Expression of Inflammatory Mediators Following Mechanical Ventilation in *Ptx3* Genetically Modified Mice

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Mechanical ventilation (MV) is a life saving therapeutic approach for patients with acute lung injury. However, this procedure represents a major cause of iatrogenic lung damage in intensive care units. Inflammation is known to be involved in the pathogenesis of the ventilator-induced lung injury (VILI) but many aspects and mediators of this process are unknown. We showed previously that MV promoted pulmonary histopathological changes underlined by a drastic alteration in local gene expression profile and that the augmented expression of the long pentraxin *Ptx3* drastically accelerates the development of VILI. This study was addressed to evaluate the expression of inflammatory mediators in the sera and lungs of *Ptx3*-transgenic (Tg(Ptx3)CD1) and knockout (*Ptx3*$^{-/-}$) mice submitted to high tidal volume ventilation. Here we show that at the time respiratory Elastance augment 50% from its basal level (~70 min in Tg(Ptx3)CD1 and ~140min in *Ptx3*$^{-/-}$ mice) the local increase of Il1b protein levels parallels the gene expression pattern. The lower levels of Il1b in *Ptx3*$^{-/-}$ in comparison with *Ptx3*$^{+/+}$-ventilated mice ascertain for the amplification loop of *Il1b* expression promoted by Ptx3. At this time point, both Tnfa lung levels in Tg(Ptx3)CD1 and Ptx3 serum levels in ventilated-*Ptx3*$^{+/+}$ although showed a significant decrease when compared to non-ventilated counterparts remained close to the basal concentration in all groups. The findings presented here support the data that the local prior to systemic temporal-regulated-balance of inflammatory mediators in the lungs plays a preponderant biological role in initiating an inflammatory cascade in the alveolar space and corroborate the central role of Ptx3 in VILI.

Key words: *Ptx3, Tnf, Il1b, VILI*.

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