Non-neutralizing humoral epitopes: What do we need for protection?

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Proposed mechanisms of protection against SARS-CoV-2
Non-neutralizing antibodies may bind all over the spike, but different epitopes may be more critical or protection.
Breaking protection – via dose-de-escalation – to define correlates of immunity

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Viral Loads

Binding Antibodies

Neutralizing Antibodies

T cells
Dose de-escalation profoundly affects Fc-effector function

**Binding Titers**
- IgG1 Log MFI
- Log MFI

**FcR2A**
- Log MFI

**Monocyte Phagocytosis**
- Cellular Phagocytosis Score

**Neutrophil Phagocytosis**
- Neutrophil Phagocytosis Score

**Complement deposition**
- Complement Deposition Score

**NK cell activation**
- MPs% of NKcells

- Group I, 1x10^11 VP, n=5
- Group II, 5x10^10 VP, n=5
- Group III, 1.125x10
- Group IV, 2x10^8 VP, n=5
- Group V, Sham, n=5

III, 1.125x10

\[ \text{sham} \]
Antibody titers and function strongly predict protection from infection and viral control.
RBD and S2-specific non-neutralizing antibodies play a dominant role in protection.
Conclusions

Antibody functions targeting the RBD (highly exposed) and the S2 (highly conserved) are likely key to protection against SARS-CoV-2 infection & disease.