

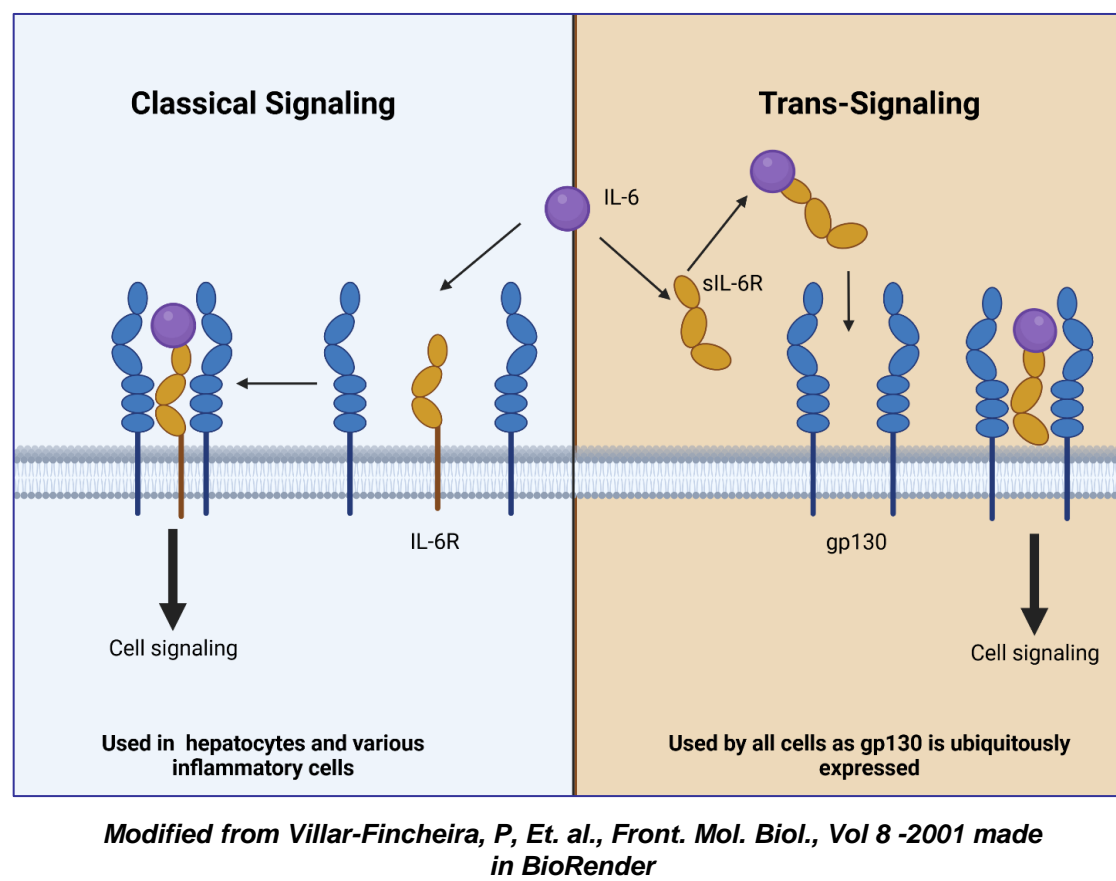
BACKGROUND

Inflammation Plays a Key Role in Venous Thromboembolism (VTE)

- Affects 1 of every 100 hospitalized children in the US each year *O'Brien, SH, Pediatrics, 1;149(3):e2021054649 (2022)*
- Pediatric hospital-acquired VTE is associated with increased mortality (up to 2%) and morbidity *Branchford, BR, Front Pediatr., 6:269 (2018)*
- Inflammatory/autoimmune disease increases the odds of VTE development (4.32, 95% CI 2.51-7.45) in children with hospital acquired-VTE *Jaffray, J, J. Pediatrics. 228:252-259.e1 (2021)*

