RETINOIC ACID REGULATES IMMUNE RESPONSES BY PROMOTING IL-22 PRODUCTION AND MODULATING S100 PROTEINS IN VIRAL HEPATITIS

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The effector T cell responses promote viral clearance and disease resolution in viral hepatitis, but can also mediate tissue damage; however, much less is known as to how the liver protects itself against the injury. We have revealed in this study a retinoic acid (RA)-mediated hepatoprotective mechanism in adenovirus-induced hepatitis in mice. We found that RA treatment promoted hepatoprotective cytokine IL-22, but inhibited the pro-inflammatory factor IL-17, from gamma delta T and double-negative T cells, and that the hepatic IL-17 and IL-22 production were regulated via the PI3K /mTORC1 signaling pathway. Moreover, RA modulated the magnitude of antigen-specific T cell responses via down-regulating dendritic cell (DC) co-stimulatory molecule expression and its migratory capacity. Mechanistically, RA treatment inhibited S100 family proteins (S100A4/6/10) and the NF-kb/ERK signaling pathways on DCs. Importantly, the inhibition of S100A4 resulted in impaired DC migration from inflamed tissues to lymph nodes for T cell priming. Collectively, our study has revealed a previously unappreciated role and molecular mechanism of RA in modulating immune responses and protecting the liver from viral hepatitis.