



## **References**

Delamarre L, Couture R, Mellman I, and Trombetta ES (2006) Enhancing immunogenicity by limiting susceptibility to lysosomal proteolysis. *J. Exp. Med.*, 203, 2049-2055.

Doel TR and Baccharini PJ (1981) Thermal stability of foot-and-mouth disease virus. *Arch. Virol.* 70: 21-32.

Jensen PE (2007) Recent advances in antigen processing and presentation *Nat. Immunol.*, 8, 1041-1048.

Moss CX TreeTI and Watts C (2007) Reconstruction of a pathway of antigen processing and class II MHC peptide capture *EMBO* 26, 2137–2147