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Fate of PEGylated antibody fragments following delivery to the lungs: Influence of delivery site, PEG size and lung inflammation

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Abstract

Pulmonary administration of anti-cytokine antibodies offers a targeted therapy in asthma. However, the rapid elimination of proteins from the lungs limits the efficacy of inhaled medications. PEGylation has been shown to increase the residence time of anti-interleukin (IL)-17A and anti-IL-13 antibody fragments in the lungs and to improve their therapeutic efficacy. Yet, little is known about the factors that affect the residence time of PEGylated antibody fragments in the lungs following pulmonary delivery. In this study, we showed that the molecular weight of polyethylene glycol (PEG), 20kDa or 40kDa, had a moderate effect on the residence time of an anti-IL-17A Fab' fragment in the lungs of mice. By contrast, the site of delivery of the anti-IL-17A and anti-IL-13 Fab' fragments within the lungs had a major impact on their residence time, with the deeper the delivery, the more prolonged the residence time. The nature of the Fab' fragment had an influence on its residence time as well and the anti-IL-17A Fab' benefited more from PEGylation than the anti-IL-13 Fab' did. Acute lung inflammation slightly shortened the residence time of the anti-IL-17A and anti-IL-13 Fab' fragments in the lungs but