Table 1. Studies providing empirical evidence for the relationship between KE3 (Event 1498) and KE4 (Event 1499).
+: Severity of Response. References available in main KER page.

Stressor (Reference)	***In vitro*/*in vivo*/*ex vivo***	**Species/Cell line**	**Exposure Conditions**	**KE3 (Event 1498) Loss of alveolar capillary membrane integrity**		**KE4 (Event 1499) Activation, T helper (Th) type 2 cells**			
Bleomycin (Kikuchi et al., 2010)	*In vivo*	Wild-type C57BL/6 and Nrf2-deficient mice	5 mg/Kg intratracheal instillation Evaluation: 1 - 28 days post-exposure	LDH in BALF	Antioxidant genes induction	Th2 cytokine expression		Expression GATA-3	
				Day 1: + Day 3: + Day 8:	Day 1: ++ Day 3: +	Day 7: + (IL-4, IL-13)		Day 7: +	
Aspergillus fumigatus extract (Haczku et al., 2006)	*In vivo*	Female BALB/c	Extract intraperitoneal injection on day 0 and day 14. Intranasal challenge on day 24. Evaluation: 12, 24, 48, 72 h post intranasal challenge.	Total BALF protein		Increased IL-4. IL-5, IL-13 in BALF			
				12 h: + 24 h: ++ 48 h: + 72 h: +		12 h: ++ 24 h: ++ 48 h: + 72 h:			
Nitrogen mustard (Venosa et al., 2016)	*In vivo*	Male Wistar rats	0.125 mg/kg intratracheal instillation Evaluation: 1, 3, 7, 28 days post-exposure.	Genes upregulated		Decreased resident macrophages	Increased infiltrating macrophages	M2 macrophages	Genes upregulated
				iNOS, IL-12α, COX-2, TNF-α, MMP9 and MMP10, CCR5, CCL2, CCL5 Day 1: +++ Day 3: ++ Day 7: ++ Day 28: +		CD11b-, CD43-, CD68+ Day 1: +++ Day 3: ++ Day 7: + Day 28: +++	CD11b+, CD43+ Day 1: + Day 3: ++ Day 7: + Day 28:	CD11b+, CD4- Day 1: + Day 3: ++ Day 7: +++ Day 28: +	IL-10, pentraxin-2, ApoE, CX3CR1, fractalkine Day 1: ++ Day 3: +++ Day 7: +++ Day 28: +
Exotoxin Pyocyanin (Caldwell et al., 2009)	*In vivo*	Wild-type FVBN mice Wild-type and STAT6-/- C57BL/6 mice	10, 25 μg intranasal challenge 3 times/ weeks, for 3, 6, 12 weeks. Evaluation: During week 3, 6, 12 of exposure.	Alveolar airspace destruction		Th2 cytokines	Decreased resident macrophages	Increased infiltrating macrophages	CD4 T cells/ml BALF
				25 μg Week 6: + Week 12: ++		25 μg IL-13, IL-4, TGF-β, IL-10	25 μg F4/80^{+}/CD 11b^{-}	25 μg F4/80^{+}/CD 11b^{+}	25 μg Week 3: +++

							Week 3: + (only IL-10) Week 6: + Week 12: +++	Week 3: Week 6: +++ Week 12: +	Week 3: Week 6: Week 12: +++	
Sodium arsenite $NaAsO_2$ (Li et al., 2017)	*In vivo*	Female C57BL/6 mice	2.5, 5, 10 mg/kg intragastrical single oral administration. Evaluation: 24 h post-exposure.	Total protein levels in BALF	MDA content in lung	Nrf2 relative protein levels in lung	Increase relative mRNA levels in lung Gata3, IL-4, Foxp3, IL-10		Decrease relative mRNA levels in lung T-bet, Ifn-γ, Ror-γt, IL-23	
				2.5: + 5: + 10: ++	2.5: + 5: ++ 10: +++	2.5: + 5: +++ 10: +++	2.5: + 5: ++ 10: +++		2.5: + 5: ++ 10: +++	
			100 mg/mL administered freely in drinking water for 2 months. Evaluation: post-exposure	Increase NF-κB, p-38, p-JNK, p-ERK relative mRNA levels			Increase IL-4, IL-23, IL-10, Ifn-γ, IL-1β mRNA levels			
NiO (Chang et al., 2017)	*In vivo*	Male Wistar rats	0.015, 0.06, 0.24 mg/Kg intratracheal instillation twice/ week, for 6 weeks Evaluation: post-exposure	Increase relative protein expression NFκ-B, IKK-α, NIK in lung tissue	Increase nitrative stress in rat lung tissue		Increase relative protein expression GATA-3		Decrease ratio of relative protein expression T-bet/GATA-3	
				0.015: 0.06: + 0.24: ++	0.015: 0.06: 0.014: +++		0.015: 0.06: + 0.024: ++		0.015: + 0.06: ++ 0.024: +++	

ApoE: Apolipoprotein E.
BALF: Bronchoalveolar lavage fluid.
CCL: C-C motif chemokine ligand.
CCR: C-C chemokine receptor.
CD: Cluster of differentiation.
COX-2: Cyclooxygenase-2.
CX3CR1: C-X3-C motif chemokine receptor 1.
Foxp3: Forkhead box P3.
Gata3: GATA binding protein 3.
Ifn-γ: Interferon gamma.
IL: Interleukin.
IKK-α: Inhibitor of NF-κB kinase subunit alpha.
iNOS: Inducible nitric oxide synthase.
LDH: Lactate dehydrogenase.
MDA: Malondialdehyde.

MMP: Matrix metalloproteinase.
NF-κB: Nuclear Factor Kappa B.
NIK: NF-κB-inducing kinase.
Nrf2: Nuclear factor erythroid 2-related factor 2.
p-38: A mitogen-activated protein kinase.
p-ERK: Phospho-extracellular signal-regulated kinase.
p-JNK: Phospho-c-Jun N-terminal kinase.
Ror-γt: Retinoic acid-related orphan receptor gamma t.
T-bet: T-box transcription factor.
TGF-β: Transforming growth factor beta.
Th: T helper.
TNF: Tumor necrosis factor.