An hRSV-neutralizing prefusion F-specific single domain antibody that binds to a membrane-proximal site on F

HRSV is an important respiratory pathogen, for which still no vaccine nor specific therapy is available. The fusion protein (F) is highly conserved and transforms during viral fusion from a metastable prefusion conformation to a postfusion conformation. Previously we identified two RSV-neutralizing prefusion F-specific single domain antibodies (VHHs), F-VHH-4 and F-VHH-L66. In this study, a new screen for RSV-neutralizing VHHs was performed. F-VHH-Cl184 was selected based on its high RSV A-neutralizing activity and its ability to bind RSV prefusion F at a different site than F-VHH-4. Crystal structures of the VHH in complex with prefusion F show that it primarily binds to antigenic site I, a site which is typically associated with poorly or non-neutralizing antibodies.

We isolated and characterized an RSV-neutralizing VHH that binds a unique prefusion F-specific epitope. The single-domain antibody has high neutralizing activity against RSV A, and limited neutralizing activity against RSV B. The VHH binds specifically and with high affinity to prefusion F. The epitope of F-VHH-Cl184 has not been described before and mainly overlaps with antigenic site I, with additional interactions with sites III and IV.

The authors declare that no competing interests exist.