Austin Journal of Clinical Immunology

Austin Publishing Group

Open Access Full Text Article

Editorial

IL-1 in Th17 Differentiation and Inflammatory Tissue Damage

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Received: January 08 2014; **Accepted:** January 10 2014; **Published:** January 14 2014

Abstract

Interleukin-1 (IL-1) is produced by innate immune cells in response to both exogenous and endogenous "danger" signals. IL-1 acts on target cells to alter their gene expression profile, which leads to various functional consequences of the cells. In the immune system, IL-1 is a major mediator that connects innate and adaptive immune responses. Recent studies have shown that IL-1 acts directly on CD4 T cells to modulate T helper cell immune responses. It can also collaborate with cytokines released by the T cells to induce tissue damage under autoimmune conditions. Under inflammatory conditions lacking adaptive autoimmune components, IL-1 also induces tissue damages. The effects of IL-1 can be negatively regulated by IL-1 receptor antagonist, making it a promising tool for modulating immune and inflammatory responses in various pathological conditions.

Introduction

How innate immune system regulates adaptive immune responses has been a major focus of immunological research. The fundamental importance of this topic in immunology is highlighted by the recent studies that demonstrate the key role of the interactions between pathogen-associated molecular patterns and the toll-like receptors in the initiation of the adaptive immune responses. However, the study of the innate immune responses has a much longer history. Interleukin-1 (IL-1) was identified 40 years ago as "endogenous pyrogen" released by leukocytes in response to endotoxin stimulation [1]. More recent studies have discovered that IL-1 can directly regulate T helper cell responses, particularly Th17 response, and cause tissue damages in many inflammatory conditions both with and without adaptive immune components. This review attempts to highlight some important findings from these studies.

Basic biology of IL-1

There are two IL-1 molecules IL-1α and IL-1β that have largely identical functions [2]. Mature IL-1α and IL- 1b molecules are generated by cleavage of pro-IL-1α and pro-IL-1β by calpain and caspase-1, respectively [3,4]. In addition to calpain, more recent studies have shown that other proteases, including granzyme B, elastase and chymase, can also process IL-1α , and the proteolysis enhances the biological activities of IL- 1a [5]. Pro- and mature IL1a are primarily membrane anchored, but they can be released to extracellular space upon cell death as a component of the cytosolic contents or on membrane fragments [6]. In contrast, mature IL-1β is secreted. The secretion of IL-1β is induced by inflammatory stimuli including microbial pathogen-associated molecular patterns (PAMPs) and endogenous "danger" signals, e.g. ATP and uric acid crystals, released by stressed or damaged cells. These stimuli trigger the intracellular "danger" receptor NLRP3 inflammasome to activate caspase-I, which in turn cleaves pro-IL-1β to produce mature IL-1β [7-9]. The inflammasome-activated production of IL-1β is negatively regulate by autophagy. The activation of autophagy by Toll-like receptor ligands also targets pro-IL-1β to autophagosome for degradation [10]. Conversely, disruption of autophagy facilitates the release of IL-1β [11]. Extracellular IL-1, including Pro-IL-1α , IL-1α and IL-1β, can bind to IL-1RI [12]. Conformational change induced by the ligand binding triggers the recruitment of IL-1 receptor accessary protein (IL-1RAcp) to the receptor, which is essential for IL-1 signaling [13]. Further signal transduction results in the formation of a multi-protein signaling complex that include MyD88 and IRAK4. A cascade of signaling events ultimately leads to the activation of NF-kB and mitogen-activated protein kinases (MAPK) that alter gene expression profiles of the host cells [14]. Apart from the receptor-mediated signaling, the propiece region of pro-IL-1α contains a nuclear localization signal so that in many cell types pro-IL-1α is predominantly localized in the nucleus [15,16]. Intranuclear pro-IL-1 a functions independently of IL-1RI [17]. Several studies have shown that intranuclear pro-IL-1α enhances IL-6 expression [18,19]. Intranuclear pro-IL-1α has also been shown to inhibit cell proliferation and induce apoptosis in some cases [20,21], but promote cell proliferation in others [22]. However, since IL-1β is the primary extracellular form of IL-1, data discussed in the following sections are mostly generated from studies using IL-1β.

