The Virome: Viral Ghost Companion, Virus Wars

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While the bacterial microbiome has been intensively investigated in recent studies, the extant viral load, the virome, colonizing the host is less well defined. As noted, one can predict that this viral protoplasm, similarly to the bacterial microbiome, will also modify host immune responses. An altered bacterial population, the composition of the bacterial microbiota, is reported to alter susceptibility to upper respiratory influenza infections. Changes in bacterial populations in the gut can similarly cause chronic intractable diarrhea and malabsorption [2,3]. In order to treat foreign invading bacteria, or perhaps to treat just a simple imbalance in native bacterial pathogens in the gastrointestinal tract, or pathogenic bacterial infestations in the gut, fecal transplants using implants of more normal gut bacterial composition into a dysfunctional gut have been used successfully to restore microbial balance and to improve host health. We would propose that, quite logically, the viral populace in a host can also alter susceptibility to other viral infections and possibly also to bacterial, fungal or parasitic infections [4]. Thus, as noted by Virgin et al., these viral and bacterial microbes can be dangerous, benign or protective (symbiotic) passengers on or in the human body. Viruses are everywhere and no part of the human body, including the brain with loss of an intact blood-brain barrier, is immune to microbes.

Based on the premise of ‘survival of the fittest microorganism’, we have postulated that one invading virus may compete with other viral invaders or even the native viral population, acting to overthrow the native viral symbiot. Conversely, the native viral populace may protect their growing fields (cells) against insurgent viruses or other microbes. This microcosm of viruses, the viral biota, may compete for space and nutrition and have a role in altering immune responses [1]. The combined genome that includes bacterial and viral genetic material in a natural symbiotic ecosystem is referred to as the metagenome. (Fungal genetic material also contributes but we will not be discussing a fungal biome here).

An ongoing negotiation, and sometimes a battle, takes place on and in our bodies, on the outer and inner surfaces of all mammals. This microbial populace living on our outer skin and the inner lining of oral and intestinal layers and the respiratory tract interact, and in turn, change or perhaps even direct immune responses to outside threats. This unseen microbe populace, bacterial and viral, determines our ability to respond to invading foreign or non-host pathogens with the potential to prevent, or conversely, encourage invasion and disease by other organisms. This microbial shell, both inner and outer, is composed of both virus and bacteria and represents at least tenfold more genetic material than our own human DNA. One would suspect in general that the bacteria work outside cells through receptors, with some exceptions such as the mycoplasma, and that viruses work as intracellular agents, or even as intra-bacterial agents (bacteriophages).

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This anti-viral activity was only detected in vivo and not in vitro in pure tissue cultures. Whether this virus-derived anti-inflammatory serpin is blocking proliferation and spread of other viruses via simple interference with immune responses or via a more direct anti-viral strategy, however, remains to be determined.

While not a definitive proof, this data suggests that viruses can use their immunomodulating capacities to block invasion and proliferation of competing viruses. This work would also suggest that viruses, similarly to bacteria, can exist as chronic commensal long-lived infectious processes and not as obligate pathogenic and disease causing infections. Several myxoma and herpesvirus-derived anti-inflammatory agents have been described and studies from a variety of labs have demonstrated reduced inflammation and plaque growth after arterial surgery such as angioplasty or after organ transplant and even in arthritis models. One cannot as yet state whether this inter-viral interaction represents either 1) an alteration of the host immune response that encourages, or prevents, invasion or infection by a foreign virus or 2) a direct virus-to-virus mediated anti-viral action. In other words, does virus-mediated immune modulation make a host more, or less, susceptible to another viral infection or is this rather a direct assault of one virus species on another. Our own work with MHV68 infections, which were modified with Myxomavirus-derived Serp-1 treatment, demonstrated both reduced detectable viral antigen and also reduced macrophage invasion. In mouse Ebola infection, a reduction in viral equivalents was also seen. Certainly other viruses such as MHV68 herpes, other herpesviruses (CMV, EBV and HSV), polyoma and HIV, among others, can chronically inhabit macrophage and T and B cells and alter immune or inflammatory responsiveness of the host cells.

Thus the answer to the question posed at the beginning of this editorial, why do some patients develop deadly disease while others do not, may lie in the immune modifying nature of the symbiotic microbes with which we share our lives. Studies on the virome and its role in host immune defences have the potential to provide new insight into effects of viral infections on responses to external infections. This may open up new fields of investigation into host immune and inflammatory responses and the selective pathways that drive these responses. Investigation into potential roles of other symbiotic organisms contributing to the metagenome, such as fungi or parasites, has received even less attention. This research may lead to new discoveries in immune responses in vascular disease or even in more basic viral interactions that modify host susceptibility to invading pathogens. Rather than submitting to a fear of being taken over by an invading virus as in Ray Bradbury’s short story, „Fever Dream“ [12], we would suggest that further investigation into virus-mediated immunomodulation and into the virome as an immune-modulating element should be encouraged. Ongoing research on the virome and its modification of host immune responses has extraordinary potential to provide extensive new insights into cardiovascular diseases or indeed any pathogenic process.

Silent host, Extant screen
Outer ghost, Unknown dream
Microbe shell, Fragile chrome
Deeper well, Life’s biome
Phosphorescent, Roiling seas
Unseen presence, Viral trees
Life untold, Inner war,
Open soul, Mystic door
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References