# A-to-I editing of miR-200b-3p in airway cells is associated with moderate-to-severe asthma



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**A genome-wide study of endogenous ADAR-mediated miRNA editing in airway cells revealed associations between A-to-I editing of miR-200b-3p and a target gene, *SOCS1*, with asthma severity, suggesting a novel mechanism and therapeutic target for severe asthma** https://bit.ly/2JWsifY

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## Abstract

***Background*** Asthma is a chronic lung disease characterised by persistent airway inflammation. Altered microRNA (miRNA)-mediated gene silencing in bronchial epithelial cells (BECs) has been reported in asthma, yet adenosine deaminase acting on RNA (ADAR)-mediated miRNA editing in asthma remains unexplored.

***Methods*** We first identified adenosine to inosine (A-to-I) edited sites in miRNAs in BECs from 142 adult asthma cases and controls. A-to-I edited sites were tested for associations with asthma severity and clinical measures of asthma. Paired RNA sequencing data were used to perform pathway enrichments and test for associations with bioinformatically predicted target genes of the unedited and edited miRNAs.

***Results*** Of 19 A-to-I edited sites detected in these miRNAs, one site at position 5 of miR-200b-3p was edited less frequently in cases compared with controls ($p_{corrected}$=0.013), and especially compared with cases with moderate ($p_{corrected}$=0.029) and severe ($p_{corrected}$=$3.9\times10^{-4}$), but not mild ($p_{corrected}$=0.38), asthma. Bioinformatic prediction revealed 232 target genes of the edited miR-200b-3p, which were enriched for both interleukin-4 and interferon-γ signalling pathways, and included the *SOCS1* (suppressor of cytokine signalling 1) gene. *SOCS1* was more highly expressed in moderate ($p_{corrected}$=0.017) and severe ($p_{corrected}$=$5.4\times10^{-3}$) asthma cases compared with controls. Moreover, both miR-200b-3p editing and *SOCS1* were associated with bronchoalveolar lavage eosinophil levels.

***Conclusions*** Reduced A-to-I editing of position 5 of miR-200b-3p in lower airway cells from moderate-to-severe asthmatic subjects may lead to overexpression of *SOCS1* and impaired cytokine signalling. We propose ADAR-mediated editing as an epigenetic mechanism contributing to features of moderate-to-severe asthma in adulthood.