Structurally modified master seed viruses to enhance conventional foot-and-mouth disease virus vaccine production

Improved master seed virus

Utilises existing production technology – introduction into the market in the short to medium term

Improved stability

-Enhanced storage characteristics of formulated products

-Reduction in losses of antigen (146S) during the liquid Nitrogen freeze/thaw cycle used in storage

-Enhanced duration of immunity when combined with depot delivery system

-Improved T cell responses as a consequence of enhanced antigen presentation

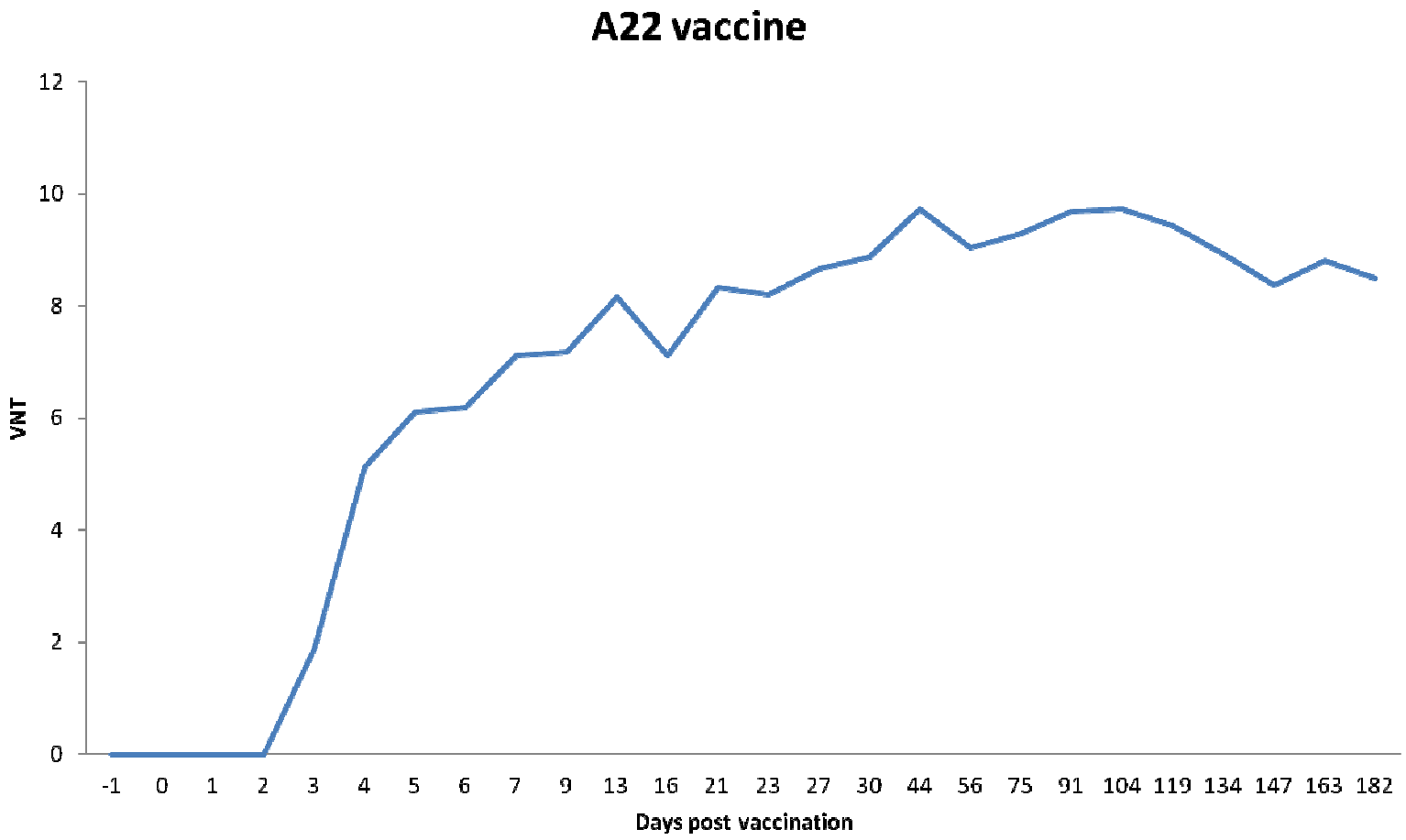
Enhanced vaccine strain adaptation

- Develop robust methods to produce infectious copy virus

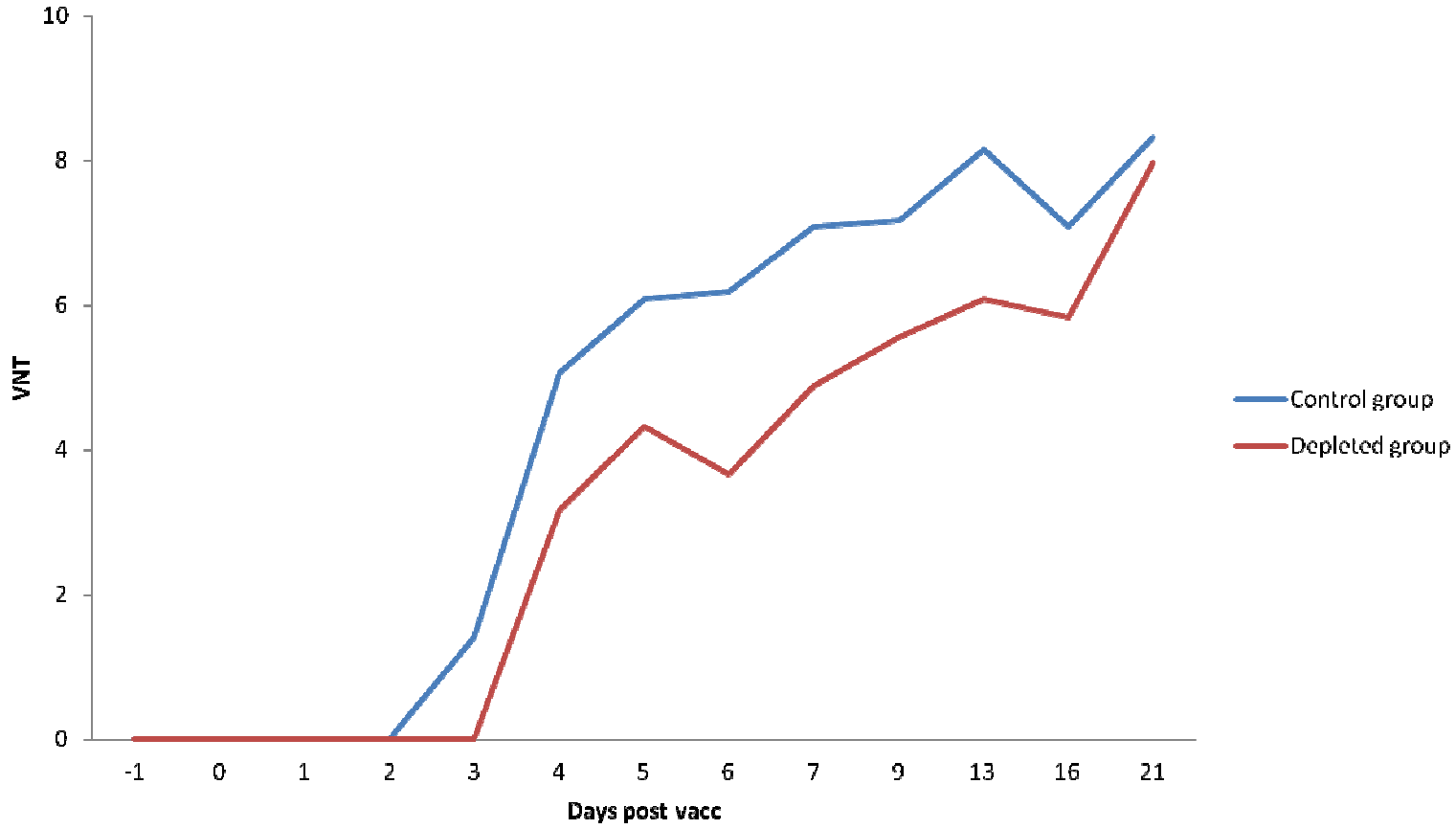
-Rapid adaptation to tissue culture

-Insert cassettes of structural protein sequences to allow rapid development of vaccines to newly emerging viruses

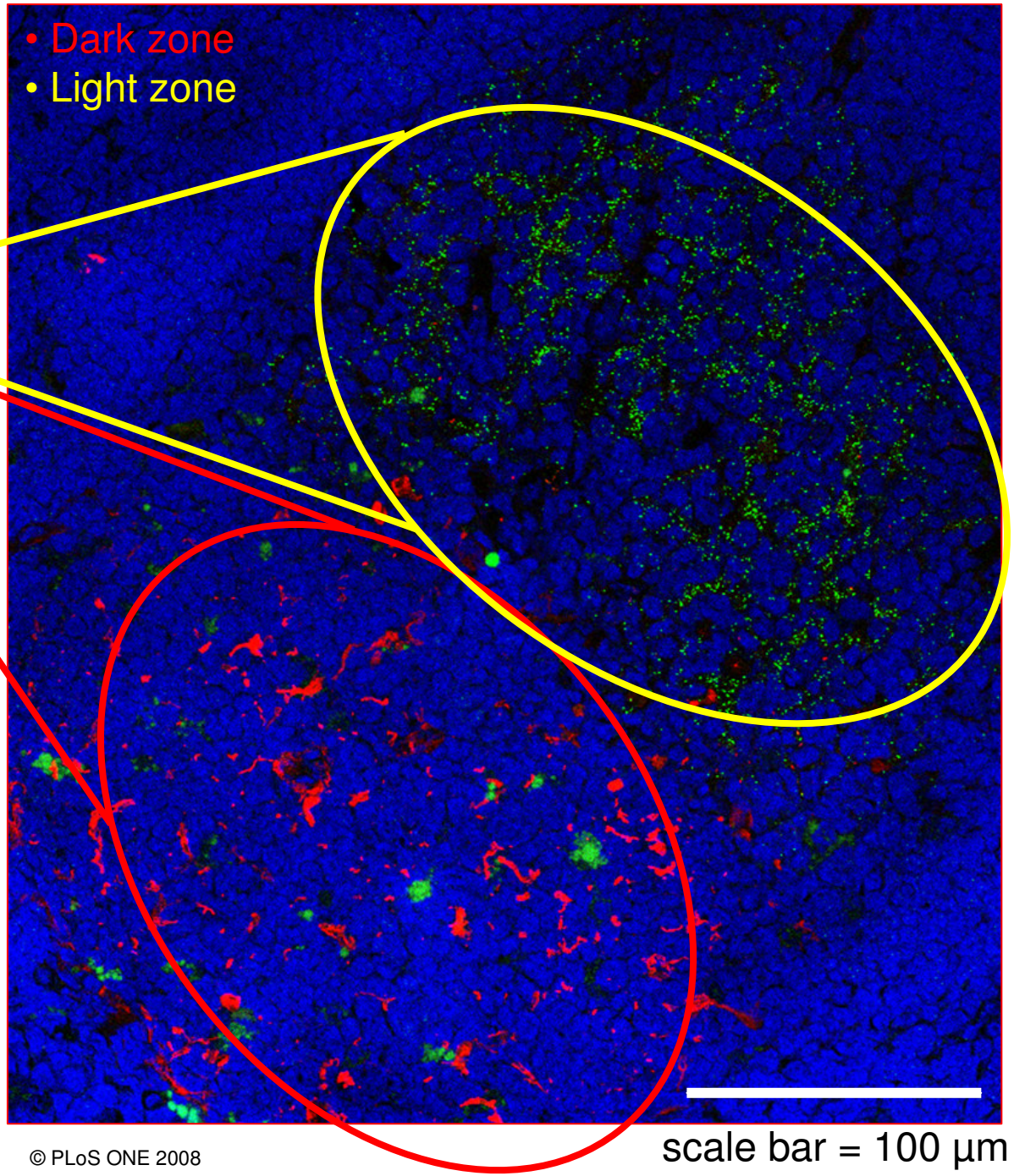
Neutralising antibody response to A22 vaccination



