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Editorial

A spoonful of sugar helps the viruses go down

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"I've put in so many enigmas and puzzles that it will keep the professors busy for centuries arguing over what I meant, and that's the only way of insuring one's immortality."
James Joyce

Keywords

Viral infection, human histo-blood group antigens, anti-adhesion molecules.

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Viral entry is the primary and often breaking point for viral infection and pathogenesis. During the millennia of viral and human (co-)evolution, the battle for life has been a back-and-forth match for survival. Increasingly sophisticated strategies have led to specific cellular structures becoming refined Trojan horses to enter cells.

The cell surface is adorned with many glycan structures, ranging from simple monosaccharides to complex sugars and glycoconjugates, with numerous branches, connections and directions [1]. The specific glycan structure varies between species and is determined by the tissue expression of particular enzymes, which transfer sugar residues to growing oligosaccharide chains [2]. Moreover, the diet and intestinal microbiota can also degrade and change the structure of glycans and change their distribution and availability in the gut [3]. In the millenary battle for life, pathogens have learned how to use host glycans for initial cell recognition, attachment and infection. These complex sugars derive through the expression of human histo-blood group antigens (HBGAs), primarily the category under control of the *FUT2* (secretor), *FUT3* (Lewis), and *ABO* genes.

Here is life lesson number one – what goes around, comes around. Breast milk contains several human maternal oligosaccharides (HMOs) [4] that are similar in structure to HBGAs. A growing amount of research has shown that HMOs are anti-adhesion molecules that operate as soluble decoy receptors, preventing pathogen attachment to newborn mucosal membranes, thus decreasing the risk of viral, bacterial, and protozoan diseases [5-7]. Mother Nature had developed this protective mechanism to shed pathogens out of breast-fed infants. At the same time, this defensive mechanism turned against the host, becoming the key to infecting human cells [8].

It is well known that the secretory status is strongly associated with susceptibility to a wide range of infectious agents [9], and the article by Mihala et al. [10] supports further scientific evidence. Infants with a secretory phenotype offer various cellular receptors for different gastrointestinal pathogens, bypassing the host defenses and entering undisturbed.

What is the deep meaning of reading the work by Mihala et al.? Indeed, knowing that secretors are at increased risk of infection does not present any practical clinical application since it is not convenient to type a population of infants to know those at higher risk of disease that should be subjected to increased surveillance or special preventive measures. However, studies that attempt to deepen how pathogens try to circumvent the immune system and stimulate understanding of the mechanisms, can boost our knowledge on the process of viral infection, immune response circumvention and disease development. The deepening of this knowledge opens up novel therapeutic and vaccine strategies, as recently demonstrated [11].

One last consideration: nowadays, viruses have never been more current, and the COVID-19 pandemic should arouse a new interest in studying preventive infection strategies. In the light of recent events, it is possible to speculate that the HBGAs, which are shared/similar between animals and humans, could be crucial not only in promoting the infectious process but especially for the viral transfer from one host to another, favoring the jump of species [12] as it happened in the case of SARS-CoV-2. Recent investigations are being conducted to determine if the binding of SARS-CoV-2 to HBGAs benefits or disadvantages each individual's sensitivity to CoVs and whether it is an additional route for the adherence of SARS-CoV-2 to human cells [9]. This insight will enable the creation of a putative vaccine and the discovery of new medications to face this and future pandemics with greater confidence.

Declaration of interest

The Author declares that there is no conflict of interest.

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