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Title: Hypoxia induces inflammasome activation and influx of neutrophils and T-cells in the lungs

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Body: Background: Inflammasomes are molecular platforms which are part of the innate immunity and activate IL-18 and IL-1β through caspase-1. They can be activated by microorganisms and physical stress (K. Schroder & J.Tschopp, Cell, 2010). Increased levels of interleukin (IL)-18 have been found during experimental alveolar hypoxia (K.O. Larsen et al. Cardiovasc Res, 2008), but it is not known whether hypoxia activates inflammasomes leading to increased IL-18 and IL-1β levels. Objectives: To study inflammasome activation and cell infiltration in mouse lungs during hypoxia exposure. Methods: Lungs were harvested from C57Bl/6j mice at 1-7 days of hypoxia exposure (10%) for histological and Western blot analyses. Active caspase-1, IL-18 and IL-1β were measured. Results: Histology revealed perivascular infiltration of inflammatory cells and inflammasome components at day 1-7, with neutrophil granulocytes dominating from day 1-3, and T-cells dominating from day 4-7. Active caspase-1 and IL-18 were significantly increased at day 3, 7 and 4 weeks of hypoxia compared to normoxic controls (both $p<0.05$). IL-1β showed upregulation, but it did not reach statistical significance. Conclusions: Active Caspase-1 was induced during hypoxia indicating activation of the innate immune system through inflammasomes. Both IL-18 and IL-1β were upregulated, but IL-1β did not reach significance. Activation of the inflammasome may play a role for the inflammatory cell influx and the cytokine mediated progression of lung disease in hypoxic patients. Acknowledgements: We are grateful to Almira Hasic and Ingeborg Løstegaard Goverud for technical assistance.