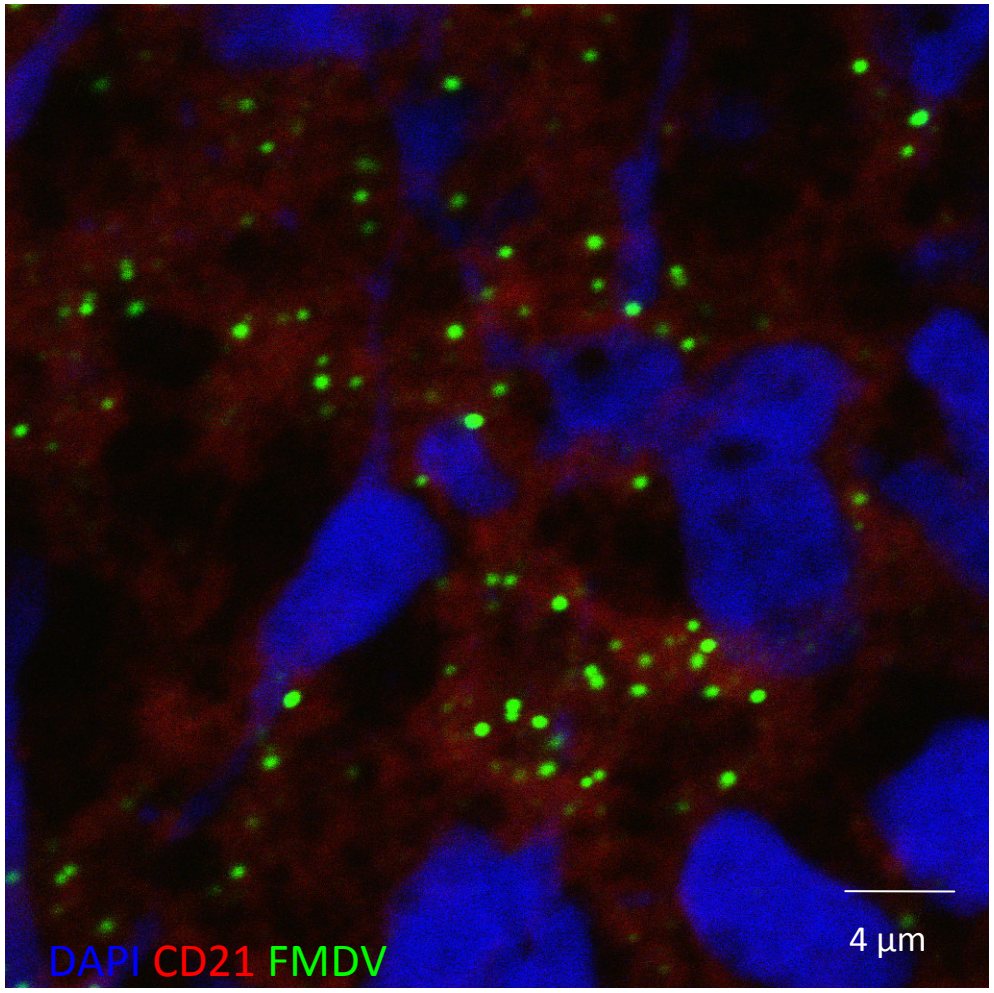
Effect of CD4 T cell depletion on neutralising antibody response to vaccination



