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Review

Inflammasomes and human autoimmunity: A comprehensive review

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ABSTRACT

Inflammasomes are multi-protein complexes composed of a NOD-like receptor (NLR)/an AIM-like receptor (ALR), the adapter molecule apoptosis-associated speck-like protein that contains a CARD (ASC), and caspase-1. Active caspase-1 cleaves pro-IL-1β and pro-IL-18 to IL-1β and IL-18, resulting in inflammation. Genetic mutations in inflammasomes were first recognized to result in autoinflammatory diseases, which are characterized by the absence of both autoantibodies and autoreactive-T/B cells. However, there is increasing attention being placed on genetic polymorphisms that are involved in the components of inflammasomes, and these have implications for innate immunity and the natural history of autoimmune diseases. For example, while the NOD-like receptor family, pyrin domain containing 1 (NLRP1) haplotypes contributes to susceptibility to developing vitiligo; there are other single nucleotide polymorphisms (SNPs) that alters the susceptibility and severity of rheumatoid arthritis (RA) and juvenile idiopathic arthritis. Indeed, there are multiple factors that contribute to lowering the threshold of immunity and inflammasomes play a key role in this threshold. For example, IL-1β and IL-18 further perpetuate Th17 responses and endothelial cell damage, which potentiate a number of autoimmune diseases, including synovitis in RA, cardiovascular disease, and systemic lupus erythematosus (SLE). There is also increasing data on the role of innate immunity in experimental autoimmune encephalomyelitis (EAE), in lupus nephritis, and in a variety of autoimmune pathologies in which activation of the innate immune system is the driver for the adaptive system. Indeed, it is likely that the chronic pathology of autoimmunity is mediated in part by otherwise innocent bystander cells, augmented by inflammasomes.

1. Introduction

Inflammasomes are multi-protein complexes composed of a NOD-like receptor (NLR)/an AIM-like receptor (ALR), the adapter molecule apoptosis-associated speck-like protein that contains a CARD (ASC), and the effector protein caspase-1 [1]. The NOD-like receptor family, pyrin domain containing 1 (NLRP1), NOD-like receptor family, pyrin domain containing 3 (NLRP3), and NLR family, CARD domain containing 4 (NLRC4) are the most studied NLRs that form inflammasomes and activate caspase-1, resulting in cleavage of pro-IL-1β and pro-IL-18 to the respective active cytokines. Multiple stimuli, including pattern recognition molecules and danger associated molecular patterns, can activate the NLRP3 inflammasome; while cytosolic double-stranded DNA (dsDNA) is a direct ligand for "Absent in melanoma 2" (AIM2) and Interferon-γ inducible protein 16 (IFI16), which are ALRs forming caspase-1-activating inflammasomes [2,3]. Furthermore, a non-canonical inflammasome using caspase-11 to process pro- IL-1β has also been reported [4].

Genetic mutations in inflammasome pathways have been found in autoinflammatory diseases, which are characterized by the absence of auto-reactive adaptive immune responses [5]. A successful adaptive response requires innate immunity and although the adaptive and innate responses would appear to be at opposite ends of the immunological spectrum, there is an integral and essential relationship [6,7]. For example, innate immune dysregulation is the driver for autoinflammatory diseases, which subsequently will lead to autoreactive T and B cell responses. More

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importantly, however, the severity and therefore the outcome of human autoimmune diseases are integrally related to inflammation and specific organ damage [8,9]. Indeed, multiple genetic polymorphisms of inflammasome components have been reported to be associated with susceptibility, activity, and treatment responses of several autoimmune diseases [10–13]. More significantly, there are now intensive efforts being placed on systems biology analysis to define these multiple and often overlapping, genetically determined inflammatory responses in both autoimmunity and infection [6,14,15]. The most well-studied genetic variants are of NLRP1 and NLRP3 inflammasomes, which have been reviewed in 2011 [16]. For example, priming of the NLRP3 inflammasome is increased in autoimmune responses by virtue of the toll-like receptor (TLR) and P2X ligand–gated ion channel 7 receptor (P2X7R) signaling, thus lowering the threshold of inflammatory responses [17,18]. IL-1β and IL-18, as the products of inflammasome activations, result in proinflammatory T cell differentiation and target organ damage [19,20]. Moreover, the level of negative regulators of inflammasomes, including activated T cells and microRNAs, have the potential to augment the inflammatory response [21,22]; and such increased inflammation can be found in both organ specific as well as organ non-specific autoimmune diseases and are also integrally related to tissue regeneration and potential fibrosis [7,23–25].

