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Impact of harvest conditions on the glycosylation profile of a therapeutic antibody

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It is essential to maintain the glycosylation profile of a protein therapeutic as it can affect its efficacy (ADCC or CDC), pharmacokinetics/pharmacodynamics, safety, and/or immunogenicity. Pilot scale experiments for an antibody manufacturing process, which used low pH during harvest step to improve the robustness of a subsequent downstream filtration step, revealed the presence of certain peaks that were not present in the harvested material without such low pH treatment. Analytical characterization of these peaks identified them to be associated with M6, M7, M8, and M9 high mannose glycoforms. Further experiments, which looked into the individual effects of the feed pump and continuous centrifuge in the pilot scale harvest set up, concluded that the glycoforms were enriched in high mannose forms during the continuous centrifugation step. Intriguingly, the same was not observed when the experiments were done using a bench top centrifuge. This led to the hypothesis that the cells were exposed to varying shear rates across scales. The hypothesis was subsequently tested using the pilot scale centrifuge and a capillary shear device, in which the cells were exposed to different levels of shear stress. The data from the experiments confirmed that it was indeed the combination of high shear and low pH that resulted in the enrichment of high mannose glycoforms in the centrifuged material. Results from subsequent experiments also suggested that the enrichment potentially occurred due to the release of immature glycoforms associated with the endoplasmic reticulum (ER) and Golgi apparatus.