Elevated IL-6 is Associated with Increased Risk of VTE

- First VTE *Reitsma, PH, J. Thromb. Haemost. 2(4):619-22. (2004)*
 - Independent of age, sex, ethnicity, and acute phase reactant, CRP *Matos, MF, Thromb. Res. 128(3):216-20 (2011)*
- Recurrent VTE *Van Aken, BE, Thromb. Haemost. 83(4):536-9 (2000)*



Platelets, IL-6, & Collagen

- Platelets utilize IL-6 trans-signaling
- IL-6 enhances signaling via low dose collagen and convulxin-induced activation marker expression

Zhou, Z, Circulation, 127(4):476-485 (2013)
Senchenkova, E, Hypertension, 81(1):e5 (2024)

- Preliminary data from our lab demonstrated that low-dose CRP, but not low-dose ADP or TRAP with IL-6 led to any changes in lectin binding (PNA or RCA1 via flow cytometry)

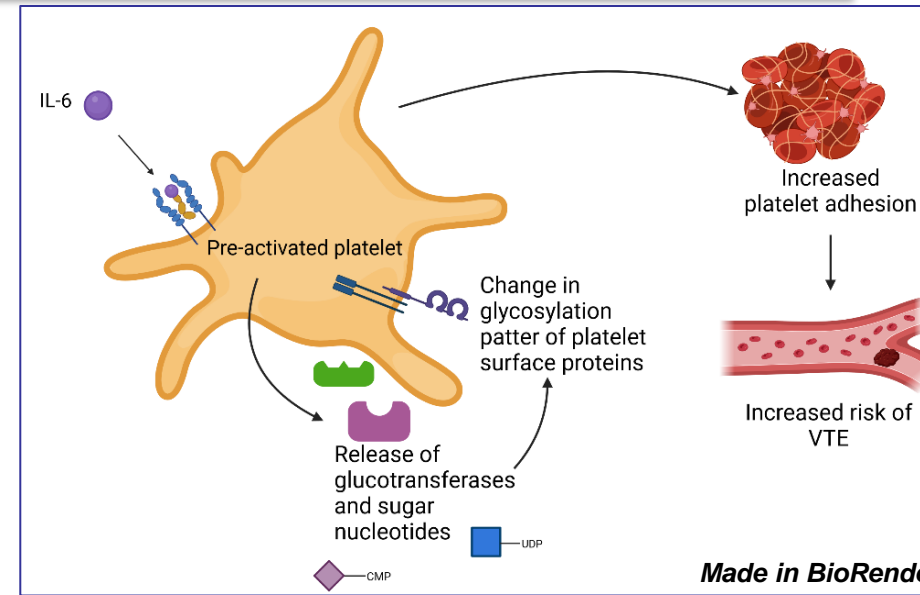
Glycosylation is Impacted in Inflammation

- Pro-inflammatory cytokines modulate cell surface glycosylation by regulating the expression of glycosyltransferases, but inflammation-associated glycan alterations on platelets themselves have not been previously studied *Dewald, JH, Cells, 29;5(4):43 (2016)*
- Platelets contain glycotransferases and sugar nucleotides necessary for altered glycosylation