2. Genetic polymorphisms and autoimmune diseases

2.1. SNPs affecting the priming of inflammasomes

Macrophages are a critical link in the inflammation that leads to tissue injury [26]. For example, infiltrating macrophages in the kidneys contribute to lupus nephritis and macrophages in the synovial membrane contribute to synovitis. Unlike monocytes, which constitutively express pro-IL-1β, priming is required for the production of IL-1β and IL-18 via the NLRP3 inflammsome in human macrophages [27]. It is thought that two signals are needed: the first signal is usually provided by TLR stimulation, which increases pro- IL-1β/pro-IL-18 levels and enhances NLRP3 expression; the second signal is induced by ATP via P2X7R [27]. Genetic polymorphisms in both TLR and P2X7R have been found to be associated with autoimmune diseases (Table 1).

The most frequently reported TLR polymorphisms associated with systemic lupus erythematosus (SLE) are TLR7 and TLR9 SNPs [28–31]. While TLR7 is known to be pathogenic, TLR9 has been reported to be protective for SLE [17]. TLR7 is expressed on macrophages, and TLR7 stimulation promotes NLRP3 activation. TLR9, however, is expressed primarily on B cells and dendritic cells (DCs), and TLR9-induced interferon-α (IFN-α) could inhibit IL-1β production via mechanisms that are at this point unknown [32]. Therefore, association of SLE susceptibility with gain-of-function TLR7 SNPs and non-functional TLR9 SNPs suggest the involvement of inflammasomes. Unfortunately, genome-wide associations in lupus and in a variety of other autoimmune diseases have been very disappointing, perhaps emphasizing the multi-factorial nature of autoimmunity. Hence, discussion of genetically specific roles depends on the genetics of the individual host and multiple environmental factors, which will lead to disease pathogenesis [33–35].

Table 1
Genetic polymorphisms affecting inflammasome priming and associated autoimmune diseases.

SNPs	Autoimmune disease (ethnicity)	Influence	Ref
P2X7R rs1718119	SLE (Chinese)	Susceptibility	[38]
P2X7R rs2230911	Lupus nephritis (Chinese)	Susceptibility	[38]
P2X7R rs17525809	Multiple sclerosis (Spanish)	Susceptibility	[18]
P2X7R rs1718119 (1068G > A)	RA (Omani Arab)	Susceptibility/ inflammatory activity	[40]
TLR7 rs179008	SLE (Brazilian)	Susceptibility	[28]
TLR9 rs351240	SLE (Northern Han Chinese)	Susceptibility	[29]
TLR9 rs187084	SLE (Taiwanese)	Susceptibility	[30]
TLR9 rs352140	Lupus nephritis (Polish)	Susceptibility	[31]

The purinergic P2X7 receptor (P2X7R) is expressed on a variety of cells, including macrophages, lymphocytes and oligodendrocytes. ATP released from damaged cells stimulates the subsequent potassium efflux that activates the NLRP3 inflammasome [36]. Previous data has suggested that the enhanced formation of neutrophil extracellular traps (NETs) or accumulated cellular debris in lupus will lead to increased inflammasome activation in macrophages via the P2X7 pathway [37]. Polymorphisms in P2X7R have been reported to be associated with susceptibility to SLE and lupus nephritis in a Chinese population [38]. Furthermore, the gain-of-function P2X7R rs17525809 polymorphism increases the risk of multiple sclerosis [18]. The association of P2X7R SNPs with rheumatoid arthritis (RA) has been investigated in Mexican and Omani Arab populations, but the results are not clear [39,40].

2.2. SNPs in inflammasome components

Genetic polymorphisms have been shown in components of both NLR- and ALR-inflammasomes, including NLRP1, NLRP3, NLRC4, CARD8, and AIM2. SNPs in NLRP1, NLRP3, and CARD8 have been found to have associations with autoimmune diseases (Table 2). The first clearly implicated association is NLRP1 and vitiligo related autoimmune diseases [10]. Since NLRP1 has been demonstrated to be expressed on Langerhans cells and T cells, it is conceivable that functional SNPs of NLRP1 could confer risks to autoimmunity of not only the skin, but also other organ systems [41]. Indeed, Pontillo et al. reported later that NLRP1 rs2670660 SNP and the NLRP1 rs12150220-rs2670660 A-G haplotype are associated with susceptibility to SLE [42]. Furthermore, NLRP1 rs878329 polymorphism upregulates NLRP1 transcription and confers a risk to RA in Chinese [43]. SNPs also correlate to other autoimmune diseases, including systemic sclerosis and autoimmune Addison's disease [44–46].

