HIV-1 ENVELOPE VACCINE PRODUCTION WITH IMPROVED YIELDS AND GLYCOSYLATION PROFILE THROUGH MANNOSE SUPPLEMENTATION

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A long-standing goal of the HIV field has been to develop a vaccine; however, there has been limited success in this pursuit, to date. The HIV-1 envelope glycoprotein (Env) is the only HIV viral protein known to elicit broadly neutralizing antibodies (bNAbs) and as such Env is the only candidate molecule for vaccine design. Recent advances have been made for stable expression of this recombinant protein in its closed, pre-fusion native viral surface conformation, with the current work focusing on the BG505-DS-SOSIP.664 construct developed at the NIH. The HIV-1 Env is a trimeric construct containing approximately 90 N-linked glycans accounting for over 50% of the protein mass. This glycan profile is an essential determinant for viral infection, with Env having a predominantly oligomannose glycan composition. Specific glycans are utilized for the binding epitopes of several bNAbs, indicating the importance of the glycosylation profile in a potential vaccine candidate. Utilizing DoE principles, a media supplement screen was carried out in shake flasks and ambr®15 micro bioreactors to investigate magnesium and manganese cations, monosaccharides, and higher nutrient supplementation on the Env glycosylation profile. These screens identified that supplementation with mannose could significantly improve the quantity and quality of the recombinant protein, but other nutrient feeds and hexose sugars, such as glucose or fructose, did not provide a similar benefit. Glycan profile analysis confirmed that the benefit of mannose can be attributed to the shift in the glycan profile to increased oligomannose species. Additional studies are planned to optimize the mannose and other monosaccharide supplementations with the ultimate goal to incorporate the results into a GMP manufacturing process.

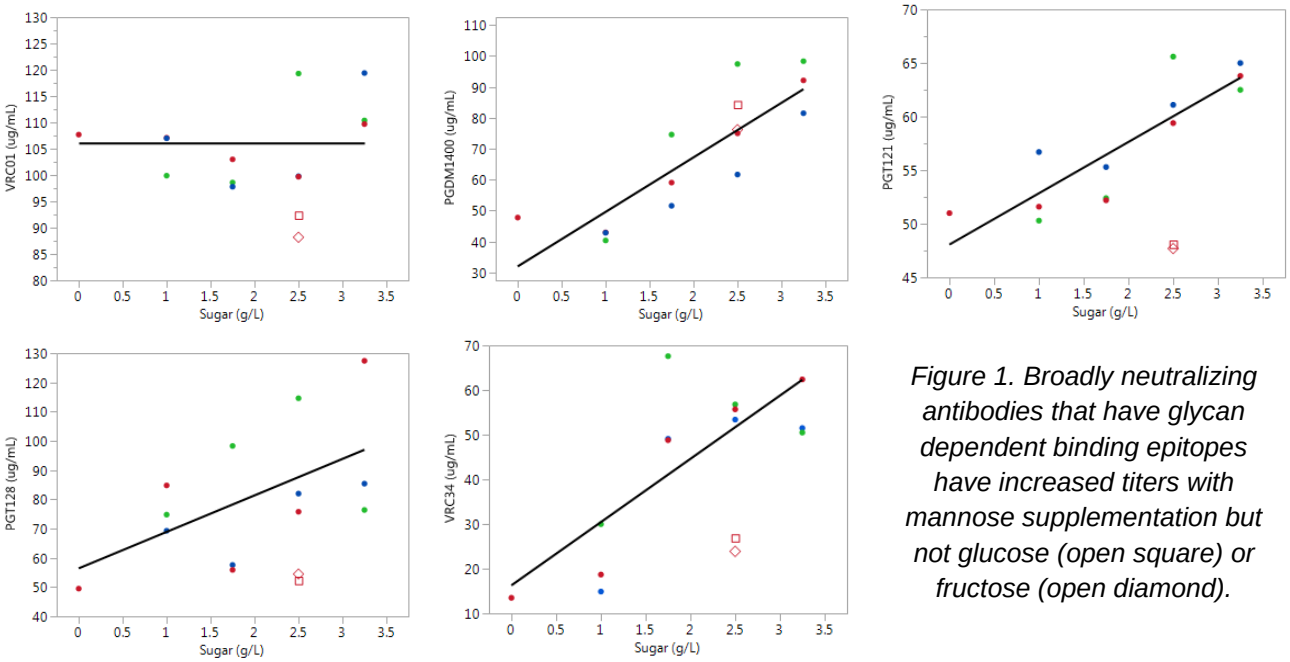

Figure 1. Broadly neutralizing antibodies that have glycan dependent binding epitopes have increased titers with mannose supplementation but not glucose (open square) or fructose (open diamond).