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Exploring the role of Klebsiella pneumoniae and bacteria-derived outer membrane vesicles (OMVs) in viral pneumonia using primary human lung models

Inhalt

Bacterial co-infections are a common complication in respiratory viral infections. ICU patients with influenza and COVID-19 frequently develop co-infections with Gram-negative bacteria, particularly *K. pneumoniae.* Beyond direct bacterial infection, host lung tissue is exposed to extracellular outer membrane vesicles (OMVs), which modulate pulmonary immune responses. Using native distal lung explants, alveolar type 2 (AT-2) organoids, and isolated alveolar macrophages, we show that both bacteria and OMVs elicit distinct immune responses in human lung tissue. While live bacteria induce a rapid pro-inflammatory cytokine response already within 1 hour post infection, accompanied by an early type I IFN response, OMVs triggered a delayed but sustained immune response. Transcriptomic profiling revealed that OMVs alone promoted an IFN-dominated, antiviral intracellular response, while simultaneously suppressing epithelial defense and regenerative pathways and attenuating neutrophil recruitment. Analysis of individual cell systems identified macrophages as the major drivers of the inflammatory response. Together, these findings demonstrate that *K. pneumoniae* OMVs alone are sufficient to reshape immune responses in human lung tissue and establish an antiviral-like transcriptional state, highlighting their potential role as modulators of pulmonary immunity that may influence host responses during bacterial–viral co-infections.

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