Table 1 | **Sterile stimuli**

Sterile inflammatory signal	Putative sensor	Associated pathology	Refs*
Endogenous			
HMGB1	TLR2, TLR4, TLR9, RAGE and CD24	Cellular injury and necrosis	26,93,98,106
HSPs	TLR2, TLR4, CD91, CD24, CD14 and CD40	Cellular injury and necrosis	11,25,106,122
S100 proteins	RAGE	Cellular injury and necrosis	19
SAP130	CLEC4E	Cellular injury and necrosis	72
RNA	TLR3	Cellular injury and necrosis	39,123
DNA	TLR9 and AIM2	Cellular injury and necrosis	40,48–50
Uric acid and MSU crystals	NLRP3	Gout	13,55
ATP	NLRP3	Cellular injury and necrosis	20,60
Hyaluronan	TLR2, TLR4 and CD44	Cellular injury and necrosis	31,32,103
Biglycan	TLR2 and TLR4	Cellular injury and necrosis	14,33
Versican	TLR2	Cellular injury and necrosis	34
Heparan sulphate	TLR4	Cellular injury and necrosis	124
Formyl peptides (mitochondrial)	FPR1	Cellular injury and necrosis	125
DNA (mitochondrial)	TLR9	Cellular injury and necrosis	125
CPPD crystals	NLRP3	Pseudogout	55
β-amyloid	NLRP3, CD36 and RAGE	Alzheimer's disease	56,94,105
Cholesterol crystals	NLRP3 and CD36	Atherosclerosis	59,105
IL-1α	IL-1R	Cellular injury and necrosis	15,22,41
IL-33	ST2	Cellular injury and necrosis	16,86
Exogenous			
Silica	NLRP3	Silicosis and pulmonary interstitial fibrosis	44,57,58
Asbestos	NLRP3	Asbestosis and pulmonary interstitial fibrosis	57

AIM2, absent in melanoma 2; CLEC4E, C-type lectin 4E; CPPD, calcium pyrophosphate dihydrate; DAMP, damage-associated molecular pattern; FPR1, formyl peptide receptor 1; HMGB1, high-mobility group box 1; HSP, heat shock protein; IL, interleukin; MSU, monosodium urate; IL-1R, IL-1 receptor; NLRP3, NOD-, LRR- and pyrin domain-containing 3; RAGE, receptor for advanced glycation end products; SAP130, spliceosome-associated protein 130; TLR, Toll-like receptor. *References may not be all inclusive.

Apoptosis
A common form of cell death that is defined by specific morphological changes and by the involvement of caspases. The morphological features include chromatin condensation, plasma membrane blebbing and DNA fragmentation into segments of ~180 base pairs. Eventually, the cell breaks up into many membrane-bound 'apoptotic bodies', which are phagocytosed by neighbouring cells.

High-mobility group box 1
(HMGB1; also known as amphoterin). A nuclear protein that binds DNA in a non-sequence-specific manner and modulates transcription and chromatin remodelling by bending DNA and facilitating the binding of transcription factors and nucleosomes, respectively.

Adjuvant
A substance that stimulates the immune system to enhance the immunogenicity of antigens or vaccines and enhance antigen-specific antibody production.

is, whether they have redundant roles or whether a predominant DAMP (the expression of which may depend on the inciting event) triggers sterile inflammation. For example, a reduction of uric acid, which is released from dying cells and has adjuvant activity *in vivo*[21], was associated with substantially reduced neutrophil recruitment in the liver after acetaminophen-induced injury in two different mouse models[13]. By contrast, in particulate-induced sterile inflammation, uric acid depletion had no effect, suggesting that uric acid may be a major pro-inflammatory DAMP that is specifically involved in cell death-related sterile inflammation[13]. However, uric acid depletion does not completely eliminate acetaminophen-induced liver inflammation or the adjuvant activity of damaged cells, which may reflect residual uric acid following depletion or redundant activities by other DAMPs.

The context of cellular injury leading to sterile inflammation may also be important. In one study, treatment of mice with HMGB1-specific antibodies during acetaminophen-induced liver necrosis ameliorated inflammatory cell recruitment[10]. However, in a peritoneal model of sterile inflammation, there was no difference between wild-type and HMGB1-deficient necrotic cells in their ability to promote neutrophilic recruitment[22]. Thus, although substantial progress has been made in identifying potential DAMPs that can elicit inflammatory responses, much remains to be learnt, such as the different biological functions of the various DAMPs during sterile inflammation, which would be important for identifying new therapeutic targets.

Mechanisms of sterile inflammation

Despite the growing list of sterile immune stimuli, the mechanisms by which these stimuli trigger an inflammatory response are still not fully understood. Even though endogenously generated DAMPs are structurally heterogeneous, the outcome of inflammatory responses to these stimuli is generally uniform. Moreover, inflammatory responses during infection are very similar to responses induced by sterile stimuli,