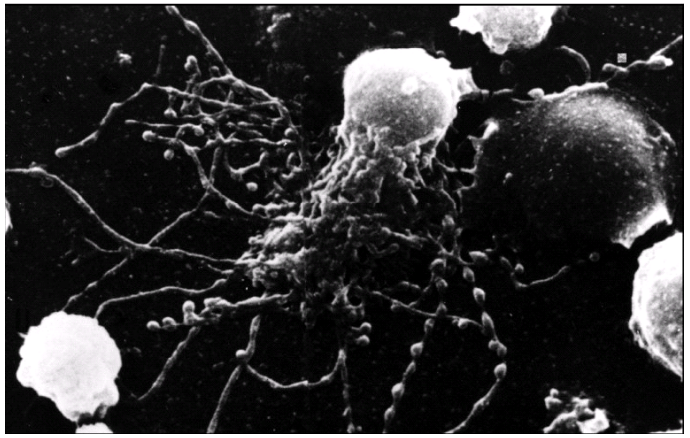
Immunohistochemistry



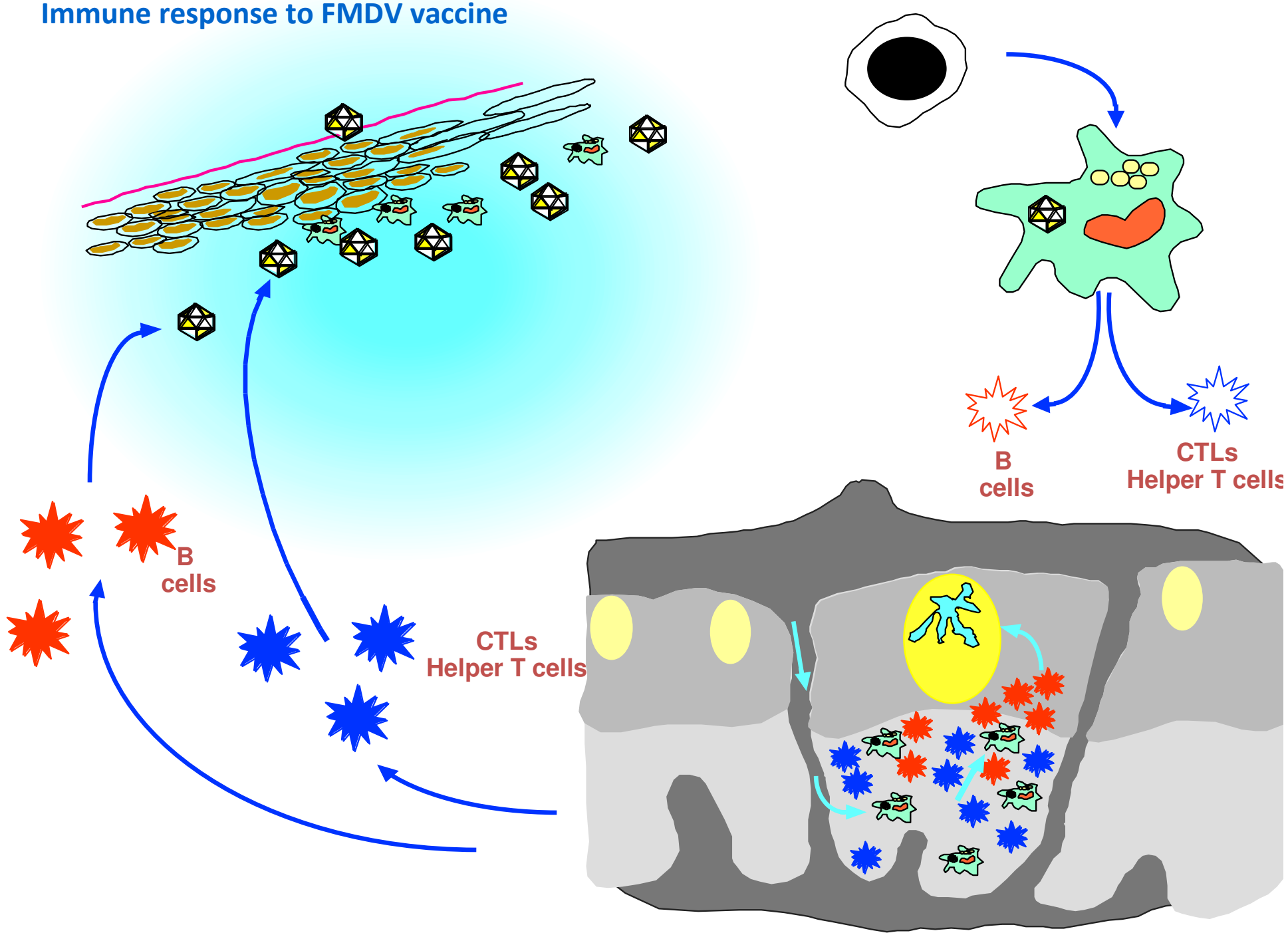
scale bar = 100 µm

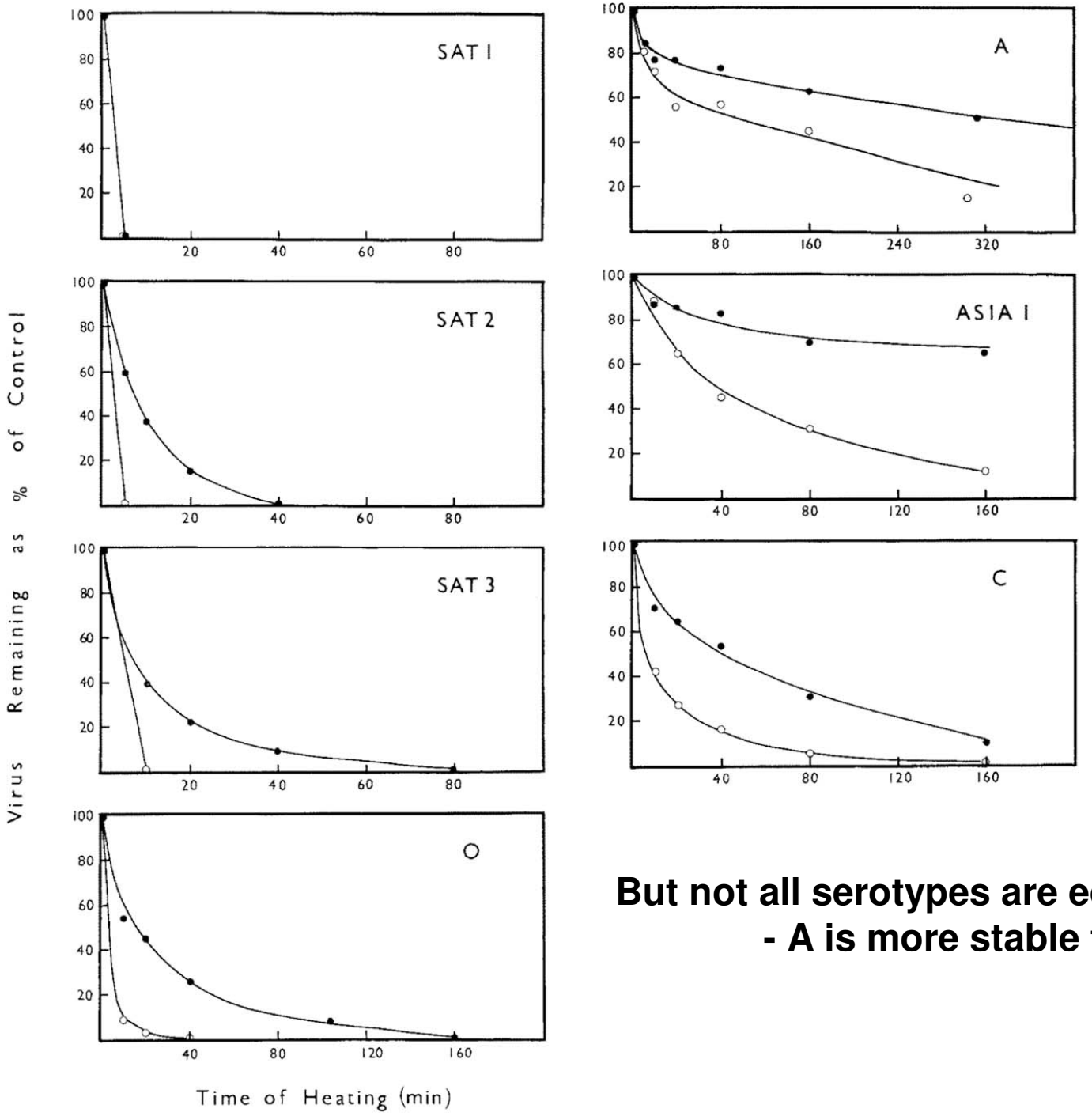


No expression of non-structural proteins:
-Non-replicating
-Extracellular



Immune response to FMDV vaccine





FMDV Serotype stability

Thermal stability at 49 degrees,

Untreated - filled circles)

