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Investigation of therapeutic potential of Cytokine IL-33 in hepatitis

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Abstract

A replacement member cytokine IL-33 has recently joined the family of IL-1 due to its 11th number within the family it's also nominated as IL-1F11. In human and mice, main source of IL-33 is liver fibrotic cells and Hepatic stellate cells (HSC) when are in their activated form. To explore the functional role of IL-33 in viral related liver pathology, murine model of hepatitis was developed by injecting Poly I:C and hepatoprotective function of IL-33 was by administration of pre-treatment of mice with recombinant IL-33 (rIL-33). The poly I:C represents a relevant hepatitis model in human, because poly I:C may be a virus-related dsRNA mimetic which plays role in increasing the IL-33 level in fulminant hepatitis. The poly I:C activates the NK cells in liver that results in induction of inflammation. this proposal was to decode the hepatoprotective role of IL-33 and underlying mechanism in viral dsRNA mimetic and poly I:C mediated acute liver diseases i.e. Hepatitis in murine model. Serum biochemical parameters like dosage of aspartate aminotransferase (AST), alanine aminotransferase (ALT) was administered by diagnostic kit in biochemistry autoanalyzer that displayed in higher amount in those mice that were challenged with Poly I:C and therefore the ir level was observed lower in post-treated rIL-33 group after Poly I:C administration and the quantitative measurement of serum INF-γ and TNF-α was performed using Albcam's INF-γ and TNF-α mice ELISA kits results of both these pro-inflammatory cytokines were same like ALT/AST. Level of those cytokines was also higher in Poly I:C challenged group and lower in post-treated rIL-33 group. These results confirmed the therapeutic effect of IL-33 in hepatitis or liver related diseases. The results were statistically analyzed by T test and a method ANOVA that proven the extent of liver biomarkers and pro-inflammatory were significantly differ in rIL-33 treated mice trials. The cytokine IL-33 is that the 11th member of the IL-1 family and is designated as IL-1F11. it's now described as a humid (damage-associated molecular patterns) or "alarmin" molecule that's normally restrained to the nuclear compartment where it could act as a nuclear factor-regulating gene expressionx but is released just in case of pathogen aggression or injury to alert the system Once released from the cells, IL-33 mediates its function through interaction with its specific receptor a dimer of ST2 (IL-1 receptor-like 1) and IL-1RacP (IL-1 receptor accessory protein) IL-33 has been described to be constitutively expressed in cell-lining tissues like endothelial cells, epithelial cells, keratinocytes, and fibroblasts but could even be induced in other cells like hepatocytes IL-33 released into the extracellular space after cell damage might be active as a full-length form (~33 kDa), but proteases are shown to manage IL-33 activity. as an example , just in case of apoptosis, caspases 3 and seven cleaved IL-33 generating two biologically inactive sort of IL-33 whereas during inflammation, neutrophil serine proteases, cathepsin G, and elastase were found to process IL-33 into mature sorts of ~20 kDa with increased biological activity (by 10-fold) The ST2 receptor is expressed in both innate and adaptive immune cells and is predominantly related to type 2 immune reaction The ST2-expressing cells, a target of IL-33, are macrophages, dendritic cells, mast cells, eosinophils, neutrophils, recently described nuocytes, or innate lymphoid cells like ILC2 Th2 cells, but could even be transient on the surface of Th1 cells and antiviral CD8+ T cellsThe IL-33/ST2 axis has been described in various pathologies and affected organs, and it induced deleterious or protective effects depending upon the immune mediators and inflammatory milieu. In liver pathology, we et al. reported increased level of serum IL-33 and ST2 not only during a cute and chronic hepatic failure in humans but also in patients chronically affected with hepatitis C and hepatitis B viruses (HCV and HBV) in correlation with liver damage Upregulated expression of IL-33 was reported in a murine model of T cell-mediated hepatitis mice infected with hepatotropic choriomeningitis virus (LCMV) In LCMV hepatitis, IL-33 induced hepatoprotective by promoting innate IFNγ production and modulating dendritic cells response, driving an antiviral CD8+ T cell response In another mouse model of adenoviral hepatitis, the expression of IL-33 and ST2 was observed within the liver within the first week of infection, and it attenuated liver injury via a rise during a number of regulatory T cells (Treg) and reduce during a number of macrophages, dendritic cells, and NK cells within the liver However, there's a paucity of knowledge regarding endogenous IL-33 deficiency on immunomodulatory effect in hepatitis . this study investigated the role of IL-33 within the natural model of acute hepatitis in mice induced by specific mouse hepatitis coronavirus (MHV3). The hepatotropic and pathogenic MHV3 strain (L2-MHV3) induced severe fulminant hepatitis in mice and their death within 3–5 days postinfection mimicking a person's hepatitis . We previously demonstrated L2-MHV3-induced overexpression of IL-33 in liver sinusoidal endothelial cells, vascular endothelial cells, and hepatocytes Here, infecting wild-type (WT) and IL-33-deficient mice (IL-33 KO) with L2-MHV3, we showed that the alarmin IL-33 ameliorated the L2-MHV3-mediated liver injury through

the regulation of IFNγ expression, survival effect on Eight- to ten-week-old wild-type (WT) C57Bl/6 (Janvier, Le Genest-sur-isle, France) and littermate IL-33 knockout (KO) C57Bl/6 mice (matched for age and sex) were provided by Dr. Jean-Philippe Girard The mice used in the study were certified as MHV3-free by the manufacturer, and they were housed under HEPA-filtered air (Forma Scientific, Marietta, OH) in the local BSL3 animal facility. The study was conducted in compliance with the French laws and the institution's guidelines for animal welfare, and the protocol was approved by the Committee on the Ethics of Animal Experiments of the French government (agreement of M. Samson number 3596). All efforts were made to immune cells, and neutrophil infiltration in hepatitis minimize suffering and pain of the animals.

Biography

Tariq Munir has completed his Graduation in MD Pathology. He is an Ambassador of European Association for Cancer Research. He has more than 58 publications in national and international journals of repute. He is a regular Reviewer of several international journals including Diagnostic Cytopathology and BMJ-Case Reports. He is also a Member of International Editorial Board of various pathology related journals and a contributor to pathology outlines.

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