The NLRP3 inflammasome receives a variety of stimuli, including crystals, ATP, and TLR ligands. Genetic mutation in NLRP3 results in classical autoinflammatory diseases: Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), chronic infantile neurological cutaneous and articular (CINCA) syndrome, and neonatal-onset multisystem inflammatory disease (NOMID) [5]. It has been recognized that NLRP3 rs35829419 (Q705K) polymorphism is a gain-of-function SNP, which might contribute to an increased activation state in autoimmune diseases [47]. CARD8 is an adapter protein of the NLRP3 inflammasome, and in a previously studied Swedish population, patients with the combined NLRP3 Q705K and CARD8 C10X (rs2043211) SNPs had elevated plasma levels of IL-1β and IL-33 [48]. The same SNP combination is associated with susceptibility and severity of RA [11]. CARD8 C10X polymorphism alone also correlates with inflammatory activity in early RA in Swedish patients [49]. Similarly, susceptibility of psoriasis in Swedish populationsis associated with CARD8 rs2043211 and NLRP3 rs10733113 variants, respectively [50]. Furthermore, other SNPs in NLRP3 and CARD8 have been found to increase the risk of RA in UK Caucasians [51]. In a study from our group, CARD8 C10X polymorphism was associated with a risk for SLE in male but not female Taiwanese patients [13]. However, it should be noted that although CARD8 C10X results in a premature stop codon, the baseline CARD8 mRNA level was not affected by the SNP [51]. The involvement of CARD8 polymorphism in autoimmunity and its interaction with NLRP3 gain-of-function SNPs requires further investigation. Interestingly, the NLRP3

Table 2
Genetic polymorphisms in inflammasome components and associated autoimmune diseases.

SNPs	Autoimmune disease (ethnicity)	Influence	Ref
NLRP1 rs6502867/rs4790797	Vitiligo-associated autoimmune diseases (USA/UK Caucasian)	Susceptibility	[10]
NLRP1 rs12150220/rs2670660	SLE (Brazilian)	Susceptibility	[42]
NLRP1 rs878329	RA (Chinese)	Susceptibility	[43]
NLRP1 rs8182352	Systemic sclerosis related fibrosingalveolitis (European Caucasian)	Susceptibility	[45]
NLRP1 rs12150220	Autoimmune Addison's disease (Polish)	Susceptibility	[46]
NLRP3 rs10159239	RA (UK Caucasian)	Susceptibility	[51]
NLRP3 rs4925648/rs4925659	RA (UK Caucasian)	Treatment response	[51]
NLRP3 rs35829419 (Q705K)	RA (Swedish), +CARD8 C10X	Susceptibility/severity	[11]
NLRP3 rs10733113	Psoriasis (Swedish)	Severity	[50]
NLRP3 rs4353135	Oligoarticular/polyarticular JIA (Taiwanese)	Susceptibility/inflammatory activity/treatment response	[12]
CARD8 rs16981845/rs10416565	RA (UK Caucasian)	Susceptibility	[51]
CARD8 rs11672725	RA (UK Caucasian)	Treatment response	[51]
CARD8 rs2043211	Early RA (Swedish)	Inflammatory activity	[49]
CARD8 rs2043211	Psoriasis (Swedish)	Susceptibility	[50]
CARD8 rs2043211	SLE (male Taiwanese)	Susceptibility	[13]

Q705K polymorphism is almost absent in Taiwan's Han Chinese population. We discovered that another NLRP3 SNP, rs4353135, which is located between the OR2B11 and NLRP3 genes, could increase lymphocyte IL-17 responses [12]. The rs4353135 variant allele carrier was associated with susceptibility to the oligoarticular and polyarticular subtypes of juvenile idiopathic arthritis (JIA) in Taiwanese [12]. JIA patients with the rs4353135 variant homozygosity also reflected an increased need for anti-TNF-αtreatment [12]. Thus, SNPs in inflammasome components contribute differentially to autoimmune diseases dependent on the ethnicities, making definitive conclusions impossible and emphasizing the widespread genetic diversity that contributes to different outcomes in various populations. This conclusion in autoimmunity [26] is similar to the diversity in response to infectious agents and, in particular, tuberculosis [52].