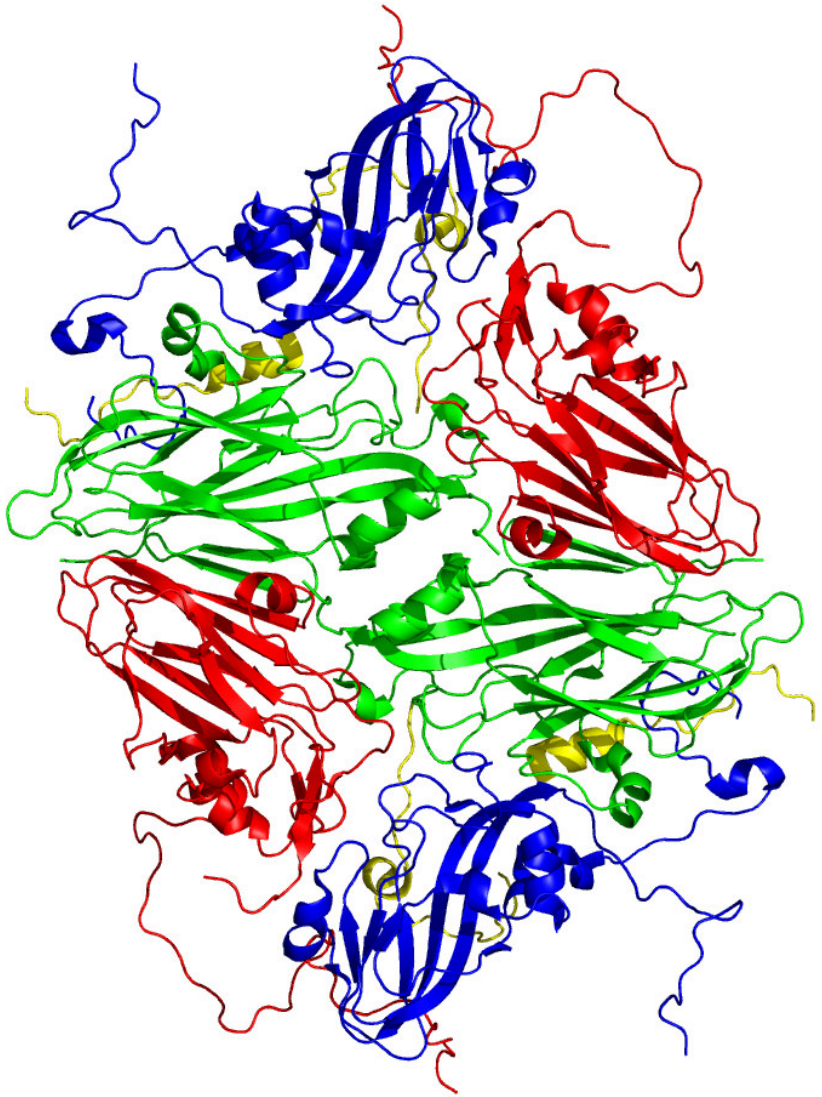
Chemically inactivated (BEI) - open circles

(Sucrose density assayed)

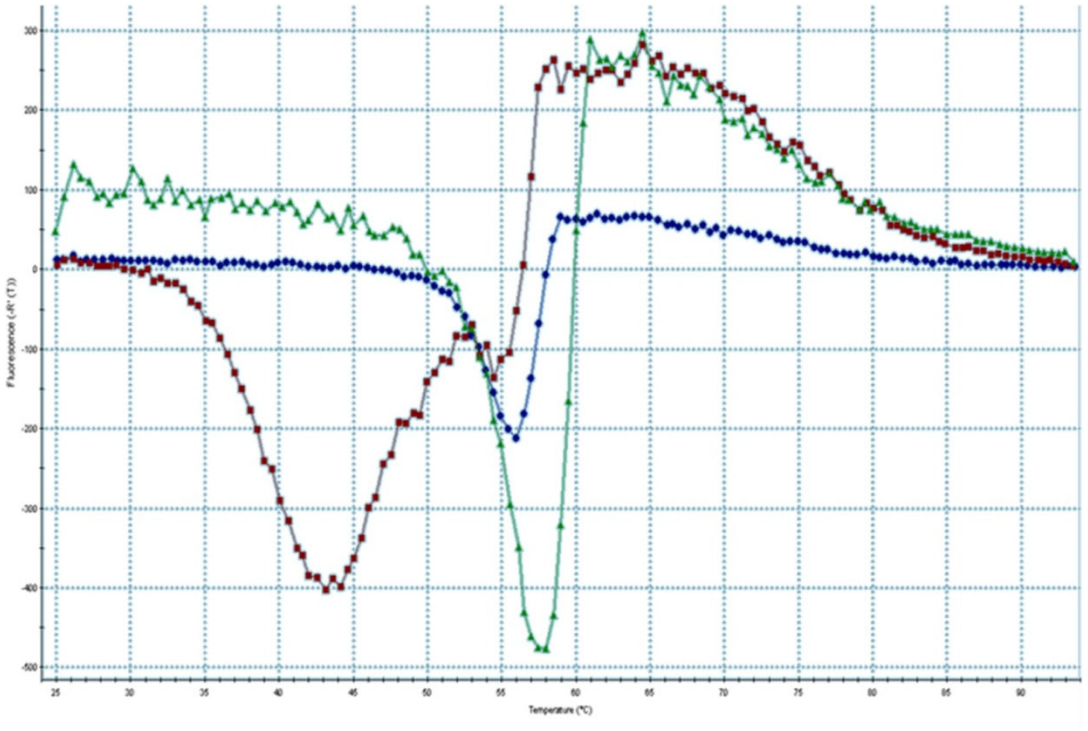
But not all serotypes are equally unstable - A is more stable than O or SAT2