Effects of IL-1 on Th17 cell differentiation

Extracellular IL-1, mainly IL-1β, plays important role in Th17 differentiation. In humans, IL-1 in combination with IL-6 and/or IL-23 induced Th17 differentiation from naïve precursors [23,24]. In mouse, in vitro Th17 differentiation from naïve conventional CD4 T (CD4 Tcon) cells is induced by IL-6 and TGF-β [25]. However, more recent studies showed that in vivo IL-6 is required for Th17 differentiation only in the mucosa and skin but not in spleen and liver. In contrast, IL-1 is indispensible for in vivo Th17 differentiation in all tissues [26]. Multiple mechanisms may be responsible for the role of

Citation: Zeng W. IL-1 in Th17 Differentiation and Inflammatory Tissue Damage. Austin J Clin Immunol. 2014;1(2): 1008.

IL-1 in Th17 differentiation. In human, IL-1 induces the expression of RORγt, the master transcriptional regulator for Th17 differentiation, in naïve CD4 T cells (24). In mouse, in vitro studies showed that IL-1 primarily stimulates the expansion of Th17 cells and the expression of IL-17 [27-29], whereas the expression of RORγt appears not affected by IL-1 signaling [27]. Th17 cells plays critical role in the pathogenesis of experimental allergic encephalomyelitis (EAE). Consistent with the positive role of IL-1 in Th17 differentiation, IL-1RI$^{-/-}$ mice were resistant to EAE [30]. Similarly, caspase 1$^{-/-}$ mice, whose ability to produce mature IL-1β were impaired, had reduced incidenceand severity of EAE [31]. In addition to Th17 differentiation, IL-1 exerts similar effect in stimulating the Antigen-driven expansion of Th1 and Th2 cells [32]. More information on the roles of IL-1 in Th1 and Th2 Cell differentiation can be found in a recent review by Santarlasci et al. [33].

The role of IL-1 in tissue damage in inflammatory conditions

Autoimmune conditions refer to inflammatory conditions that are initiated by adaptive immune responses. Not only does IL-1 play critical roles in shaping the adaptive immune response by regulating T helper cell differentiation, it also collaborates with cytokines produced by T helper cells to induce apoptosis to cause tissue damages. Many studies have shown that in type 1 diabetes (T1D), IL-1 can synergize with IFN-γ produced by pancreatic antigen-reactive Th1 cells to induce apoptosis in pancreatic β cells [34,35]. More recently similar synergistic effect has also been reported between IL-1 and IL-17 produced by Th17 cells [36]. While the mechanism for the collaboration of IL-1 and IL-17 is not well understood, considerable details have been learnt about the collaboration between IL-1 and IFN-γ. Exposure of b cells to IL-1β and IFN-γ activates the MAPK JNK hence its target c-Jun, which up regulates the expression of the apoptosis sensitizer DP5 [37,38]. DP5 binds and deactivates pro-survival factor Bcl-XL. Bcl-XL functions to sequester the apoptosis activator Puma. Thus, deactivation of Bcl-XL by DP5 releases Puma [39]. In addition, IL-1 and IFN-γ induce the synthesis of nitrite oxide (NO) that triggers ER stress (40). ER stress up regulates DP5 and Puma [37,41], and suppresses the translation of the pro-survival factor Mcl-1 [42]. Like Bcl-XL, Mcl-1 sequesters Puma, therefore down-regulation of Mcl-1 further facilitate the release of Puma. Once released, Puma binds and activates pro-death protein Bax, which leads to the release of cytochrome c from mitochondria that starts the cascade of caspase activation [43]. Importantly, IL-1 also plays an important role in tissue damage caused by inflammation with apparent adaptive immune components, for example, b cell death in type 2 diabetes (T2D). In contrast to T1D, T2D is not considered as an autoimmune disease. Nonetheless, high glucose levels in T2D can stimulate IL-1β Production by pancreatic β cells. Such b cell-derived IL-1 has a suicidal effect on the b cells by inducing b cell apoptosis through Fas expression [44]. IL-1 is a major cytokine found in the acute inflammation during Ischemia-reperfusion (I/R) [45], and is responsible for the apoptosis of various tissue parenchymal cells in I/R injury, most notably the death of cardiomyocytes [46,47]. Although the details of the mechanism have not been fully elucidated, it appears that under these circumstances IL-1 ultimately induces the expression of Bax and Bak to activate the mitochondrial apoptosis pathway [47,48].

