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Lung alert

Pathogenetic mechanisms involved in viral-induced exacerbations of COPD

Viruses have been shown to be important causes of exacerbations in patients with chronic obstructive pulmonary disease (COPD). Evidence suggests that innate immune responses play a key role in the pathogenesis of airway inflammation in cigarette smoke (CS)-exposed individuals. However, the precise immune pathways and viral pathogen-associated molecular patterns that trigger these responses have not been previously elucidated.

This study used dsRNA (polyinosine-polycytidylic acid (poly(I:C))) as a surrogate to define responses elicited by viral infections in a murine model. Significantly increased airway inflammatory responses and increased alveolar remodelling were observed in CS-exposed mice receiving poly(I:C) compared with mice breathing room air (RA). Poly(I:C) was a potent stimulator of bronchoalveolar lavage fluid levels of type I and II interferon (IFN), interleukin (IL)-18 and IL-2/IL-23 p40 (all known to have roles in viral responses in patients with COPD). These responses were significantly greater in CS-exposed mice than in RA-exposed mice.

Furthermore, CS + poly(I:C)-induced inflammation and alveolar remodelling was significantly diminished in the airways of mice with separate null mutations of IL-18Rα, IFNγ, PKR (double-stranded RNA-dependent protein kinase), TLR-3 (toll-like receptor 3) or MAVS (mitochondrial antiviral signalling protein) compared with wild-type mice.

This intriguing study provides a novel insight into the mechanisms involved in viral-induced exacerbations of COPD and suggests potential therapeutic targets to control virus-induced responses in smokers with COPD. However, the applicability of this murine model to human patients who have been exposed to many years of CS and a variety of respiratory viruses remains to be seen.

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