From Tim Doel

Residues Near 2-Fold



O1M Mut

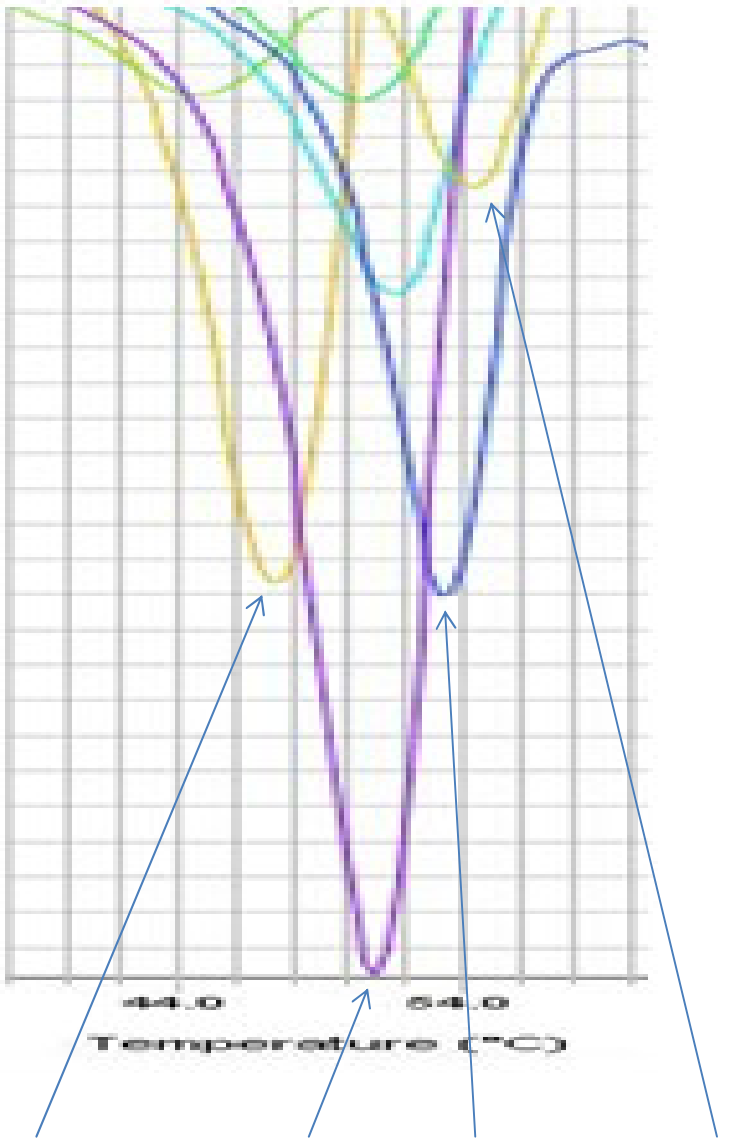


Wt

Mut-O

A

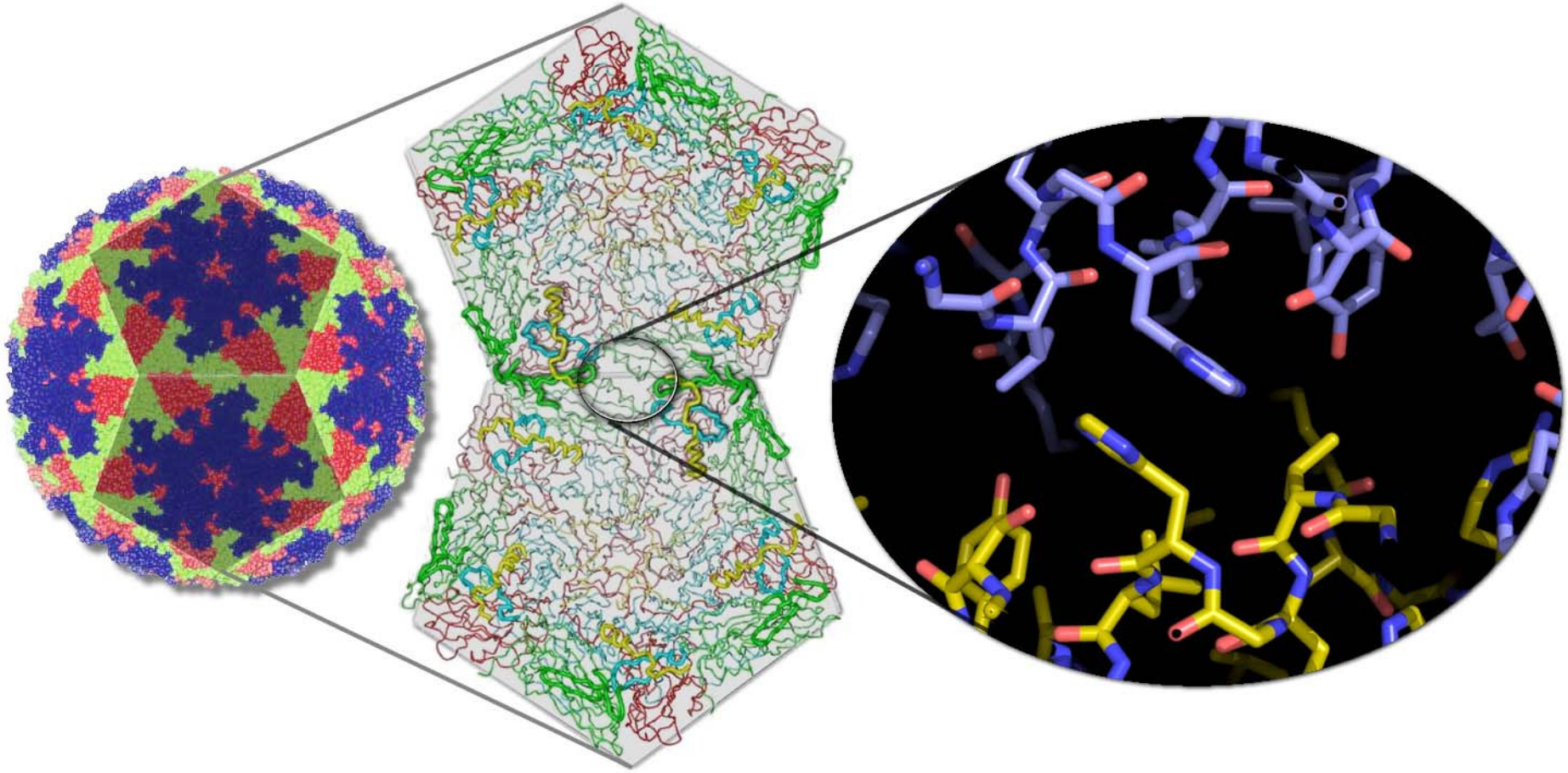
SAT2 Mut



Vaccination

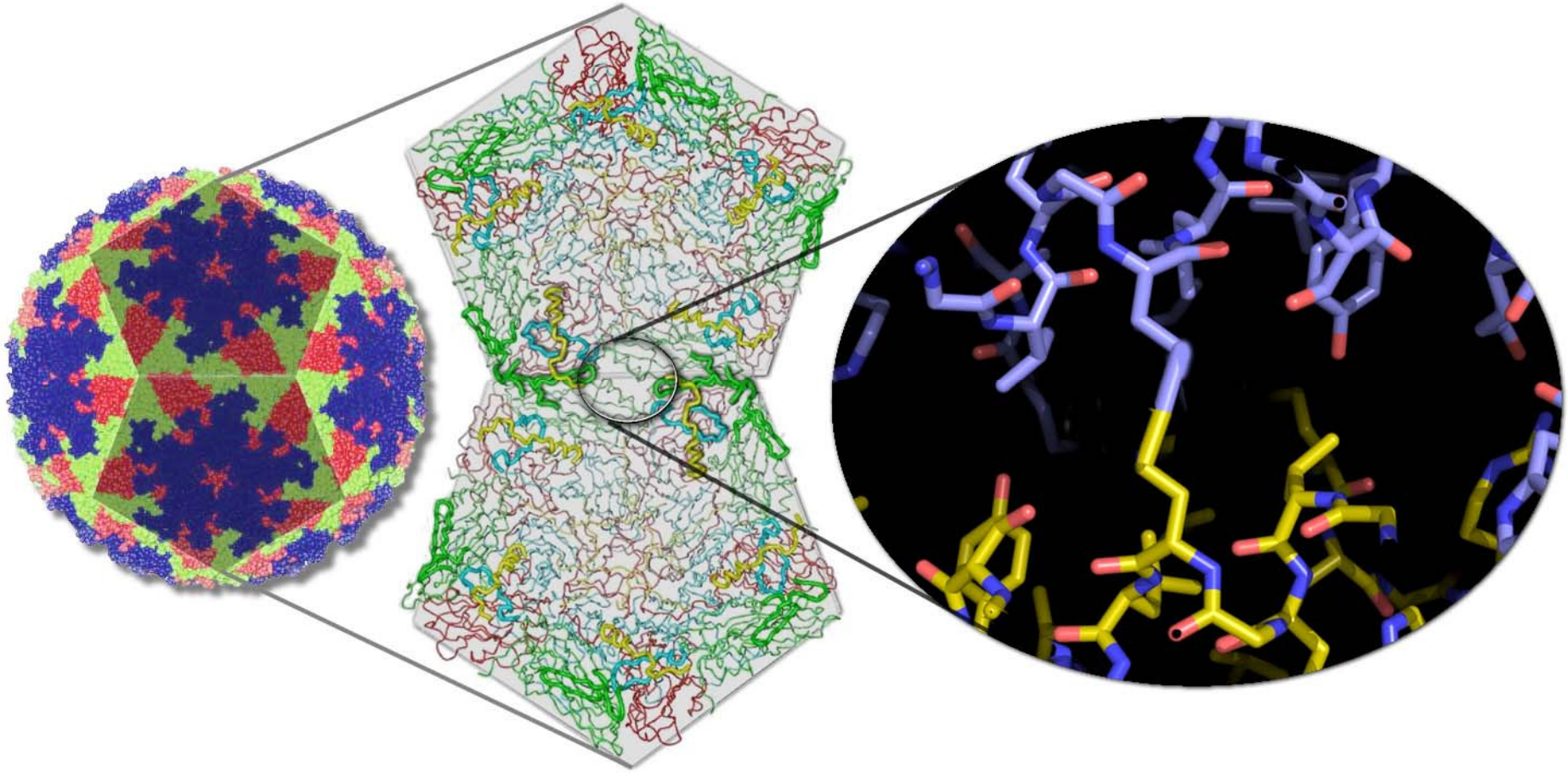
- Stabilise antigen (Persistence of antigen)
- Target antigen
- Provide co-stimulation (Danger signals)

Structure-based stabilisation of FMDV capsids



Proof of principle that an engineered mutation (his to cys) is consistent with capsid assembly.
Similar approaches can be used for infectious copies.