Negative control of the effects of IL-1 by IL-1Ra

IL-1 signaling and its biological effects can be inhibited by IL-1R antagonist (IL-1Ra), a naturally produced protein of the IL-1 family [2]. IL-1Ra includes secreted and intracellular isoforms [49]. The secreted IL-1Ra binds to IL-1RI but does not recruit IL-1RAcp to the receptor, thereby competitively inhibits receptor dependent IL-1 signaling [50]. Thus, the biological functions of IL-1Ra 3 are to counterbalance those of IL-1. Consistent with the effect of IL-1 on Th17 differentiation discussed above, IL-17 production was elevated in IL-1Ra $^{-/-}$ mice [51-53]. In addition, the IL-1Ra $^{-/-}$ mice developed spontaneous arthritis, the severity of which is closely correlated with the levels of IL-17 expression [51]. These mice are also more susceptible than wild type mice to the induction of EAE in the absence of pertussis toxin [53]. Pertussis toxin is known to mimic the actions of IL-1 such that it serves to overcome the effect of IL-1Ra in the induction of EAE in the wild type mice. IL-1Ra is naturally expressed in the b cells in healthy individuals. Its expression is reduced in type 2 diabetic patients, and down-regulation of IL-1Ra by siRNA increases b apoptosis [54]. Conversely, anakinra, the clinically approved recombinant human IL-1Ra, protects b cells from apoptosis induced by high glucose or IL-1 plus IFN-γ [54,55]. Similarly, IL-1Ra expression was induced in ischemic cardiomyocytes as a protective mechanism [56,57]. Indeed, transfection of cardiomyocytes with IL-1Ra gene and administration of anakinra have both been shown to protect cardimyocytes from I/R induced apoptosis [47,58]. Interestingly, not only the secreted IL-1Ra can attenuate IL-1 induced apoptosis, intracellular isoform IL-1Ra can also inhibit apoptosis of ischemic cardiomyocytes by directly binding and preventing the activation of caspase 9 [48].

Conclusion

IL-1 has emerged as a positive regulator of the adaptive immune responses, particularly the T helper cell immune responses. As the T helper cells are critically involved in many immunological diseases such as autoimmune diseases, IL-1 is an important target for controlling the pathological immune responses under such conditions. In addition to the immune regulatory functions, IL-1 alone or in collaboration with other cytokines can directly induce apoptosis of tissue parenchymal cells. Conditions where IL-1 induces tissue damages include both autoimmune diseases with active adaptive immune components and inflammatory conditions without apparent adaptive immune components. Therefore dampening IL-1 activity, such as by IL-1Ra, is beneficial for these conditions.

References

1. Dinarello CA. IL-1: discoveries, controversies and future directions. European journal of Immunology. 2010; 40: 599-606.

2. Dinarello CA. Immunological and inflammatory functions of the interleukin-1 family. Annual Review of Immunology. 2009; 27: 519-550.

3. Kobayashi Y, Yamamoto K, Saido T, Kawasaki H, Oppenheim JJ, Matsushima K. Identification of calcium-activated neutral protease as a processing enzyme of human interleukin 1 alpha. Proceedings of the National Academy of Sciences of the United States of America. 1990; 87: 5548-5552.

4. Thornberry NA, Bull HG, Calaycay JR, Chapman KT, Howard AD, Kostura MJ, et al. A novel heterodimeric cysteine protease is required for interleukin-1 beta processing in monocytes. Nature. 1992; 356: 768-774.

5. Afonina IS, Tynan GA, Logue SE, Cullen SP, Bots M, Lüthi AU, et al. Granzyme B-dependent proteolysis acts as a switch to enhance the proinflammatory activity of IL-1α Ipha. Molecular cell. 2011; 44: 265-78.

6. Chen CJ, Kono H, Golenbock D, Reed G, Akira S, Rock KL. Identification of a key pathway required for the sterile inflammatory response triggered by dying cells. Nat Med. 2007; 13: 851-856.

7. Goldbach-Mansky R. Current status of understanding the pathogenesis and management of patients with NOMID/CINCA. Curr Rheumatol Rep. 2011; 13: 123-131.

8. Hoffman HM, Mueller JL, Broide DH, Wanderer AA, Kolodner RD. Mutation of a new gene encoding a putative pyrin-like protein causes familial cold autoinflammatory syndrome and Muckle-Wells syndrome. Nat Genet. 2001; 29: 301-305.

9. Martinon F, Burns K, Tschopp J. The inflammasome: a molecular platform triggering activation of inflammatory caspases and processing of proIL-beta. Mol Cell. 2002; 10: 417-426.

10. Harris J, Hartman M, Roche C, Zeng SG, O'Shea A, Satoh T, et al. Autophagy controls IL-1βeta secretion by targeting pro-IL-1βeta for degradation. J Biol Chem. 2011; 286: 9587-9597.

