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The Immune Response in Covid-19

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Perspective

The mucosal system is that the largest component of the whole system, having evolved to supply protection at the most sites of infectious threat: the mucosae. As SARS-CoV-2 initially infects the upper tract, its first interactions with the system must occur predominantly at the respiratory mucosal surfaces, during both inductive and effector phases of the response. However, most studies of the immune reaction in COVID-19 have focused exclusively on serum antibodies and systemic cell-mediated immunity including innate responses. This article proposes that there's a big role for mucosal immunity and for secretory also as circulating IgA antibodies in COVID-19, which it's important to elucidate this in order to comprehend especially the asymptomatic and mild states of the infection, which appear to account for the majority of cases [1]. Moreover, it's possible that mucosal immunity is often exploited for beneficial diagnostic, therapeutic, or prophylactic purposes.

Although the COVID-19 pandemic has been ongoing now for several months, little or no attention has been given to mucosal immunity in SARS-CoV-2 infection. Yet this virus primarily infects the mucosal surfaces of the tract (and possibly also the digestive tract) a minimum of until advanced stages of the disease when viral RNA may become detectable in the circulation. The virus can also be acquired through the mouth, and at the conjunctival surface of the attention whence it drains into the nasal passages through the lachrymal duct. This means that its interactions with the immune system, during both inductive and effector phases, must first occur predominantly if not exclusively at the respiratory and oral mucosae. This has profound implications for the outcomes and will guide our approach to investigating and comprehending adaptive immunity in COVID-19 disease, including its diagnosis, treatment, and effective vaccine development. In terms of both the deployment of immune cells and therefore the production of immunoglobulin's, the mucosal system is far and away the most important component of the whole system, having evolved to supply protection at the most sites of infectious threat: the mucosae [2]. Secretory IgA (S IgA) is produced in quantities far exceeding those of all other immunoglobulin isotopes combined. Together with the serum counterpart, which springs from a definite source, the bone marrow, IgA is that the most heterogeneous of immunoglobulin isotopes, occurring in three molecular forms (secretory, polymeric, and monomeric), two subclasses (IgA1 and IgA2), and numerous glycoforms, collectively indicating marked differences in physiological function relating partly to the locations in which they occur. Whereas circulating IgA is usually monomeric, and consists predominantly of IgA1 subclass, S IgA is dimeric and consists of variable proportions of IgA1 and IgA2 [3]. Few functional differences are attributed to the IgA subclasses, aside from their being preferentially induced by protein vs. carbohydrate antigens and the longer hinge of IgA1 gives it greater flexibility to reach separated antigenic epitopes. However, different effector functions of IgA subclasses are ascribed to their different glycosylation profiles.

It is possible that responses might also be induced through mucosal inductive sites in the lacrimal duct or the oral cavity, although the quantitative contribution of such sites to mucosal immune responses

in humans is uncertain. Bronchus-associated lymphatic tissue (BALT) isn't normally present in adult humans, but is often found in children and adolescents, and should be induced to make by infections. This raises interesting questions on whether responses induced in BALT might contribute to the reported greater resistance of children to COVID-19 disease, or whether BALT could be induced by SARS-CoV-2 with consequences for the course of infection. All such mucosal inductive site tissues generate IgA-producing mucosal B cells that home to varied remote mucosal effector sites where they differentiate into polymeric (p) IgA-secreting plasma cells. In addition, systemic IgG-producing B cells also are induced within the tonsils and these home to peripheral lymphoid tissues where they differentiate and secrete IgG for the circulation. In the sub epithelial spaces of the mucosae and associated glands, mucosal plasma cells produce p IgA which is selectively transported into the secretions by the polymeric immunoglobulin receptor-mediated pathway, being released as S IgA [4]. Both within the nasal passages and because it descends into the trachea and bronchi, the virus encounters a S IgA-dominated environment, which is generated through the mucosal system and maintains an essentially non-inflammatory milieu.

S IgA antibodies are known to be effective against various pathogens, including viruses, by such mechanisms as neutralization, inhibition of adherence to and invasion of epithelial cells, agglutination and facilitation of removal in the mucus stream. Intracellular mechanisms of inhibiting viral replication have also been described. Moreover, S IgA is actually non-inflammatory, even anti-inflammatory, in its mode of action. IgA doesn't activate complement by the classical pathway and alternative pathway activation by IgA is essentially art factual, while the lectin pathway depends on the terminal sugar residues in the glycan structures. Furthermore, IgA antibodies have even been shown to inhibit complement activation mediated by IgM or IgG antibodies. Interestingly, results from a person's systemic HIV immunization trial suggest that prime levels of serum IgA responses compromised the protective function of IgG antibodies with an equivalent antigenic specificity and were related to a better risk of HIV infection [5].

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Conflict of Interest

None

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