

P005 Rapid changes in MicroRNA-146a expression negatively regulate the IL-1 β -induced inflammatory response in human lung alveolar epithelial cells

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Posttranscriptional regulation of gene expression by microRNAs (miRNAs) has been implicated in the regulation of chronic physiological and pathological responses. In this report, we demonstrate that changes in the expression of miRNAs can also regulate acute inflammatory responses in human lung alveolar epithelial cells. Thus, stimulation with IL-1 β results in a rapid time- and concentration-dependent increase in miRNA-146a and, to a lesser extent, miRNA-146b expression, although these increases were only observed at high IL-1 β concentration. Examination of miRNA function by overexpression and inhibition showed that increased miRNA-146a expression negatively regulated the release of the proinflammatory chemokines IL-8 and RANTES. Subsequent examination of the mechanism demonstrated that the action of miRNA-146a was mediated at the translational level and not through the down-regulation of proteins involved in the IL-1 β signaling pathway or chemokine transcription or secretion. Overall, these studies indicate that rapid increase in miRNA-146a expression provides a novel mechanism for the negative regulation of severe inflammation during the innate immune response.