11. Saitoh T, Fujita N, Jang MH, Uematsu S, Yang BG, Satoh T, et al. Loss of the autophagy protein Atg16L1 enhances endotoxin-induced IL-1βeta production. Nature. 2008; 456: 264-268.

12. Vigers GP, Anderson LJ, Caffes P, Brandhuber BJ. Crystal structure of the type-I interleukin-1 receptor complexed with interleukin-1beta. Nature. 1997; 386: 190-194.

13. Wesche H, Korherr C, Kracht M, Falk W, Resch K, Martin MU. The interleukin-1 receptor accessory protein (IL-1RAcP) is essential for IL-1-induced activation of interleukin-1 receptor-associated kinase (IRAK) and stress-activated protein kinases (SAP kinases). J Biol Chem. 1997; 272: 7727-7731.

14. Weber A, Wasiliew P, Kracht M. Interleukin-1 (IL-1) pathway. Sci Signal. 2010; 3: cm1.

15. Luheshi NM, Rothwell NJ, Brough D. Dual functionality of interleukin-1 family cytokines: implications for anti-interleukin-1 therapy. Br J Pharmacol. 2009; 157: 1318-1329.

16. Luheshi NM, Rothwell NJ, Brough D. The dynamics and mechanisms of interleukin-1alpha and beta nuclear import. Traffic. 2009; 10: 16-25.

17. Heguy A, Baldari C, Bush K, Nagele R, Newton RC, Robb RJ, et al. Internalization and nuclear localization of interleukin 1 are not sufficient for function. Cell Growth Differ. 1991; 2: 311-315.

18. Kawaguchi Y, McCarthy SA, Watkins SC, Wright TM. Autocrine activation by interleukin 1alpha induces the fibrogenic phenotype of systemic sclerosis fibroblasts. J Rheumatol. 2004; 31: 1946-1954.

19. Werman A, Werman-Venkert R, White R, Lee JK, Werman B, Krelin Y, et al. The precursor form of IL-1α lpha is an intracrine proinflammatory activator of transcription. Proc Natl Acad Sci U S A. 2004; 101: 2434-2439.

20. Palmer G, Trolliet S, Talabot-Ayer D, Mézin F, Magne D, et al. Pre-interleukin-1alpha expression reduces cell growth and increases interleukin-6 production in SaOS-2 osteosarcoma cells: Differential inhibitory effect of interleukin-1 receptor antagonist (icIL-1Ra1). Cytokine. 2005; 31: 153-160.

21. Pollock AS, Turck J, Lovett DH. The prodomain of interleukin 1alpha interacts with elements of the RNA processing apparatus and induces apoptosis in malignant cells. FASEB journal: official publication of the Federation of American Societies for Experimental Biology. 2003; 17: 203-213

22. Kawaguchi Y, Nishimagi E, Tochimoto A, Kawamoto M, Katsumata Y, Soejima M, et al. Intracellular IL-1α lpha-binding proteins contribute to biological functions of endogenous IL-1α lpha in systemic sclerosis fibroblasts. Proc Natl Acad Sci U S A. 2006; 103: 14501-14506.

23. Acosta-Rodriguez EV, Napolitani G, Lanzavecchia A, Sallusto F. Interleukins 1beta and 6 but not transforming growth factor-beta is essential for the differentiation of interleukin 17-producing human T helper cells. Nature immunology. 2007; 8: 942-949

24. Cosmi L, De Palma R, Santarlasci V, Maggi L, Capone M, et al. Human interleukin 17-producing cells originate from a CD161+CD4+ T cell precursor. J Exp Med. 2008; 205: 1903-1916.

25. Bettelli E, Carrier Y, Gao W, Korn T, Strom TB, Oukka M, et al. Reciprocal developmental pathways for the generation of pathogenic effector TH17 and regulatory T cells.Nature. 2006; 441: 235-238

26. Hu W, Troutman TD, Edukulla R, Pasare C. Priming microenvironments dictate cytokine requirements for T helper 17 cell lineage commitment. Immunity. 2011; 35: 1010-1022.

27. Chang J, Burkett PR, Borges CM, Kuchroo VK, Turka LA, Chang CH. MyD88 is essential to sustain mTOR activation necessary to promote T helper 17 cell proliferation by linking IL-1 and IL-23 signaling. Proc Natl Acad Sci U S A. 2013; 110: 2270-2275.