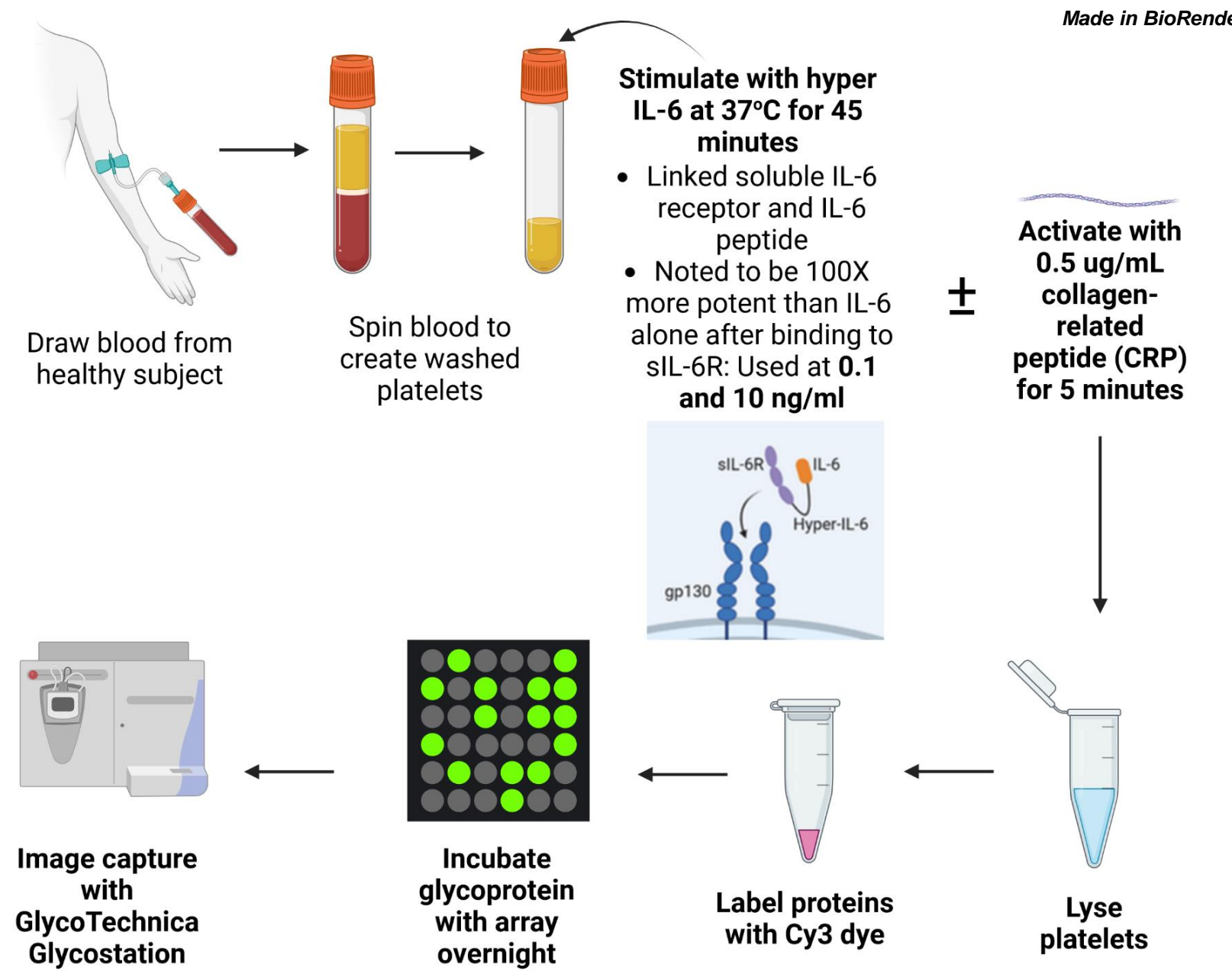
Wandall, HH, Blood, 19;120(3):626-35 (2012)
Lee-Sundlov, MM, Glycobiology, 27(2):188-198 (2017)
Lee MM, J Biol Chem, 289(13):8742-8 (2014)

HYPOTHESIS

IL-6 enhances the contribution of activated platelets to thrombosis via glycosylation changes of the platelet surface



