

P011 microRNAs mediated the resolution of inflammation
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We have examined the role of miRNAs in the inflammatory response by investigating their actions during the innate immune response and in the mechanism of action of the potent anti-inflammatory glucocorticoids. Initial studies of the differential expression profile of 156 miRNAs in the acute response to aerosilised LPS in the mouse lung showed a rapid and time dependent increase in the miRNA expression profile, which peaked at 3 hrs. Crucially, this increase was correlated with a reduction in the expression of $TNF\alpha$, KC and MIP-2 suggesting a potential role for increased miRNAs in the resolution of the inflammation. Expression studies *in vitro* involving IL-1 β stimulation of the lung airway epithelial A549 cell line, caused up-regulation of miR-146a/b. Significantly, biochemical and pharmacological studies showed that miR-146a/b attenuated the IL-1 β induced release of IL-8, IL-6 and RANTES through negative feedback inhibition involving the down-regulation in the expression of Traf-6 and IRAK-1 protein. Exposure to the glucocorticoid, dexamethasone had little effect upon the profile of miRNA expression and did not influence the LPS and IL-1 β stimulated changes in mouse lung or A549 cells. Overall, these investigations imply a role for miRNA mediated translational inhibition and down-regulation of regulator proteins in the resolution of inflammation. In contrast, glucocorticoids act primary during the activation phase of inflammation through their actions at the transcriptional level.