28. Chung Y, Chang SH, Martinez GJ, Yang XO, Nurieva R, Kang HS, et al. Critical regulation of early Th17 cell differentiation by interleukin-1 signaling. Immunity. 2009; 30: 576-587.

29. Gulen MF, Bulek K, Xiao H, Yu M, Gao J, Sun L, et al. Inactivation of the enzyme GSK3Î± by the kinase IKKi promotes AKT-mTOR signaling pathway that mediates interleukin-1-induced Th17 cell maintenance. Immunity. 2012; 37: 800-812.

30. Sutton C, Brereton C, Keogh B, Mills KH, Lavelle EC. A crucial role for interleukin (IL)-1 in the induction of IL-17-producing T cells that mediate autoimmune encephalomyelitis. J Exp Med. 2006; 203: 1685-1691.

31. Furlan R, Martino G, Galbiati F, Poliani PL, Smiroldo S, Bergami A, et al. Caspase-1 regulates the inflammatory process leading to autoimmune demyelination. J Immunol. 1999; 163: 2403-2409.

32. Ben-Sasson SZ, Hu-Li J, Quiel J, Cauchetaux S, Ratner M, Shapira I, et al. IL-1 acts directly on CD4 T cells to enhance their antigen-driven expansion and differentiation. Proc Natl Acad Sci U S A. 2009; 106: 7119-7124.

33. Santarlasci V, Cosmi L, Maggi L, Liotta F, Annunziato F. IL-1 and T Helper Immune Responses. Frontiers in immunology. 2013; 4: 182.

34. Eizirik DL, Mandrup-Poulsen T. A choice of death--the signal-transduction of immune-mediated beta-cell apoptosis. Diabetologia. 2001; 44: 2115-2133.

35. Gurzov EN, Eizirik DL. Bcl-2 proteins in diabetes: mitochondrial pathways of Î²-cell death and dysfunction. Trends Cell Biol. 2011; 21: 424-431.

36. Arif S, Moore F, Marks K, Bouckenooghe T, Dayan CM, Planas R, et al. Peripheral and islet interleukin-17 pathway activation characterizes human autoimmune diabetes and promotes cytokine-mediated Î²-cell death. Diabetes. 2011; 60: 2112-2119.

37. Gurzov EN, Ortis F, Cunha DA, Gosset G, Li M, et al. Signaling by IL-1βeta+IFN-γamma and ER stress converge on DP5/Hrk activation: a novel mechanism for pancreatic βeta-cell apoptosis. Cell Death Differ. 2009; 16: 1539-1550.

38. Moore F, Naamane N, Colli ML, Bouckenooghe T, Ortis F, Gurzov EN, et al. STAT1 is a master regulator of pancreatic {beta}-cell apoptosis and islet inflammation. J Biol Chem. 2011; 286: 929-941.

39. Kim H, Rafiuddin-Shah M, Tu HC, Jeffers JR, Zambetti GP, Hsieh JJ, et al. Hierarchical regulation of mitochondrion-dependent apoptosis by BCL-2 subfamilies. Nat Cell Biol. 2006; 8: 1348-1358.

40. Oyadomari S, Takeda K, Takiguchi M, Gotoh T, Matsumoto M, Wada I, et al. Nitric oxide-induced apoptosis in pancreatic βeta cells is mediated by the endoplasmic reticulum stress pathway. Proc Natl Acad Sci U S A. 2001; 98: 10845-10850.

41. Gurzov EN, Germano CM, Cunha DA, Ortis F, Vanderwinden JM, Marchetti P, et al. p53 up-regulated modulator of apoptosis (PUMA) activation contributes to pancreatic βeta-cell apoptosis induced by proinflammatory cytokines and endoplasmic reticulum stress. The Journal of biological chemistry, 2010; 285: 19910-19920.

42. Allagnat F, Cunha D, Moore F, Vanderwinden JM, Eizirik DL, Cardozo AK. Mcl-1 downregulation by pro-inflammatory cytokines and palmitate is an early event contributing to Î²-cell apoptosis. Cell Death Differ. 2011; 18: 328-337.

43. Kim H, Tu HC, Ren D, Takeuchi O, Jeffers JR, Zambetti GP, et al. Stepwise

activation of BAX and BAK by tBID, BIM, and PUMA initiates mitochondrial apoptosis. Mol Cell. 2009; 36: 487-499.

44. Maedler K, Sergeev P, Ris F, Oberholzer J, Joller-Jemelka HI, Spinas GA, et al. Glucose-induced beta cell production of IL-1βeta contributes to glucotoxicity in human pancreatic islets. J Clin Invest. 2002; 110: 851-860.

