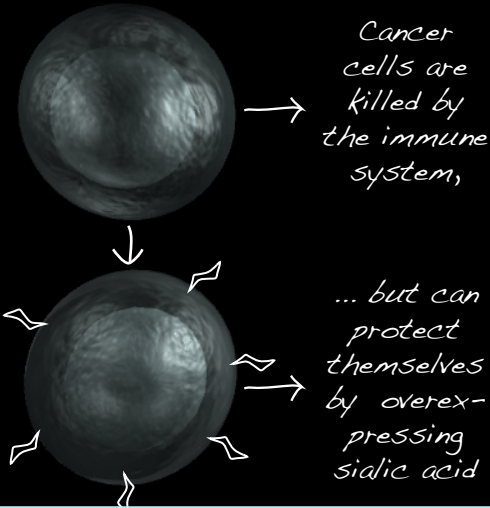


# Glycocalyx engineering reveals a Siglec-based mechanism for NK cell immunoevasion

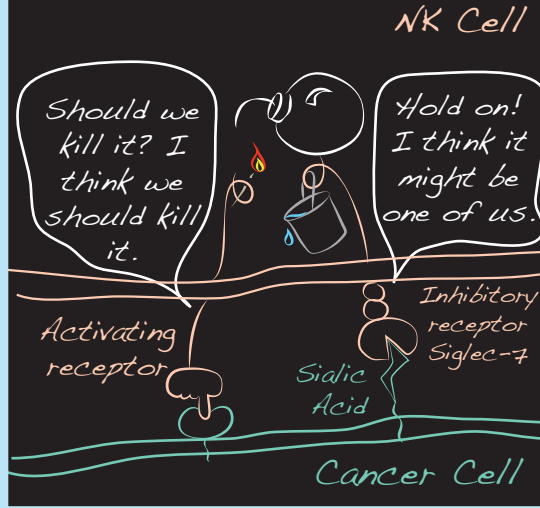
Hudak J.E., Canham S.M., Bertozzi C.R. *Nat. Chem. Biol.* 2014 Jan;10(1):69-75

doi: 10.1038/nchembio.1388. Epub 2013 Nov 24.

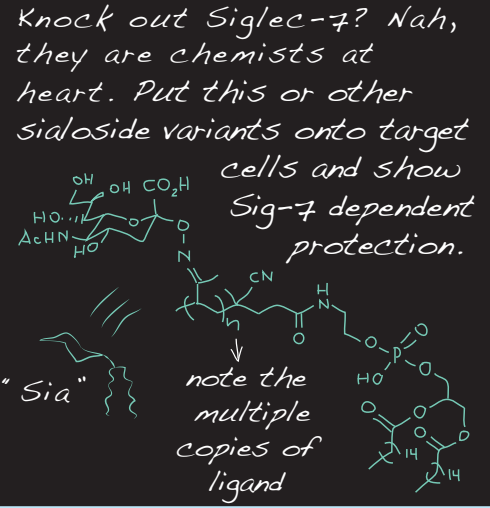
## background:



## hypothesis:



## approach:



## evidence:

① Increase in phosphorylation and SHP-1 recruitment by western blot and co-ip = Sig7 activation

② Fluorescence microscopy shows Siglec-7 accumulating where the cells touch each other.

③ Sia incorporation inhibits NK cell degranulation and release of interferon-γ.

④ Flow cytometry shows Siglec-7-Fc chimera binding to Sia-incorporated cells.

Inhibition of Cytotoxicity

Amt. of Sia on membrane

note: Sia was the most promising ligand, even though GD3 would be expected to be.

© O'Reilly Science Art

## 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.