

## **IMMUNOMODULATORY EFFECTS OF L-CITRULLINE ADMINISTRATION IN A RAT MODEL OF MODERATE HYPEROXIA-INDUCED LUNG INJURY**

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Previous studies have shown that L-citrulline shows beneficial effects on histopathological changes of experimental models of bronchopulmonary dysplasia (BPD). The aim of the present work was to evaluate possible immunomodulatory effects of L-citrulline in an hyperoxia-induced model of BPD. All experimental groups consisted of newborn rats sacrificed at the postnatal day 14 and included: 1) newborn rats raised in normoxia; 2) pups exposed to 60% hyperoxia throughout the experiment without any treatment; 3) pups exposed to normoxia and treated daily with intraperitoneal L-citrulline; 4) rats exposed to 60% hyperoxia and treated daily with L-citr. Hyperoxia-induced changes in lung morphometric parameters (increased mean linear intercept and less numerous secondary crests) and increase in MMP-12 immunostaining were significantly reversed by L-citrulline. Hyperoxia exposure increased the number of lung macrophages and L-citrulline treatment counterbalanced this change. Hyperoxia did not significantly modify the levels of GM-CSF, TNF- $\alpha$ , IL-1 $\beta$ , CXCL10, IL-10 and Arginase 1. Conversely, L-citrulline treatment increased the lung expression of IL-10 and Arginase 1 (markers of M2 macrophages), in the absence of significant changes in main M1 markers. In conclusion, our findings suggest that the therapeutic effects of L-citrulline could at least partially rely on modulation of macrophage proliferation and cytokine release.