2.3. SNPs in end products

Activation of inflammasomes leads to caspase-1 mediated synthesis of the effecter cytokines IL-1β and IL-18. Association of genetic polymorphisms in these cytokines with autoimmune diseases has been studied with mixed results [53,54]. A functional IL-1β polymorphism +3953 (C/T)has been reported to be associated with susceptibility to SLE in a Colombian population, but the result requires validation [55]. In the central nervous system (CNS), inflammasomes are expressed not only on infiltrating macrophages and microglia, but also on neurons and astrocytes [56,57]. Inflammasome-mediated pyroptosis has been implicated in neuroinflammatory diseases, one of which is multiple sclerosis (MS). In a cuprizone-induced demyelination mouse model resembling MS, NLRP3 was found to play an important role in exacerbating neuroinflammation, partly via caspase-1 and IL-18. IL-1β knock-out mice, however, did not show a difference in demyelination as compared with wild-type controls [58]. While IL-18 genetic polymorphism was reported to confer risk for MS in a Turkish population; a meta-analysis failed to show an association of IL-1 SNPs with MS [59,60]. Studies on genetic polymorphisms of inflammasome end products and associated autoimmune diseases are summarized in Table 3.

3. Inflammasomes and specific tissue injury in autoimmune diseases

3.1. The effect(s) of cytokines

IL-1β, along with IL-6 and IL-23, drive the differentiation of T helper 17 (Th17) cells [19], which are major players in organ-specific autoimmunity (Table 4). SLE patients have increased IL-17 producing T cells in peripheral blood, and IL-17 is involved in the tissue injury of glomerulonephritis [61,62]. Furthermore, IL-17 attracts neutrophils, CD4+ T cells, and B cells to the site of synovial inflammation, which promotes the transition from the acute phase to the chronic phase of RA [63,64]. In vitiligo skin lesions, active Th17 cells have also been detected [65]. IL-18, the other effector cytokine of inflammasome-mediated caspase-1 activation, has been implicated in the dysfunction of endothelial progenitor cells in SLE, impairing vascular repair [20]. IL-18 augments CD4+T cell interferon-γ production and contributes to secondary progressive MS and RA joint inflammation [66,67]. IL-18 is an important cytokine stimulating leukocyte chemotaxis, angiogenesis, and cartilage destruction [67].

3.2. Direct involvement of inflammasomes in autoimmunity

A high level of NLRP1 has been found in T cells and Langerhans cells, and upregulation of NLRP1 in Langerhans cells has been detected in the leading edge of vitiligo skin [41,65]. NLRP1 inflammasome activation in the skin has been suggested to increase IL-1β release, dermal-epidermal junction apoptosis, and Th17 axis activation [65] (Table 4). In addition to its potential role in RA, NLRP3 has been implicated in the pathogenesis of experimental autoimmune encephalomyelitis (EAE) [68]. The NLRP3 inflammasone mediates EAE progression via augmenting T cell chemotactic activity to migrate to the CNS, rather than increasing the population of Th17 cells [69]. CD4+ T cells primed by antigen presenting cells with an activated NLRP3 inflammasome upregulates the chemotactic protein CCR2, which has been shown to be elevated in the peripheral blood of MS patients during relapse [70,71].

AIM2 differs from NLRP1 and NLRP3 in that it is an intracellular DNA sensor which forms an inflammasome complex with the adapter protein ASC and caspase-1 [72]. The ability of apoptotic body clearance is altered in SLE patients, and self-DNA together with corresponding autoantibodies triggers type-I interferon (IFN) production [73]. While endosomal nucleic acids stimulate TLR7/TLR9, cytoplasmic DNA directly activates the AIM2 inflammasome [3]. A correlation between AIM2 expression and disease severity was found in lupus patients and apoptotic-DNA-induced SLE mice [74]. Furthermore, the blockading of AIM2 expression has been demonstrated to reduce macrophage activation and lupus symptoms [74]. Since aberrant macrophage activation in response to apoptotic-DNA has been proposed to result in lupus nephritis, AIM2 inflammasome activation in infiltrating macrophages has the potential to contribute to kidney injuries in SLE [75]. In humans, male SLE patients have been reported to suffer from more severe

Table 3
Genetic polymorphisms in inflammasome end products and associated autoimmune diseases.

