Most studies to date have investigated this discrepancy in terms of gender-specific immune responses, and the results have shown that females have a greater ability to elicit immune responses against infection (Moulton, 2018; Ortona et al., 2019). Some hypotheses, which are mainly discussed in the review, suggest a direct effect by male sex hormones on pathogen infection. TMPRSS2, which is expressed in an androgen-dependent manner, is utilized by SARS-CoV-2 for the priming of viral spike (S) protein, which is essential for viral entry into primary target cells and for viral spread in the infected host (Mjaess et al., 2020). Similarly, TMPRSS2 acts as the major hemagglutinin (HA)-activating protease of influenza A virus (IAV) in human airway cells and of influenza B virus (IBV) in type II pneumocytes (Limburg et al., 2019). To the early-stage infection of other viruses, AR is involved in the coordinated activation of Src/RSK1/EphA2 Ser897 signaling, which promotes primary infection by KSHV (Wang et al., 2017). On the contrary, 17β-estradiol (E2) can inhibit HCV spread and/or entry by activating G-protein-coupled estrogen receptor, GPR30, increasing matrix metalloproteinase 9 (MMP-9) activation and exporting to the extracellular space leading to cleavage of occludin in Domain D (Ulitzky et al., 2016). The well-documented role of HBV in hepatocellular carcinoma (HCC) indicates that a virus–host feedback loop between the X gene of HBV and AR is established in HBV-infected male hepatocytes (Zhu et al., 2011).