45. Abbate A, Bussani R, Amin MS, Vetrovec GW, Baldi A. Acute myocardial infarction and heart failure: role of apoptosis. Int J Biochem Cell Biol. 2006; 38: 1834-1840.

46. Barrier A, Olaya N, Chiappini F, Roser F, Scatton O, Artus C, et al. Ischemic preconditioning modulates the expression of several genes, leading to the overproduction of IL-1Ra, iNOS, and Bcl-2 in a human model of liver ischemia-reperfusion. FASEB journal: official publication of the Federation of American Societies for Experimental Biology. 2005; 19: 1617-1626

47. Suzuki K, Murtuza B, Smolenski RT, Sammut IA, Suzuki N, Kaneda Y, et al. Overexpression of interleukin-1 receptor antagonist provides cardioprotection against ischemia-reperfusion injury associated with reduction in apoptosis. Circulation. 2001; 104: I308-308I3.

48. Vecile E, Dobrina A, Salloum FN, Van Tassell BW, Falcione A, Gustini E, et al. Intracellular function of interleukin-1 receptor antagonist in ischemic cardiomyocytes. PLoS One. 2013; 8: e53265.

49. Gabay C, Porter B, Fantuzzi G, Arend WP. Mouse IL-1 receptor antagonist isoforms: complementary DNA cloning and protein expression of intracellular isoform and tissue distribution of secreted and intracellular IL-1 receptor antagonist in vivo. Journal of immunology. 1997; 159: 5905-5913

50. Dripps DJ, Brandhuber BJ, Thompson RC, Eisenberg SP. Interleukin-1 (IL-1) receptor antagonist binds to the 80-kDa IL-1 receptor but does not initiate IL-1 signal transduction. J Biol Chem. 1991; 266: 10331-10336.

51. Koenders MI, Devesa I, Marijnissen RJ, Abdollahi-Roodsaz S, Boots AM, Walgreen B, et al. Interleukin-1 drives pathogenic Th17 cells during spontaneous arthritis in interleukin-1 receptor antagonist-deficient mice. Arthritis Rheum. 2008; 58: 3461-3470.

52. Lamacchia C, Palmer G, Seemayer CA, Talabot-Ayer D, Gabay C. Enhanced Th1 and Th17 responses and arthritis severity in mice with a deficiency of myeloid cell-specific interleukin-1 receptor antagonist. Arthritis Rheum. 2010; 62: 452-462.

53. Matsuki T, Nakae S, Sudo K, Horai R, Iwakura Y. Abnormal T cell activation caused by the imbalance of the IL-1/IL-1R antagonist system is responsible for the development of experimental autoimmune encephalomyelitis. Int Immunol. 2006; 18: 399-407.

54. Maedler K, Sergeev P, Ehses JA, Mathe Z, Bosco D, Berney T, et al. Leptin modulates beta cell expression of IL-1 receptor antagonist and release of IL-1βeta in human islets. Proc Natl Acad Sci U S A. 2004; 101: 8138-8143.

55. Schwarznau A, Hanson MS, Sperger JM, Schram BR, Danobeitia JS, Greenwood KK, et al. IL-1βeta receptor blockade protects islets against pro-inflammatory cytokine induced necrosis and apoptosis. J Cell Physiol. 2009; 220: 341-347.

56. Patti G, D'Ambrosio A, Mega S, Giorgi G, Zardi EM, Zardi DM, et al. Early interleukin-1 receptor antagonist elevation in patients with acute myocardial infarction. J Am Coll Cardiol. 2004; 43: 35-38.

57. Patti G, Mega S, Pasceri V, Nusca A, Giorgi G, Zardi EM, et al. Interleukin-1 receptor antagonist levels correlate with extent of myocardial loss in patients with acute myocardial infarction. Clin Cardiol. 2005; 28: 193-196.

58. Abbate A, Salloum FN, Vecile E, Das A, Hoke NN, eStraino S, et al. Anakinra, a recombinant human interleukin-1 receptor antagonist, inhibits apoptosis in experimental acute myocardial infarction. Circulation. 2008; 117: 2670-2683.

Austin J Clin Immunol - Volume 1 Issue 2 - 2014
ISSN : 2381-9138 | www.austinpublishinggroup.org

Citation: Zeng W. IL-1 in Th17 Differentiation and Inflammatory Tissue Damage. Austin J Clin Immunol. 2014;1(2): 1008.