immune response against SARS-CoV-2. These results can contribute to the development of therapeutics, preventive medication against hyperinflammatory syndromes as well as alternative vaccine constructs and adjuvants.

Theobald SJ, Simonis A, […], Rybniker J. (2021) **Long-lived macrophage reprogramming drives spike protein-mediated inflammasome activation in COVID-19**. *EMBO Molecular Medicine* 13(8): e14150

P033

MicroRNA-223 dampens neutrophil-mediated lung inflammation during pneumococcal pneumonia

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Community acquired pneumonia remains a leading cause of communicable disease-related mortality globally, despite the widespread use of protective vaccines and effective antibiotics. Neutrophils play a major role in containing bacterial growth, while also orchestrating detrimental pulmonary inflammation when dysregulated. Here we aimed to elucidate the role of myeloid cell-derived microRNA-223 in regulating pulmonary inflammation during pneumococcal pneumonia.

Serum microRNA-223 was quantified in pneumococcal pneumonia patients and healthy subjects. Wild-type and microRNA-223 knockout mice were intranasally infected with *Streptococcus pneumoniae*, followed by evaluation of pulmonary inflammation in terms of clinical disease course, histopathology, immune cell chemotaxis and inflammatory protein and gene signatures. Single-cell RNA sequencing was utilized to evaluate the transcriptomic repercussions of the absence of microRNA-223 during murine pneumococcal pneumonia.

Cell-free serum microRNA-223 was reduced in pneumococcal pneumonia patients relative to healthy subjects, which was correlated with increased disease severity. MicroRNA-223 knockout mice exhibited enhanced neutrophilic influx into the lungs and bronchoalveolar lavage, leading to histopathological aggravation and increased production of pro-inflammatory mediators following *Streptococcus pneumoniae* infection. MicroRNA-223 was induced in the lungs and sorted lung neutrophils of wild-type mice by *Streptococcus pneumoniae* in a time-sensitive manner, while its absence resulted in a dysregulated transcriptome of pulmonary neutrophils involving anti-microbial and cellular maturation genes.

Altogether, our findings indicate that in the absence of microRNA-223, alterations in the neutrophil transcriptome provoked exacerbated acute lung injury in mice, while reduced levels in the serum correlated to increased disease severity in pneumococcal pneumonia patients.