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Current Opinion in Virology

Editorial overview: Viral immunology

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Current Opinion in Virology 2019, **34**:vii–viii

For a complete overview see the Issue

https://doi.org/10.1016/j.coviro.2019.03.003

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This issue of *Current Opinion in Virology* features six outstanding reviews covering findings and concepts critically relevant for understanding the interaction of emerging and reemerging viruses with their infected host and how this knowledge can be harnessed to develop novel therapeutics and vaccines.

Virus entry into susceptible cells is a critical initial step in the lifecycle of any virus. Multiple cell surface proteins serve as attachment points on host cells to facilitate tethering and entry of viruses into cells. In addition to proteinaceous receptors, cell surface glycans can also serve as primary binding moieties on the surface of susceptible host cells. The review by Thompson *et al.*, highlights glycan receptor usage by various virus families and the role the diversity of glycan receptors plays as determining factors for virus host and cellular tropism. The authors highlight how both enveloped and non-enveloped viruses can utilize glycan receptors for cell attachment and entry. Moreover, the authors speculate what the future holds for targeting glycan-virus interactions to treat and prevent major virus outbreaks and their associated morbidity and mortality.

Natural killer (NK) cells play a central role in the initial response to many viral infections by restricting virus multiplication at early times of infection and stimulating adaptive immune responses. NK cells control viral infection through different mechanisms including lysis of virus infected cell, cytokine production and optimal activation of adaptive T and B cell responses. A detailed understanding of the specific mechanisms by which NK cells promote control of specific viral infections can facilitate the development of better strategies to treat patients both therapeutically and through the creation of optimal prophylactic vaccines. Ali *et al.* review different mechanism by which NK cells promote control of viral infection. They also highlight the ongoing battle between the NK cell response to viral infection and the counter adaptations viruses have employed to subvert NK cell-mediated immunity. Finally, the nascent concepts of NK cell memory and exhaustion are discussed and how they relate to the host response to viral infections.

Monoclonal antibodies (MAbs) with neutralizing activity have moved to the front row as potential therapeutics against viral infections for which licensed vaccines or effective therapeutics are not available. In addition, these MAbs provide investigators with unique tools to identify and characterize conserved viral targets for the development of antiviral drugs and design of novel vaccine strategies, topics that are discussed in two papers within this issue of *Current Opinion in Virology*. The first paper is by Chen *et al.* and reviews the current knowledge about the genetic and structural features of a

group of broadly neutralizing MAbs (bnMAbs) that share an immunoglobulin heavy chain variable region (V_H1-69) and that have been documented for influenza virus, HCV and HIV-1, three viruses with great impact in human health. The development of vaccines with broad spectrum of cross-protection against these highly variable viruses would represent a major breakthrough in public health. Structural knowledge of viral epitopes targeted by these bnMAbs can guide rational design of immunogens that could provide the bases for broadly cross-protective vaccines for viruses whose genetic diversity facilitate escape from host antibody responses targeting immunogenic, but highly variable, epitopes. The second paper is by King *et al.* and reviews the structural features of MAbs that target the filovirus glycoprotein (GP) and are broadly cross-reactive against different ebolaviruses, with some of them having shown to be protective in non-human primate models of Ebola virus (EBOV) disease (EVD). This paper illustrates how structural knowledge about the interaction of these MAbs with their GP targets, together with investigation of the mechanisms by which these broadly cross-reactive MAbs protect against infection, can advance the development of Ab-based therapeutics against filovirus infections, as well as provide design templates to develop broadly protective filovirus vaccines, which will play a critical role to counteract the unpredictable time, location and virus genetic makeup of future filovirus outbreaks. Despite great progress in development of vaccines to combat hemorrhagic fever-causing filoviruses, there is an urgent and unmet need for therapeutics against filoviruses and detailed characterization of filovirus bnMAbs can provide critical knowledge for the development of safe and effective Ab-based therapeutics.

Dengue virus (DENV) infects approximately 400 million people yearly causing about 2 million cases of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) and a larger number of dengue fever (DF) cases. Notably, the worldwide incidence of DENV infections has risen 30-fold in the past 30 years, and more countries are experience their first outbreaks of DENV associated disease. The majority of adults infected with Zika virus (ZIKV) remain asymptomatic or develop a self-limited febrile disease, but ZIKV infection *in utero* can cause Congenital Zika Syndrome (CZS), manifested as microcephaly, cerebral malformations, arthrogryposis and ophthalmological and hearing defects. Despite the impact DENV, and to lesser degree ZIKV, infections have in human health, no licensed vaccines or specific therapies are available for these pathogens, underscoring an existing unmet need for novel therapeutics against DENV and ZIKV, a task that would be facilitated by a detailed understanding of virus–host interactions underlying DENV and ZIKV pathogenesis. The paper by Carlin and Shresta reviews current state-of-the-art genomic approaches, including CRISPR-Cas9 based screens, to dissect host-virus interactions in Dengue (DENV) and Zika (ZIKV) virus infections and advance our understanding of DENV and ZIKV pathogenesis.

Viral zoonoses are responsible for many human infectious diseases. Zoonotic viruses often establish asymptomatic chronic infections in their natural reservoirs, but upon a zoonotic event, these viruses can subvert the innate immune responses in the infected individual and prevent the development of effective adaptive immune responses, which results in unrestricted virus multiplication and associated pathology and disease manifestations. Detailed understanding of the biogeography, genetic diversity and evolution of zoonotic viruses in their natural environment can facilitate the implementation of surveillance and diagnostic methods to counteract their impact on human health. An example of this situation is illustrated by Lassa virus (LASV), a mammarenavirus highly prevalent in West Africa and the etiological agent of Lassa fever (LF), a hemorrhagic fever (HF) disease associated with high morbidity and significant mortality. The paper by Pontremoli *et al.* reviews the use of current next generation sequencing technologies to examine the geographic origin and evolutionary dynamics of arenaviruses, and how this knowledge can be harnessed to assess the zoonotic and pathogenic potential of known and yet to be discovered mammarenaviruses.