Karolina Benesova
Dr. med.

Bedeutung der Eisenhomöostase für die inflammatorische Antwort bei entzündlichen Atemwegserkrankungen

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Iron is an indispensable element for metabolism and oxygen transport in mammals; however, it is also an essential nutrient of most microbial pathogens. To protect the host from infection, the regulation of iron homeostasis and the immune response are closely interlinked. The consequences of disturbed iron homeostasis on this interrelationship are not fully understood. In this study we investigate how imbalanced systemic iron homeostasis in *Hfe* deficient mice (*Hfe*$^{-/-}$), the mouse model of hereditary hemochromatosis affects the inflammatory response in the lung, an organ that copes with constant exposure to both, airborne pathogens and iron particles.

Acute pulmonary inflammation was induced in *Hfe*$^{-/-}$ and wild-type mice by intratracheal instillation of lipopolysaccharide and local and systemic inflammatory responses and iron-related parameters were evaluated at 4 h post-challenge. We show that the inflammatory response in *Hfe*$^{-/-}$ mice is dysregulated with attenuated neutrophil recruitment to the alveolar space on the one hand and hyper-induced mRNA expression and protein secretion of inflammatory mediators on the other hand. This effect is only partially preserved in mice with selective *Hfe* deficiency in macrophages and neutrophils (*Hfe*^{LysMCre}).

Our results suggest that the underlying molecular mechanisms are likely multifactorial and include elevated systemic iron levels, iron depletion of alveolar macrophages and subsequent impairment of TLR4- and/or NFκB-signaling. Additionally, our data implicate a possible role for Hfe in macrophages and nonhematopoietic cells.

Collectively, our findings provide novel insight into the consequences of *Hfe* deficiency and imbalanced iron homeostasis for the inflammatory response of the host.