Abstract:
Overall asthmatic symptoms can be controlled with diverse therapeutic agents. However, certain symptomatic individuals remain at risk for serious morbidity and mortality, which prompts the identification of novel therapeutic targets and treatment strategies. Thus, using an adjuvant-free T helper type 2 (Th2) murine model, we have deciphered the role of interleukin (IL)-1 signalling during allergic airway inflammation (AAI). Because functional IL-1? depends on inflammasome activation we first studied asthmatic manifestations in specific inflammasome-deficient [NACHT, LRR and PYD domains-containing protein 3 (NLRP3(-/-) ) and apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC(-/-) )] and IL-1 receptor type 1(-/-) (IL-1R1(-/-) ) mice on the BALB/c background. To verify the onset of disease we assessed cellular infiltration in the bronchial regions, lung pathology, airway hyperresponsiveness and ovalbumin (OVA)-specific immune responses. In the absence of NLRP3 inflammasome-mediated IL-1? release all symptoms of AAI were reduced, except OVA-specific immunoglobulin levels. To address whether manipulating IL-1 signalling reduced asthmatic development, we administered the IL-1R antagonist anakinra (Kineret®) during critical immunological time-points.
sensitization or challenge. Amelioration of asthmatic symptoms was only observed when anakinra was administered during OVA challenge. Our findings indicate that blocking IL-1 signalling could be a potential complementary therapy for allergic airway inflammation.