Pan-HA ANTIBODIES CONFER PROTECTION IN MICE AGAINST INFLUENZA

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The elderly population is one of the most vulnerable groups to influenza infection and influenza-related complications. Unfortunately, vaccination exhibits reduced efficacy in this population. Immunization and treatment with passive antibody transfer could therefore be a valuable alternative.

In this project, we have generated antibodies against a constant region of hemagglutinin (HA), the main protein found at the surface of the virus. In vitro, two lead candidates (mAb 10A9 and mAb 11H12) were able to detect strains belonging to 13 subtypes of Influenza A as well as B strains (1). In order to facilitate large scale production, stable CHO pools were generated for pan-HA antibody production. Biophysical characteristics of antibodies produced in CHO cells were similar to the ones of antibodies generated using mouse hybridomas. The antibodies were further tested in a mouse model of influenza to evaluate their protective potential.

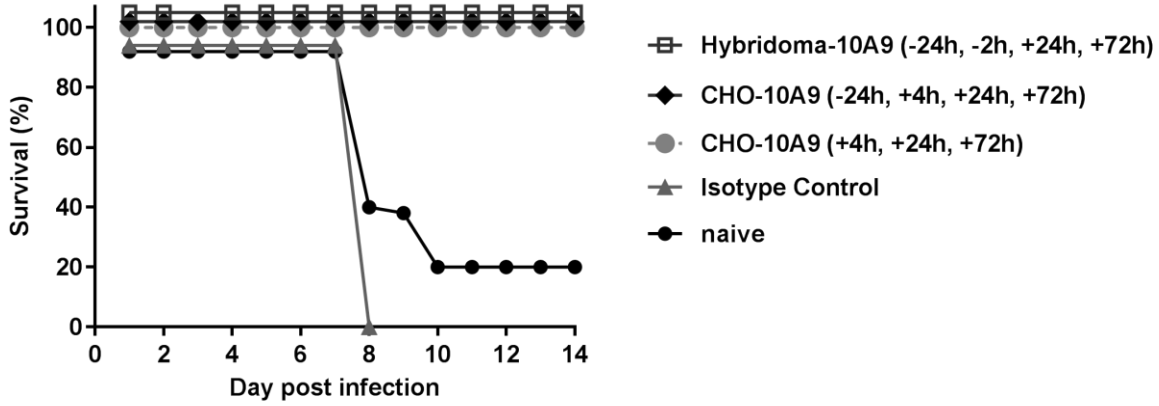

Figure 1 – Protective effect of 15 µg/g body weight of mAb 10A9 (produced from mouse hybridoma or CHO cells) against H3N2 A/Hong Kong/8/68 in BALB/c mice (n= 5 per group).Mice were infected with 10^4PFU virus by intranasal challenge. The different injection times relative to infection are shown in the legend in brackets.

The antibodies offered protection against influenza regardless of their production platform (Figure 1). The CHO-produced antibody was tested in prophylactic mode (first injection 24hrs before the challenge) and as a therapeutic (first treatment 4hrs after viral infection). In both cases, all mice survived. Other viral strains and treatment regimens have to be tested but these preliminary results are encouraging.

Finally, multiple repeated administrations of the mAb in at-risk population would be impractical and too expensive. Therefore, recombinant Adeno-Associated-Virus (rAAV) is being considered as a delivery system. Using rAAV would allow delivering the genes encoding for the mAb and ensuring their long-term expression. The heavy chain and light chain of the pan-HA antibodies are expressed on the same cassette and transfected into suspension HEK293SF cells, along with two other plasmids to form the AAV particles. After purification, the AAV will be injected in mice for long term production of the antibodies (experiments ongoing). This would represent a cost effective delivery route in immunocompromised or elderly individuals.

Manceur AP et al, Generation of monoclonal pan-hemagglutinin antibodies for the quantification of multiple strains of influenza. PLoS One. 2017 Jun 29;12(6)