

Review of: "[Review] Dr Jekyll and Mr Hyde: From Two Branches of Immune Response to Three Types of Interferon Response"

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Potential competing interests: No potential competing interests to declare.

The current article by Dr. Brent Brown provides comprehensive information about interferon (IFNs) from their first discovery to current research status. The article discusses all three IFN types and their immunoregulatory role under diverse infections, including COVID-19, and inflammatory conditions such as cancers. The introduction of the TLR3, cGAS/STING, and RIG-1-like receptor (RLR) signaling pathways in the production of IFNs has been well introduced, revolutionizing IFN research in infection and immunity. The article is good to read for researchers involved in IFN or immunology research. However, I have found some minor suggestions for the author as follows:

The immune system also senses pathogenic antigens through pattern recognition receptors (PRRs), as well as cellular endosomally expressed Toll-like (TLR) receptors. The authors should correct this statement, as PRRs do not recognize antigens but associated molecules such as LPS, LTA, flagellin, and their genetic material. Antigens differ from these pathogen-associated molecular patterns (PAMPs) recognized by PRRs. Furthermore, endosomal TLRs comprise the endosomal part of TLRs, which is present in the endosomal membrane and in the cytosol in endosomes, endolysosomes, phagolysosomes, etc. Besides cytosolic TLRs, other PRRs such as NLRs, ALRs, cGLRs (cGAS/STING signaling pathway), and RIG-1-like receptors (RLRs) are also part of cytosolic PRRs, recognizing cytosolic PAMPs and DAMPs.

Type I IFNs include IFN- β , IFN- δ , IFN- ϵ , IFN- κ , IFN- τ , IFN- ω , and IFN- ζ , amongst others. In this statement, the author should mention IFN- α .

The author should explain VARV as Variola virus for smallpox.

With regard to SARS-CoV-2 infection, viral host entry is sensed through PRRs and TLRs (e.g., TLR3, TLR7/8/9), as well as pathogen-associated molecular patterns (PAMPs). The author should not mention TLRs separately, as they are critical members of the PRR family.

I hope the author will incorporate these suggestions into his article.