The Role of Hyaluronan Synthase 3 in Ventilator-induced Lung Injury

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摘要

Abstract

We recently found that low-molecular-weight hyaluronan was induced by cyclic stretch in lung fibroblasts and accumulated in lungs from animals with ventilator-induced lung injury. The low-molecular-weight hyaluronan produced by stretch increased interleukin-8 production in epithelial cells, and was accompanied by an upregulation of hyaluronan synthase-3 mRNA. We hypothesized that low-molecular-weight hyaluronan induced by high VT was dependent on hyaluronan synthase 3, and was associated with ventilator-induced lung injury. Effects of high VT ventilation in C57BL/6 wild-type and hyaluronan synthase-3 knockout mice were compared. Significantly increased neutrophil infiltration, macrophage inflammatory protein-2 production, and lung microvascular leak were found in wild-type animals ventilated with high VT. These reactions were significantly reduced in hyaluronan synthase-3 knockout mice, except the capillary leak. Wild-type mice ventilated with high VT were found to have increased low-molecular-weight hyaluronan in lung tissues and concomitant increased expression of hyaluronan synthase-3 mRNA, neither of which was found in hyaluronan synthase-3 knockout mice. We conclude that high VT induced low-molecular-weight hyaluronan production is dependent on de novo synthesis through hyaluronan synthase 3, and plays a role in the inflammatory response of ventilator-induced lung injury.