Role of HIF-1α in the inflammatory response at the alveolar epithelium and macrophages

In the lung, alveolar macrophages and alveolar epithelium cells release mediators like cytokines, nitric oxide and other substances upon stimulation of bacterial toxins. These mediators inhibit fluid reabsorption by decreasing the level of sodium and water transport from the alveolar space, and increase barrier leakage to cause pulmonary edema, which further inhibits alveolar reabsorption. HIF (hypoxia inducible factor) is heterodimer with subunits HIF-1α and 1β. HIF-1α plays important role in the activation and inflammation response at the alveolar epithelium and macrophages both in normal and hypoxic conditions.

Our aim is to test the aggravating effect of hypoxia in the activation of HIF-1α and inflammatory response both in macrophages and alveolar epithelium cells. Effects of inflammatory response and HIF role were studied by exposing to primary alveolar epithelium cells with absence of HIF-1α (silencing HIF-1α by viral transfer). Nitric oxide production and cytokine expression plays important role in inflammation and inhibition of ion transport in the alveolar epithelium. Upon with stimulation of lipopolysaccharides, alveolar macrophages produce high amounts of nitric oxide which cause many physiological changes and affect the function of the cells. By dialysis, we removed nitric oxide from the media. Our results show that alveolar epithelial type II cells cannot produce nitrite where as macrophages produce.

To check the role of HIF-1α, we used silenced HIF-1α From this, we found that Hif-1α has some role with influences of cytokines like Interleukin-6, Interleukin-1beta and tumour necrosis factor-alpha and also inducible nitric oxide synthase m-RNA expression under hypoxia conditions.This is gives a idea about the signaling pathway for inflammation and inhibition of ion transport in the alveolar epithelium. In future, we will test cytokines relevant for sodium transport inhibition, signaling molecules (nitric oxide) and the role for HIF in the inflammatory response of macrophages and their consequences for sodium-reabsorption.

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