SNPs	Autoimmune disease (ethnicity)	Influence	Ref
IL-1β rs1143634 (−511A > G)	RA (UK Caucasians)	Susceptibility	[53]
IL-1β rs1143634 (+3953 C > T)	SLE (Colombian)	Susceptibility	[55]
IL-18 rs187238 (−137G > C)	RA (Europeans)	Susceptibility	[54]
	SLE (Asians)	Susceptibility	[54]
IL-18 rs187238/rs1946518	Multiple sclerosis (Turkish)	Susceptibility	[59]

symptoms (including lupus nephritis) than their female counterparts [76]. Indeed, in our previous study we observed elevated AIM2 mRNA expression in resting macrophages of male SLE patients [13].

4. Pathogenesis

4.1. Inflammasome activation in autoimmune diseases

Inefficient clearance of cellular debris in SLE will result in the elevation of reactive oxygen species (ROS), which participates in the U1-small nuclear ribonucleoproein (U1-snRNP) mediated NLRP3 inflammasome activation in the presence of the anti- U1-snRNP autoantibody [77]. Furthermore, impaired NET clearance in a subset of SLE patients stimulates the NLRP3 inflammasome via P2X7R-mediated potassium efflux [37]. Accumulation of cytosolic self DNA in autoimmunity triggers AIM2 inflammasome-mediated IL-1β production, and cytosolic IFI16-induced type-I interferons [72]. Alternatively, IFI16 forms an activating inflammasome complex following stimulation with viral DNA [2]. Whether self DNA can activate the nuclear IFI16 inflammasome requires further investigation. Activation of inflammasomes leads to the release of IL-1β and IL-18, and these promote the differentiation of Th17 cells and impair the function of lupus endothelial progenitor cells, respectively [19,20]. CD4+ T cells primed by NLRP3-activated antigen presenting cells upregulate chemotaxis-related proteins, such as CCR2 and CXCR6, resulting in T cell CNS migration [69]. There are thus multiple steps in inflammasome pathway activation (Fig. 1).

4.2. Dysregulation of inflammasome

Both priming and activation of inflammasomes require tight regulations to prevent an excessive inflammatory response. Inflammasome pathways are negatively regulated at multiple levels [9,21,78,79]. Type I interferons could decrease pro-IL-1β/pro-IL-18 levels and inhibit NLRP1/NLRP3 inflammasome activation [32,79]. The anti-apoptotic proteins Bcl-2 and Bcl-X(L) bind and suppress the NLRP1 inflammasome [80]. Furthermore, the autophagy protein Atg16L1 has been suggested to regulate lipopolysaccharide-induced inflammasome activity in the gut [81] and may contribute to the role of microbiota [82]. It is well known that type I interferons, apoptosis, and autophagy are implicated in the sustained activation of autoreactive cells [83–85]. Recently, tumor necrosis factor α-induced protein 3 (A20/TNFAIP3) was found to be another negative regulator of the NLRP3 inflammasome, and specific deletion of A20 in myeloid cells resulted in spontaneous arthritis in mice that resembled human RA [86].

CD4+T cells and microRNA miR-223 have been demonstrated to suppress NLRP inflammasome activity. Murine effector and memory CD4+ T cells inhibit NLRP1 and NLRP3 inflammasomes of macrophages in a contact-dependent manner [87]. Human CD4+ memory T cells dampen NLRP3 activation via down-regulation of P2X7R signaling [88]. miR-223 has been shown to directly decrease NLRP3 protein expression, thus reducing NLRP3 inflammasome activity [22,89]. MiR-223 is differentially expressed in myeloid cells, making fine-tuning of NLRP3 activity possible [89]. In RA, miR-223 is highly expressed on naïve CD4+ T cells but barely expressed on Th17 cells [90]. Moreover, miR-223 is overexpressed in RA T lymphocytes, and is found in a higher concentration in RA synovial fluid than in osteoarthritis [91,92]. Of note, elevated levels of plasma circulating miR-223 have been found in both RA and SLE as compared with healthy controls, suggesting dysregulation of inflammasome pathways [93].

