Improving Quality Assurance along the FMD Vaccine Production and Supply Chain

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The effectiveness of FMD vaccines is influenced by multiple factors such as route of vaccination, dose, similarity to circulating virus and adjuvant. Antigen integrity is also imperative for vaccine efficacy; FMD vaccines that are comprised of dissociated viral particles do not elicit adequate levels of protective neutralising antibodies. This problem is exacerbated by the fact FMDV capsids (146S particles) readily dissociate at mild acidic conditions and at room temperature into their constituent subunits (12S particles). In addition, chemical inactivation further decreases the stability of the FMDV capsid (Doel and Baccarini, 1981).

A research team headed by Bryan Charleston at The Pirbright Institute in the UK has recently focused on (i) the development of alternative FMDV vaccines based on virus-like particles (VLPs), and (ii) the generation and characterization of more stable infectious virions and VLPs. To quantify the antigen content and integrity of these new vaccine candidates two different assays have been developed. The first, termed the thermofluor assay, is a qPCR-based technique that monitors viral genome release as an indicator of capsid disassembly using a dye sensitive to the presence of nucleic acid during a slow increase in temperature. The second assay is ELISA-based and uses llama single-domain antibodies (VHHs) that are specific for intact viral capsids. Michiel Harmsen and Aldo Dekker at the Central Veterinary Institute Wageningen UR, The Netherlands (CVI), have developed the selection of such 146s specific VHHs using phage display libraries derived from llamas immunized against FMDV. Both assays are user -friendly and can be quickly performed with minimal training using standard laboratory equipment. In combination, the techniques complement each other and have the potential to be applied for quality control of FMDV vaccines, both during and after the production process, as well as for the characterisation of optimal vaccine storage conditions.

At the 2014 EuFMD meeting in Croatia, the use of both techniques as diagnostic tools for FMDV capsid stability was presented, generating a lot of interest amongst the FMDV community. This has led to a successful application for EuFMD-FAR funding. The collaborative project combines the technical expertise of Julian Seago and Eva Perez at TPI in performing the assays with established methodologies at CVI in the production of VHHs. The project will develop and assess the assays on FMD vaccine strains currently being produced in East Africa by vaccine companies, with the intention of transferring the technologies for their future application; this will be mediated through Nick Lyons at TPI and Vish Nene at the International Livestock Research Institute (ILRI) in Kenya.

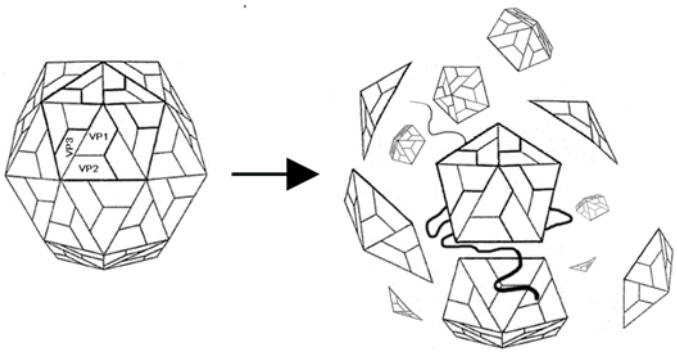

Figure 1: *Schematic representation of a FMDV virion (146S) dissociating into its constituent pentameric subunits (12S) and RNA genome. Positions of the three structural proteins (VP1-3) on the external surface of the capsid are*

Foot-and-mouth Disease Vaccine Antigen Engineering to Promote Cell Culture Adaptation, Capsid Stability and Antigen Immunofocussing to Innovate Vaccine Candidates

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FMD is not simply a contagious disease of cloven-hooved livestock, but can be considered as a complex of diseases caused by numerous genetic and antigenic variants with different geographic distributions and epidemiologies, belonging to the seven serotypes, A, O, C, Asia-1, Southern African Territories (SAT) type 1, SAT2 and SAT3 . In Africa, the epidemiology of FMD is influenced by two different patterns, i.e. a cycle involving wildlife, in particular the African buffalo (Syncerus caffer), and an independent cycle maintained within livestock. Another unique feature of FMD epidemiology in Africa is the presence of the three SAT serotypes, which are maintained within the African buffalo populations. Therefore, the presence of large numbers of African buffalo provides a potential source of sporadic infection to livestock and other wildlife species.