DEVELOPMENT OF A STABILIZED TRIMER PRE-FUSION RSV F RECOMBINANT VIRAL GLYCOPROTEIN VACCINE

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It has been known that the RSV fusion protein F is a target vaccine protein to produce a protective immune response. The VRC has shown (Ngwuta, et.al.) through binding competition assays that the amount of pre-fusion site Ø–specific antibodies correlates with neutralizing (NT) activity, whereas the pre/post-fusion site II mAbs does not correlate with neutralization. Our results indicate that RSV NT activity in human sera is primarily derived from pre-F–specific antibodies, and therefore, inducing or boosting NT activity by vaccination will be facilitated by using pre-F antigens that preserve site Ø. Therefore, the instability of the RSV pre-fusion conformation has limited the potential of this as a vaccine antigen. Therefore, the VRC has designed a structurally stabilized glycoprotein pre-fusion RSV F trimer vaccine antigen and has shown it to be highly immunogenic in preclinical studies. A description of challenges in the development of a high productivity CHO cell line, production process and product quality and antigenic characterization assays for Phase I clinical material will be presented along with comparison of pre-clinical results of research to development material.

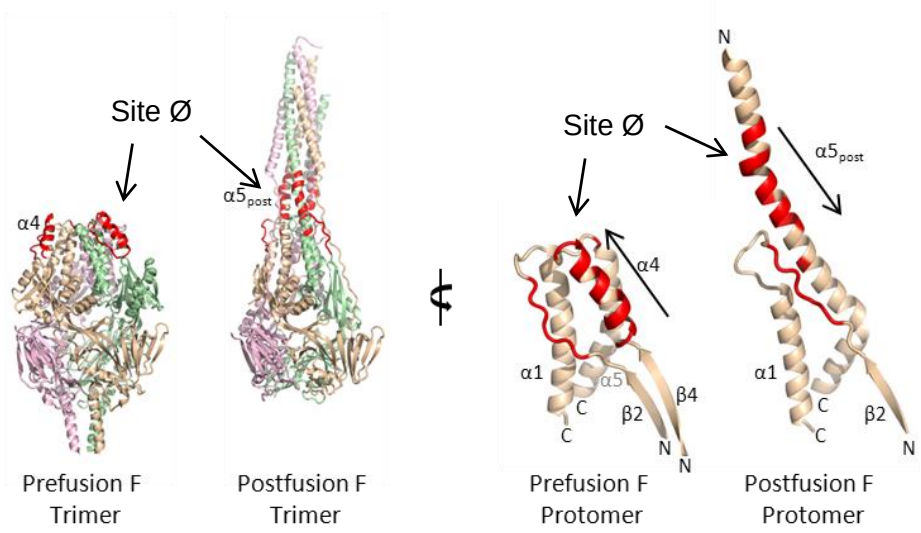

Figure 1. Antigenic Site Ø on pre-fusion and post-fusion RSV-F. Trimer on the left and monomer on the right. (McLellan et al. Science 2013).