Downstream of NLRP1 and NLRP3 proteins, Caspase-recruitment-domain (CARD)-only decoys, such asCARD-only protein (COP), inhibitory CARD (INCA), and ICEBERG, interfere with inflammasome assembly [94,95]. Furthermore, it has been reported that caspase-12 associates with caspase-1 and inhibits its activity [96]. In the AIM2 inflammasome pathway, p202, another member of the HIN-family, competes with AIM2 for dsDNA binding, thus antagonizing AIM-2-dependent caspase-1 activation [97]. Negative regulators of NLRP1/3 and AIM2 inflammasomes are summarized in Fig. 2.

5. Conclusion

In conclusion, priming of inflammasomes is increased in autoimmune diseases, either because of the functional genetic polymorphisms of TLR/P2X7R, or due to the proinflammatory microenvironment, including stimuli released from damaged cells. NLRP1, NLRP3 and AIM2 inflammasomes are activated in autoimmune diseases, all three of which play important roles in tissue injury and organ damage. Understanding the complex regulatory network of inflammasome activation in autoimmunity will shed

Table 4
Inflammasome pathway proteins and specific tissue injury in autoimmune diseases.

Protein	Site of action	Response	Disease	Ref
IL-1β	Macrophage	Activation	RA (joint destruction)	[98]
	Th17	Differentiation/activation	SLE (lupus nephritis)	[61,62]
	Th17	Differentiation/activation	RA (joint destruction)	[63,64]
	Th17	Differentiation/activation	Vitiligo (skin inflammation)	[65]
IL-18	Endothelial progenitor cell	Dysfunction	SLE (atherosclerosis)	[20]
	CD4+T cell	IFN-γproduction	Multiple sclerosis (CNS inflammation)/RA (joint destruction)	[66,67]
	Synovial fibroblast	Chemokine secretion	RA (joint destruction)	[67]
	Leukocyte	Extravasation	RA (joint destruction)	[67]
	Endothelial cell	Angiogenesis	RA (joint destruction)	[67]
NLRP1	Langerhans cell	Activation	Vitiligo (skin inflammation)	[65]
NLRP3	T cell	Chemotaxis	Multiple sclerosis (CNS inflammation)	[69]
AIM2	Macrophage	Activation	SLE (lupus nephritis)	[13,74,76]