Structure-based stabilisation of FMDV capsids



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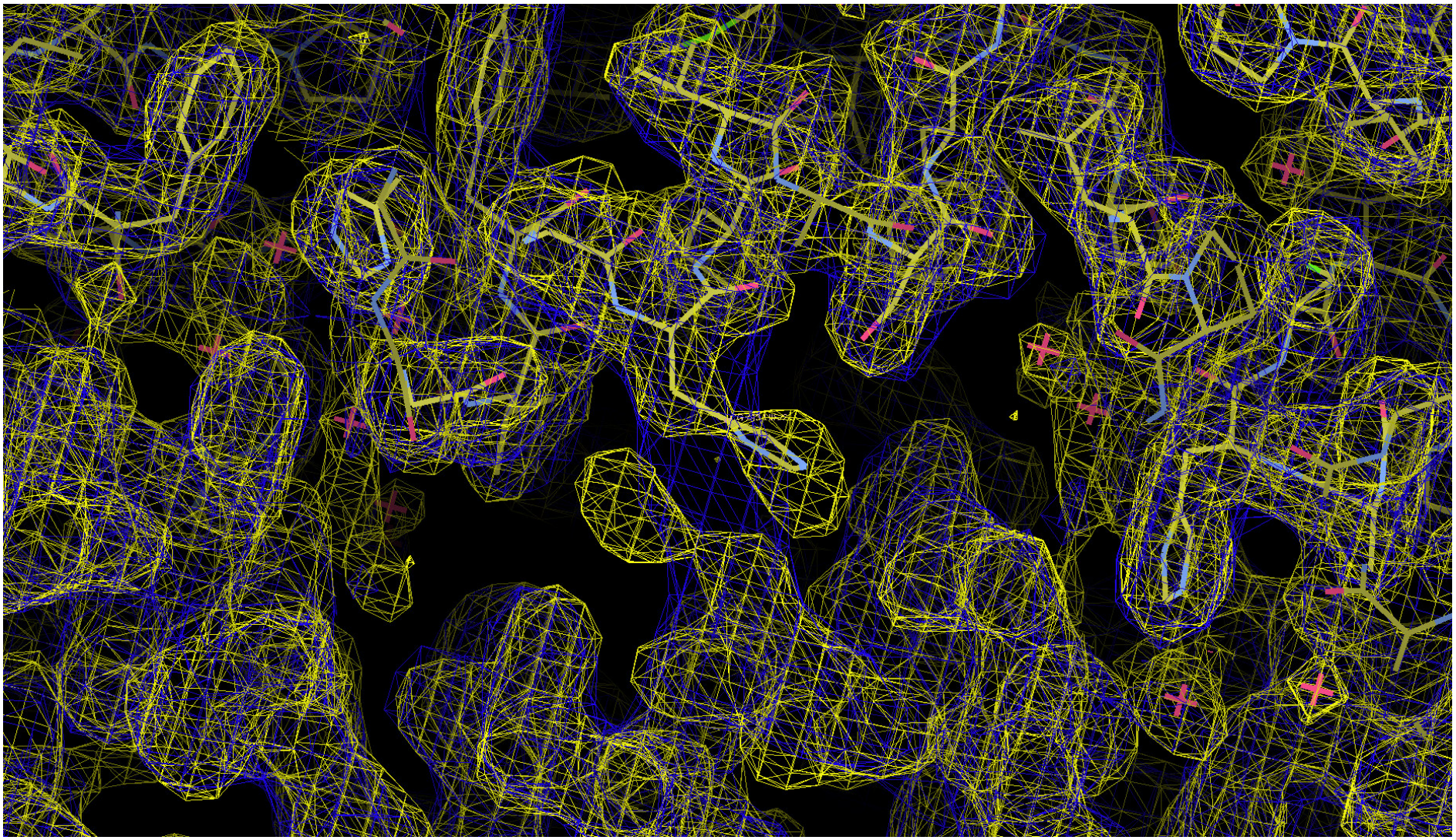
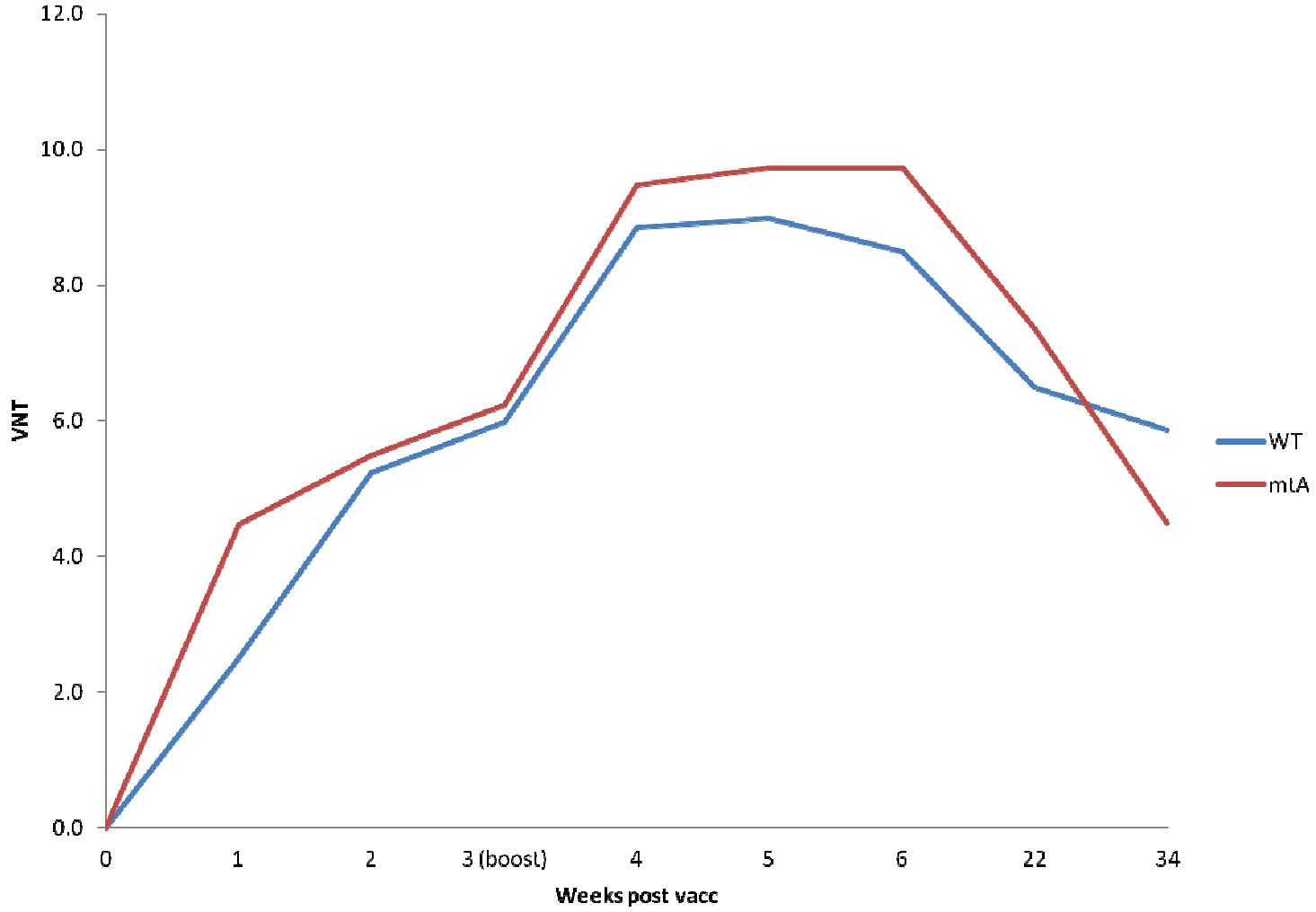
Overlay of wild-type and stable capsid structures



Cattle vaccinated with 12ug of Baculovirus derived FMDV capsids in commercial oil adjuvant Day 0 and Day 21



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-Improved B cell responses as a consequence of enhanced antigen presentation


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Excellence in Research and Development
USDA
BBSRC
bioscience for the future
wellcome trust