Recognition of viral infection and the ensuing inflammatory response

Viral infections pose a constant threat to human health but are countered by our immune response. Upon recognition of an invading virus by the immune system, infected cells produce several cytokines including interferon (IFN). IFNs are cytokines with dual functions: They induce the expression of hundreds of antiviral proteins, which act as an effective first line defense against the intruding virus, and they mobilize professional immune cells of both the adaptive and innate immune response. This mobilization of immune cells, many of which are capable of killing virus-infected cells, is referred to as an inflammatory reaction, which is necessary to clear the virus but it is also a major cause of morbidity and mortality during viral infections. Therefore, the immune system needs to balance the response in a manner, which achieves efficient control over the virus but limits the pathology caused by the inflammatory response. Type I and type III IFNs (also known as IFNαs) regulate a similar set of genes but where type I IFNs act globally, type III IFNs primarily target mucosal epithelial cells and protect them against the frequent viral attacks that are typical for barrier tissues. Furthermore, proper production of type III IFNs during the early phases of a viral infection is of critical importance to limit the damage caused by the inflammatory response. Type III IFNs also exhibit a strong antiviral effect in the human liver and has potent anti-hepatitis C viral effect. However, the recently discovered IFNλ4 isoform appears to behave fundamentally differently: It impairs the clearance of hepatitis C virus and fundamentally changes the inflammatory responses in the liver. The effects of IFNλ4 extend beyond viral hepatitis and may play an important role in non-viral inflammatory disorders of the liver, like non-alcoholic fatty liver disease (NAFLD).

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