Inhibition of inflammasome activation improves lung acute injury induced by carrageenan in a mouse model of pleurisy

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The NLRP3 inflammasome is a molecular pathway activated by a wide range of cellular 'danger' to elicit innate immune defences through the activation of Caspase-1 and the maturation of pro-inflammatory cytokines as IL-1β and IL18. The expression of NRLP3 is abnormally elevated in numerous human inflammatory diseases, including pulmonary diseases. An injection of carrageenan into the pleural cavity triggered an acute inflammatory response: tissue damage, inflammatory exudates, leukocyte infiltration and increased MPO activity. The aim of this study was to assess the effect of BAY 11-7082 (30 mg/Kg i.p.) or Brilliant Blue G (BBG 45.5 mg/Kg i.p.), two inflammasome blocking agents, in a mouse model of carrageenan-induced pleurisy. Treatments with BAY 11-7082 or BBG 1 hour after carrageenan injection attenuated pulmonary membrane thickening and polymorphonuclear leukocytes infiltration, reduced NFkB translocation in the nucleus and inhibited the assembly of the NRLP3/ASC/Caspase-1 complex. BAY 11-7082 or BBG administrations also down-regulated iNOS, nitrotyrosine and PARP expression and inhibited carrageenan-induced apoptosis. In conclusion we demonstrate that treatments with inflammasome blocking agents significantly reduce the development of acute lung injury carrageenan-induced.