METHODS



RESULTS

Hyper IL-6 Increases α -linked Fucosylation

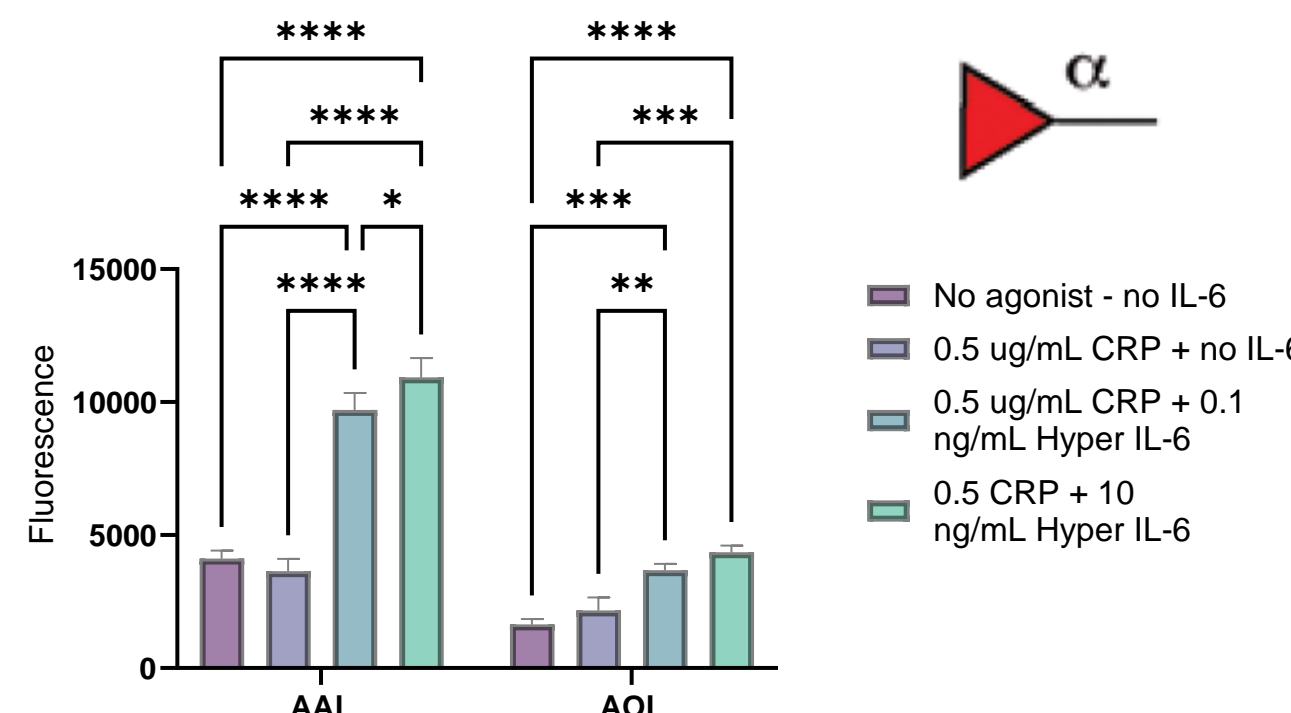


Figure 1: Hyper IL-6 increases α -linked fucosylation via increased binding of AAL and AOL lectins

