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Commentary

Significance of Sialoglycans in SARS-CoV2 Infection

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ABSTRACT

The second wave of coronavirus disease 19 (COVID-19) has hit India badly with a rapid surge of cases. One of the greatest challenges in managing infections from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the incomplete knowledge regarding the disease course, hypersensitivity, and relative resistance in a number of individuals. Recently, it has been reported that besides the Angiotensin-converting enzyme 2 (ACE2), certain sialic acids present on the cell surface may also function as potential receptors for binding the spike protein of SARS-CoV-2. In this brief commentary we briefly discuss the role of sialic acids in SARS-CoV-2 infection and suggest more research investigations pertaining to this arena. This may pave the way for breakthrough solutions to combat the current pandemic more effectively by developing specific drug-targeted therapies.

Key words: Coronavirus, N-acetylneuraminic acid, salivary diagnostics, sialic acid, targeted drug therapy

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COVID-19 WAVE

The second wave of coronavirus disease 19 (COVID-19) has hit India badly with a rapid surge of cases. All the health care workers, named front-line COVID warriors, strive hard to combat the COVID-19 infection in patients. On the other hand, researchers thoroughly investigate the disease to discover a one-stop drug solution. One of the greatest challenges in managing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections is the incomplete knowledge regarding the disease course, hypersensitivity, and relative resistance in a number of individuals in terms of the immune response[1].

VIRULENCE FACTORS

The high virulent potential of human coronaviruses is intimately related to the invasive mechanisms underlying the adhesion and viral entry to the host cells. It has been proven that the Angiotensin-converting enzyme 2 (ACE2) is the primary receptor for entry of the SARS-CoV2. Nevertheless, recently another receptor known as sialic acid has been implicated in a significant role in binding the spike protein of the SARS-CoV2[2]. Literature evidence suggests that the sialylated compounds of the cellular glycocalyx can serve as a crucial factor in mediating the coronavirus infection. Further, the sialic acid-mediated cross-reactivity with the host immune response exhibits varying intensities in specific pathological events[1].

ROLE OF SIALIC ACIDS

Sialic acids are nine-carbon sugars found attached to the terminal position of N and O linked glycans, which are polysaccharide structural components ubiquitously present on eukaryotic and prokaryotic cells[3]. The sialo-glycoconjugates present on the host cell surface have served as ligands or receptors for several viruses in the past, including the influenza A virus and Middle East respiratory syndrome-related coronavirus (MERS-CoV)[3]. It has also been demonstrated that N-acetylneuraminic acid, considered the most abundant form of sialic acid in nature, exhibits an affinity towards the SARS-CoV-2 spike protein[4]. More recently, it has been hypothesised that the high salivary expression of pivotal enzymes involved in sialic acid biosynthesis may also have a possible role in the SARS-CoV-2 infection; however, this needs to be elucidated[5].

SIALOME-MODULATING MACHINERY- RESEARCH SCOPE

It has also been claimed that sialoglycans act as self-associated molecular patterns (SAMPs) in mammalian cells resulting in the potential interaction with specific immune receptors present on the cell membranes and the amplification of inflammatory reactions within affected tissues[6]. The literature review reveals a plethora of research on the significance of ACE2 receptors in SARS-CoV2 entry, but limited evidence is available on the role of sialic acid. Higher

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ACE2 expression has been reported in the epithelial cells of the oral mucosa, tongue, and salivary glands[7]. Similarly, more research studies can be undertaken to assess the role of sialic acid receptors in the SARS-CoV2 infection, focusing on its expression in the oral epithelial cells and salivary glands. This may pave the way for some breakthrough solutions to better understand the coronavirus disease 2019 (COVID-19) and to effectively combat the current pandemic by developing targeted drug therapies. Further, the sialome-modulating machinery may inhibit the invasion of the virus through the prevention of virus-host interaction and immunomodulation, in addition to other mechanisms as rightly stated by Kuchipudi *et al.*[3].

ABBREVIATIONS

ACE2: Angiotensin-converting enzyme 2
COVID-19: Coronavirus disease 19
MERS-CoV: Middle East respiratory syndrome-related coronavirus
SAMPS: Self-associated molecular patterns
SARS-CoV2: Severe acute respiratory syndrome coronavirus 2

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The authors declare that they have no competing interests.

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