Glycocalyx engineering reveals a Siglec-based mechanism for NK cell immunoevasion

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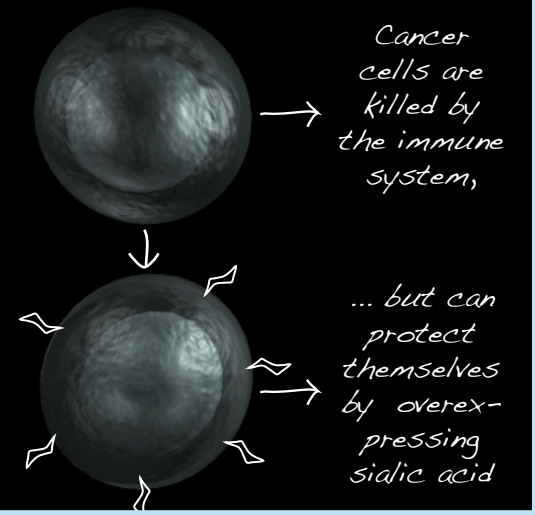
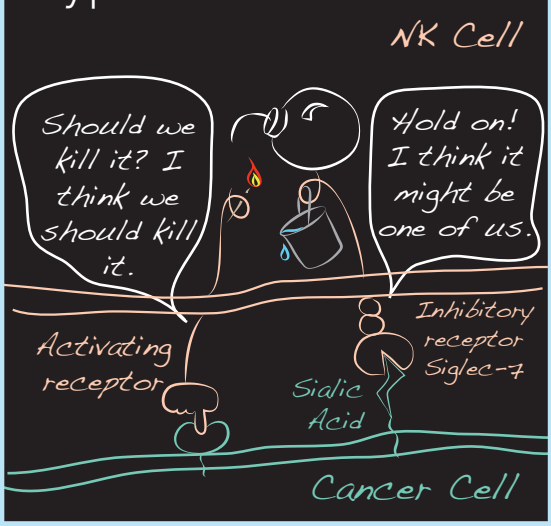
background:

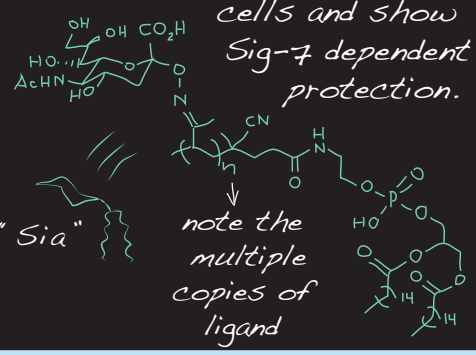


hypothesis:

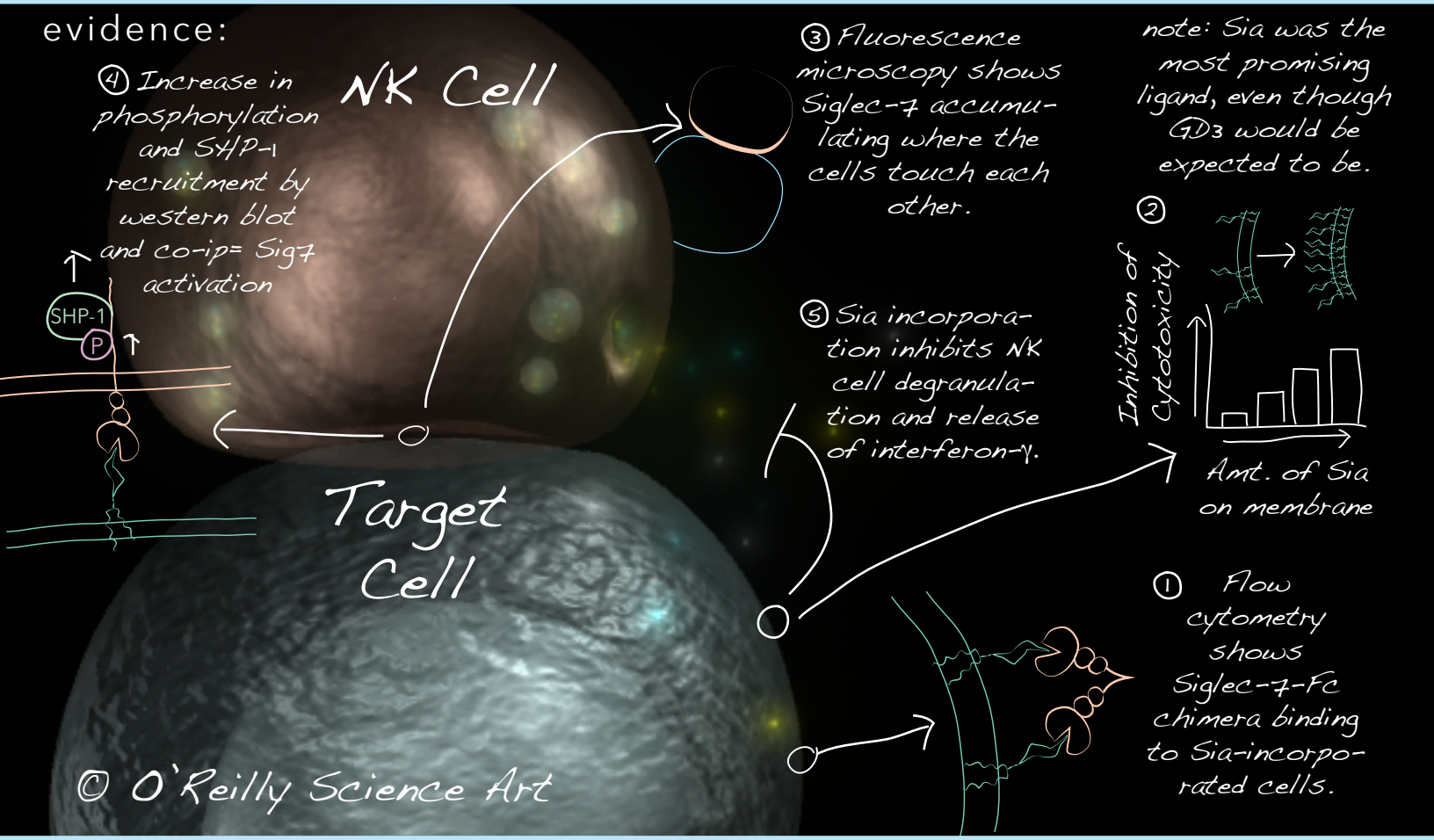


approach:

Knock out Siglec-7? Nah, they are chemists at heart. Put this or other sialoside variants onto target cells and show Sig-7 dependent protection.



evidence:



conclusions and questions:

By providing ligands for Siglec-7, target cells can trigger a silencing effect on natural killer cells in a Siglec-7 dependent manner, thus protecting themselves from a lethal attack.

One question remaining is how the levels of incorporated glycopolymer compare to the levels of native Siglec-7 ligands on cells, both cancerous and non-cancerous. Interestingly, when native ligands were removed, cytotoxicity increased, as expected, and when glycopolymers were added back, cytotoxicity dropped well below untreated. Does this mean that more than native levels incorporated? Could be, but so many other things could be going on there that I would hesitate to say that with any certainty. Nevertheless, I don't think that it undermines the results and I am excited to see this role for Siglec-7.