

**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 at day 0 and day 14. Intranasal challenge at day 24. Evaluation: 12, 24, 48, 72 hours 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-12 α , COX-2, TNF- α , MMP9 and MMP10, CCR α , CCR5, CCL2, CCL5 Day 1: +++ Day 3: ++ Day 7: ++ Day 28: +	CD11b-, CD43-, CD68+	CD11b+, CD43+	CD11b+, CD4-	IL-10, pentraxin-2, ApoE, CX3CR1, fractalkine Day 1: ++ Day 3: +++ Day 7: +++ Day 28: +		
Exotoxin Pyocyanin (PCN) (Caldwell et al., 2009)	In vivo	WT FVBN mice	10, 25 μ g intranasal challenge 3 times/ weeks, for 3, 6, 12 weeks.	Alveolar airspace destruction		Th2 cytokines		Decreased resident macrophages	Increased infiltrating macrophages	CD4 T cells/ml BALF
		WT and STAT6-/- C57BL/6 mice	Evaluation: During week 3, 6, 12 of exposure.	25 μ g PCN Week 6: + Week 12: ++	25 μ g PCN IL-13, IL-4, TGF- β , IL-10	25 μ g PCN F4/80 $^+$ /CD11b $^-$	25 μ g PCN F4/80 $^+$ /CD11b $^+$	25 μ g PCN F4/80 $^+$ /CD11b $^+$	25 μ g PCN Week 3: +++	

							Week 3: + (only IL-10) Week 6: + Week 12: +++	Week 3: Week 6:+++ Week 12: +	Week 3: Week 6: Week 12: +++	
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- γ t, 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- κ B, p-38, p-JNK, p-ERK relative mRNA levels			Increase IL-4, IL-23, IL-10, Ifn- γ , IL-1 β 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 NF κ -B, IKK- α , NIK in lung tissue	Increase Nitritative 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: +++			