THE SHORT ANSWER

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Microbial glycan microarrays define key features of host-microbial interactions

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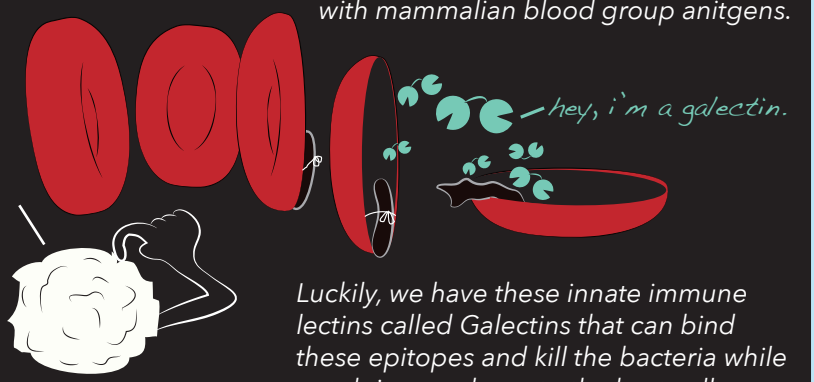
background:

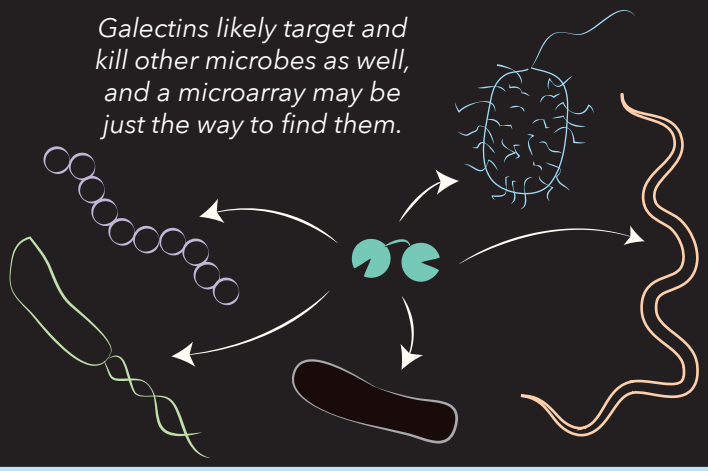
Certain types of E. coli try to trick our immune system by masking themselves with mammalian blood group anitgens.



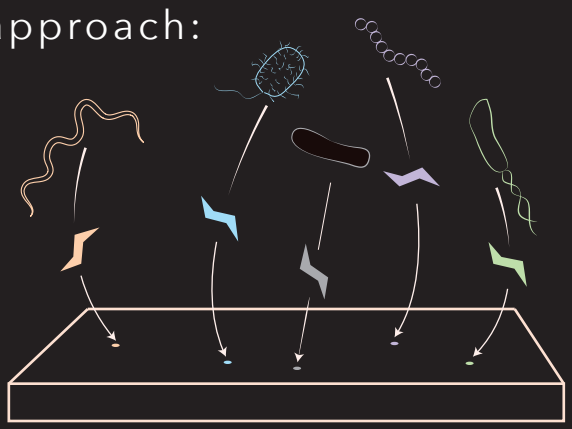
Luckily, we have these innate immune lectins called Galectins that can bind these epitopes and kill the bacteria while not doing any harm to the host cells.

hypothesis:

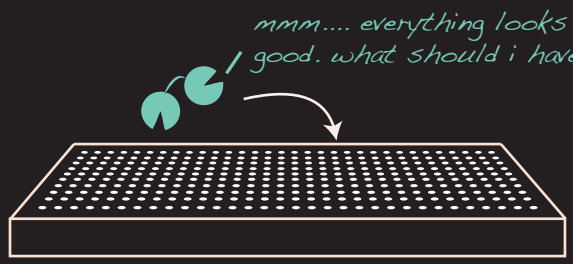
Galectins likely target and kill other microbes as well, and a microarray may be just the way to find them.



approach:



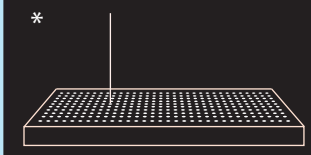
First, extract glycan epitopes from hundreds of microbes, then conjugate them to a plate, aka the Microbial Glycan Array



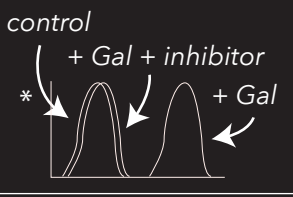
Then, probe the array with galectins (or antibodies, other lectins, etc.) to see what glycans they prefer to bind to.

evidence:

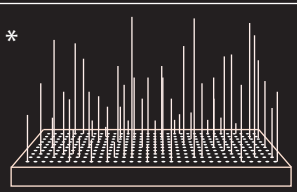
At around 0.1-0.2 μM, galectin only binds to a very specific O-antigen found on Providencia alcalifaciens O5.



Binding to P. alcalifaciens O5 is verified by flow cytometry



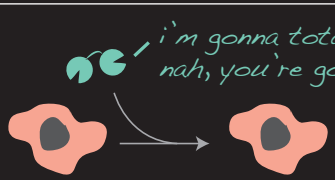
And galectin is show to disrupt viability of P. alcalifaciens O5. It does not affect a related strain of this species, but does affect other species with the same O-antigen.



At higher concentrations of galectin (5 μM), lots of other hits pop up. Interestingly, all of the glycan hits are associated with self-like antigens.

** Not actual data!*

Even more interesting, the galectins do not affect the viability of mammalian cells that have these same epitopes!



conclusions:

The innate immune function of galectins is generalizable to many different species of microbes and may be an important first line of defense, particularly for microbes that use molecular mimicry to evade the traditional, antibody-based immune system. One questions I have is how the concentrations used here relate to the physiological concentration of galectins. Maybe they get upregulated upon microbial challenge. This work opens the door to a lot of really interesting follow up, and I am looking forward to it!