4-4-2022

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DEVELOPING METHODS FOR THE PRODUCTION OF ANTIVIRAL VHH-Fc ANTIBODIES IN PICHIA PASTORIS FOR FAST PANDEMIC RESPONSE

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Antibodies are effective in the treatment and prevention of emerging infectious diseases. Nevertheless, their rapid deployment is hampered by the expensive and time-consuming production process in CHO cells. Yeast expression of classical hIgG mAbs often results in relatively low expression yields. We report that the fusion of the variable domain of single domain antibodies (VHH or nanobody) with the human IgG Fc, VHH-Fc, is a much more suitable format for expression in *Komagatella phaffii* (aka *Pichia pastoris*) as compared to full hIgG. We investigated the production of broadly neutralizing VHH-Fcs against SARS-CoV-2 infections. The Fc part of the antibody was re-engineered to make it yeast-compatible, to tune effector function and to obtain favourable stability. We will present data illustrating that, given appropriate engineering, production of VHH-Fc in *P. pastoris* can result in protein quality on par with that obtained in CHO cells. In addition, these *Pichia*-optimized antibodies showed to be as protective as the CHO-produced antibodies in animal models. These results set the stage for a future yeast-based single domain antibody platform for rapid response to pandemic outbreaks.