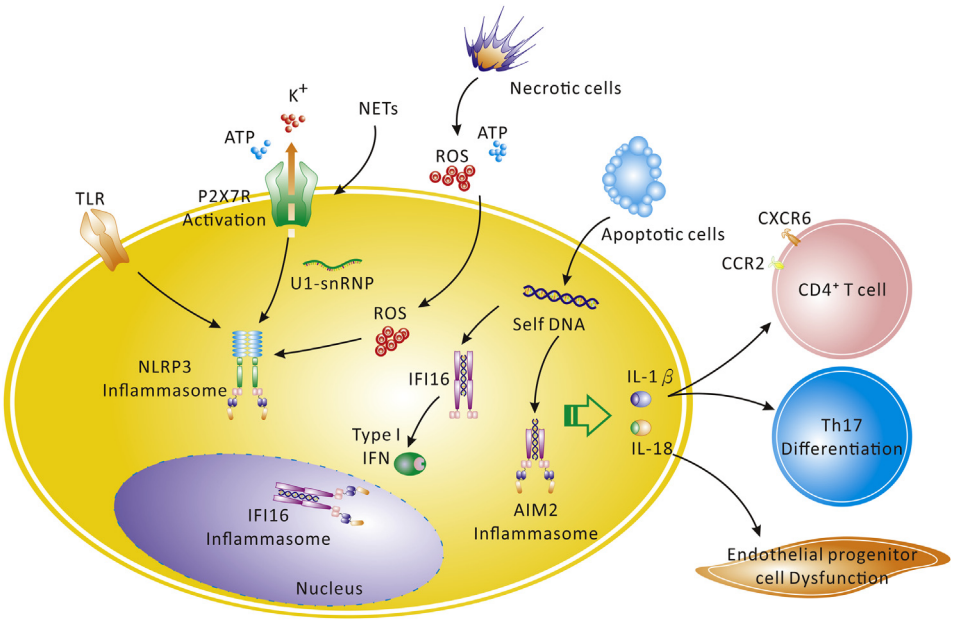

Fig. 1. Infammasome activation in autoimmune diseases. Defective clearance of NETs, damaged cells, and apoptoticcells in autoimmune diseases can prime the NLRP3 inflammasome via P2X7R activation and generation of ROS. Genetic polymorphisms in TLR and P2X7R may also contribute to increased priming. U1-SnRNP, in the presence of its autoantibody, activates the NLRP3 inflammasome. Cytosolic self DNA activates the AIM2 inflammasome and induces IFI16-mediated type-I IFN production. Whether the nuclear IFI16 inflammasome plays a role in autoimmunity requires further investigations. Activation of both NLRP3 and AIM2 inflammasomes leads to IL-1β and IL-18 secretion, which then mediates CD4+ T cell chemotaxis, Th17 cell polarization, and endothelial progenitor cell dysfunction.

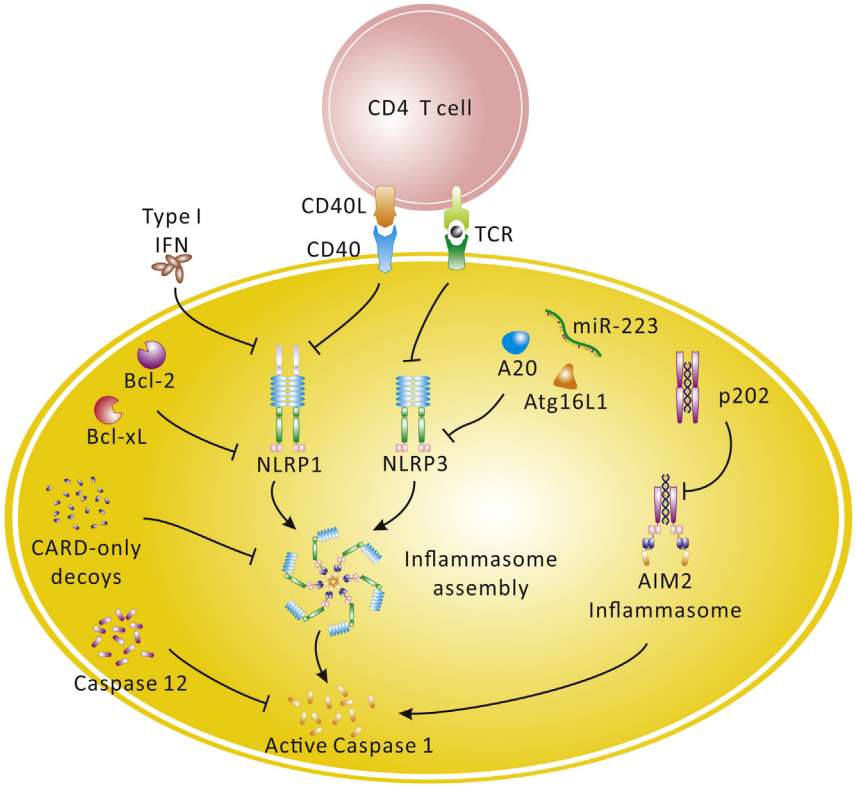

Fig. 2. Negative regulators of inflammasomes. Type I IFN, autophagy, and apoptosis are all implicated in autoimmune diseases. Type I IFN and anti-apoptotic proteins Bcl-2/Bcl-X(L) inhibit the NLRP1 inflammasome. Type I IFN and the autophagy protein Atg16L1 can suppress the NLRP3 inflammasome, resulting in decreased IL-1β and IL-18 production. In addition, A20 and miR-223 suppress NLRP3 inflammasome activity. Knockdown of A20 in mice results in spontaneous arthritis. miR-223 is elevated in the synovial fluid of RA. While CD4+T cells inhibit macrophage NLRP1 and NLRP3 inflammasome activation via contact-dependent mechanisms, caspase-12 can associate with caspase-1 directly and prevent its activation. Furthermore, CARD-only decoys and the HIN-family protein p202 interferes with NLRP inflammasome assembly and suppresses the AIM2 inflammasome.

light on the development of new target therapy. Yet, more significantly, large population genetic association studies concerning SNPs in inflammasome component and autoimmune diseases need to be done to validate current data. Further, understanding the mechanism of inflammasome dysregulation in autoimmune diseases may shed light on new treatments.

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