Table 1. Studies providing empirical evidence for the relationship between MIE (Event 1495) and KE1 (Event 1496). +: Severity of Response. References available in main KER page.

Stressor (Reference)	***In vitro*/ *in vivo*/ *ex vivo***	**Species/cell line**	**Exposure conditions**	**MEI (Event 1495) Interaction with the lung resident cell membrane components**		**KE1 (Event 1496) Increased, secretion of pro-inflammatory and pro-fibrotic mediators**
Silica (Chan et al., 2018)	*In vitro*	U937-differentiated macrophages	2.5 µg/cm^2 for 0 - 24 h	TLR4 mRNA expression level 0 h: 0.5 h: 2 h: 8 h: 16 h: + 24 h: ++ TLR4 Protein expression level 24 h: + MyD88, TIRAP protein expression level 24 h: +		An increase in the release of IL-1β, IL-6, IL-10, and TNF-α 24 h: +
Zinc oxide nanoparticles (Roy et al., 2014)	*In vitro*	Primary mice macrophages	2.5 µg/ml for 0.5 - 24 h	TLR6 mRNA expression level, MyD88, TRAF mRNA, and protein expression level 0.5 h: + 3 h: + 6 h: ++ 12 h: +++ 24 h: +++		Increased mRNA and protein expression of IL-1β, IL-6, and TNF-α 24 h: +
Crystalline silica (Brown et al., 2007)	*In vitro*	Mouse bone marrow-derived mast cells	6.25 - 50 µg/cm^2 for 0.5 - 24 h	Scavenger receptor MSR2 mRNA expression increased (2 h) µg/cm^2 6.25: + 12.5: + 25: ++ 50: +++	Scavenger receptor MSR2 mRNA expression increased (50 µg/cm^2) 30 min: + 1 h: ++ 2 h: +++	Increased TNF-α, IL-13, MCP-1 (24 h) µg/cm^2 6.25: + 12.5: ++ 25: +++ 50: ++++
Thapsigargin (Suwara M et al., 2014)	*In vitro*	Primary human bronchial epithelial cells (16HBE14o)	Conditioned medium obtained from 6HBE14o treated with thapsigargin 20 µM for 2 h	16HBE14o cells Release IL-1α (alarmin)		MRC5 treated with conditioned medium from 16HBE14o cells. Increased IL-6, IL-8, MCP-1 and GM-

		Human lung fibroblast (MRC5)	MRC5 treated with conditioned medium for 5 h.		CSF gene expression
Cigarette smoke (Heijink I et al., 2015)	*In vitro*	Human peripheral blood neutrophils Normal human bronchial epithelial cells	Cell-free supernatant collected from smoke-treated neutrophils (bubbled 1 min with cigarette smoke, rested 2 h). Normal human bronchial epithelial cells treated with conditioned medium for 24 h.	Neutrophils Released HMGB1	Normal human bronchial epithelial cells treated with conditioned medium from neutrophils Released CXCL8
Acetaminophen (Martin-Murphy et al., 2010)	*In vivo*/*in vitro*	C57BL/6J mice RAW 264.7 cells	350 mg/Kg intraperitoneal injection for 3 and 6 h (Mice) (Liver perfusate) RAW 264.7 cells treated for 3 h with liver perfusate (6 h acetaminophen treated mice)	Increased HSP-70 and HMGB1 levels in liver perfusate	Increased mRNA expression in RAW 264.7 cells treated with liver perfusate
				3 h: + 6 h: +	MCP-1: + IL-1β: +
Silica (Rabolli et al., 2014)	*In vivo*	Female C57BL/6 mice	Instillation 2.5 mg/mouse Evaluation: 1 – 24 h post-exposure	Release IL-1α (alarmin)	Increased mRNA expression pro IL-1β
				1 h: ++ 3 h: +++ 6 h: +++ 12 h: ++ 24 h: +	1 h: 3 h: 6 h: ++ 12 h: ++ 24 h: +++
Bleomycin (Xu J. et al., 2016)	*In vivo*	Kunming strain mice	5 mg/Kg intratracheal instillation Evaluation: 3 – 28 days post-exposure	Release of IL-33	Release of IL-4 and IL-13
				Day 3: ++ Day 7: ++ Day 14: + Day 28: +	Day 3: Day 7: + Day 14: ++ Day 28: ++

CXCL: C-X-C motif chemokine ligand.
GM-CSF: Granulocyte-macrophage colony-stimulating factor.
HMGB1: High mobility group box 1.
HSP: Heat shock protein.
IL: Interleukin.
MCP-1: Monocyte chemoattractant protein-1.
MSR2: Macrophage scavenger receptor.
MyD88: Myeloid differentiation primary response 88.
TIRAP: Toll-interleukin-1 receptor domain containing adaptor protein.
TLR: Toll-Like Receptor.
TNF: Tumor necrosis factor alpha.
TRAF: TNF receptor-associated factor