A cell-based, SARS-CoV-2 spike protein binding assay reveals differential impact of RBD-targeting antibodies

Neale Harrison[1], Elizabeth Jinks[1], Chiara Pallini[1], Ines Morano[1], Connie Akiror[1], Andrea Lavado[1], Ana Teodosio[1], Harriet Hill[2], Catherine Brady[1], John Gordon[1], Nicholas M. Barnes[3], Lawrence S. Young[4], Tim Dafforn[5], Zania Stamataki[2] and Omar Qureshi[1]

[1] Celentyx Ltd, Birmingham Research Park, Vincent Drive, Birmingham, UK.

[2] Institute for Immunology and Immunotherapy, University of Birmingham, Birmingham, UK.

[3] Institute of Clinical Sciences, College of Medical and Dental Sciences, University of Birmingham, Vincent Drive, Edgbaston, Birmingham, UK.

[4] Warwick Medical School, University of Warwick, Coventry, UK.

[5] School of Biosciences, University of Birmingham, Edgbaston, Birmingham, UK

Entry of SARS-CoV-2 into host cells relies upon the interaction of spike (S) protein with host cell membrane proteins such as the ACE2 receptor. We have developed a high-throughput, immunofluorescence microscopy-based assay that allows direct investigation of spike binding to ACE2 expressed in cells that are also susceptible to SARS-CoV-2 infection. Using this assay system, we have identified differential binding of a range of recombinant spike proteins. Using two of these recombinant spike protein formats, we have characterised the impact of antibodies that recognise ACE2 and spike protein upon the spike protein binding. The results reveal a range of antibody activities from enhancement to blockade of spike protein binding. We propose this assay will be a useful cell-based system for the development of molecules that block the Spike/ACE2 interaction to prevent SARS-CoV-2 infection.