RESULTS

Differential Sialylation in CRP-stimulated Platelets with Hyper IL-6

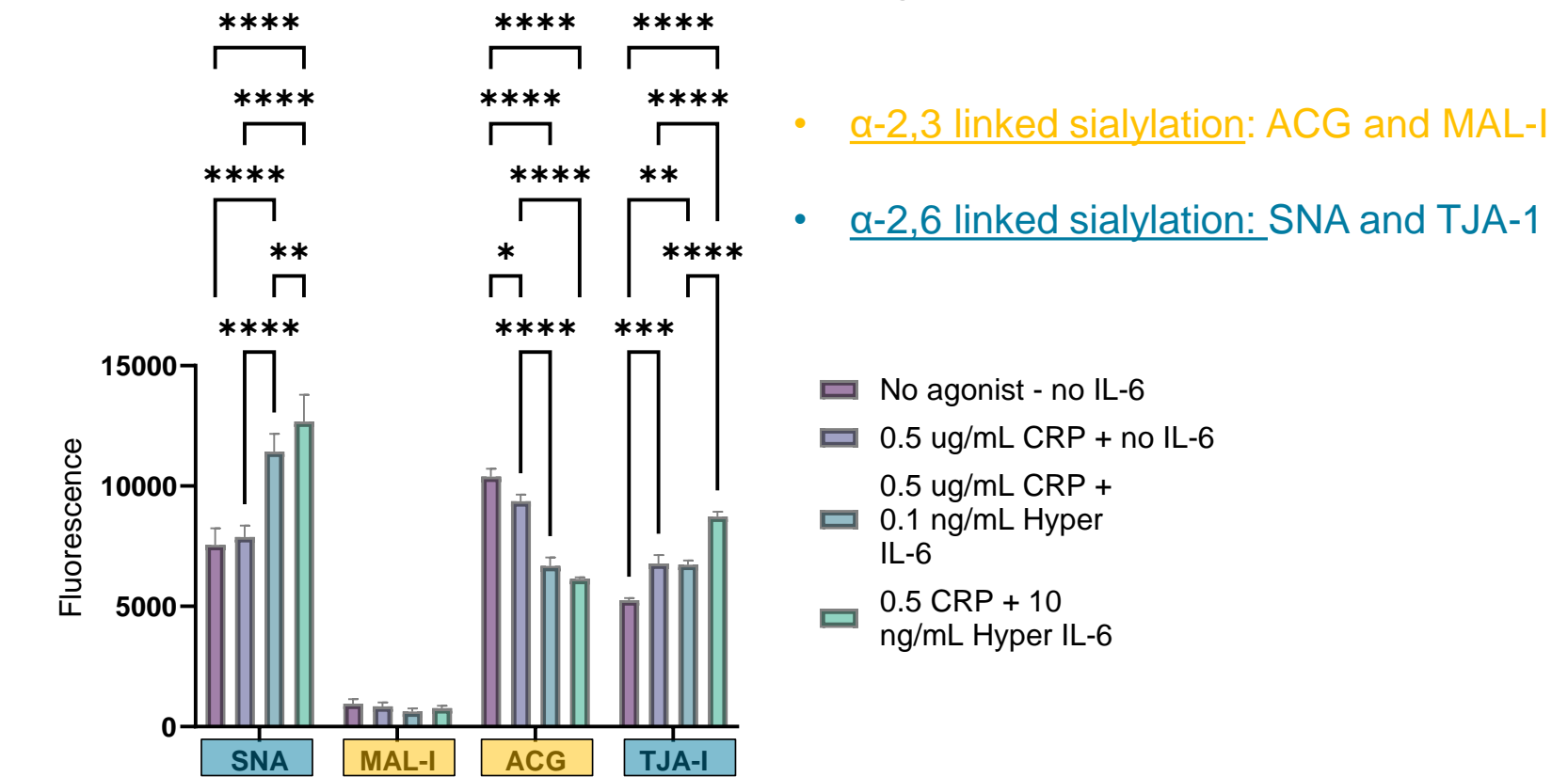


Figure 2: α -2,3 linked sialylation is significantly decreased based on decreased binding of ACG lectin and α -2,6 sialylation is significantly increased based on SNA and TJA-1 lectin binding

CONCLUSIONS

- α -Fucosylation is increased in CRP-stimulated platelets with additional IL-6
 - May impact Lewis antigens and platelet adhesion
- α -2,6 linked sialylation is increased in CRP-stimulated platelets with additional IL-6 as seen in other inflammatory conditions
- α -2,3 linked is decreased in CRP-stimulated platelets with additional IL-6

FUTURE DIRECTIONS

- Lectin immunoblotting of specific platelet glycoproteins to assess which glycoproteins are impacted
 - Focus on Lewis antigen structures and O-glycans related to adhesion of platelets and functional adhesion with Venaflex microfluidics platform

ACKNOWLEDGEMENTS

- K12 scholar in Translational Glycomics Program for Career Development in Glycoscience
- Versiti Blood Research Institute T32 training grant in Transfusion Medicine and Classical Hematology