Effect of Chemerin Deficiency on Quasi-Static Elastic Properties of the Respiratory System

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RATIONALE: Chemerin, a non-chemokine chemoattractant for natural killer cells, macrophages, and plasmacytoid dendritic cells, is a ligand for three different seven-transmembrane domain receptors: C-C chemokine receptor like-2, chemerin-like receptor 1 (CMKLR1), and chemerin-like receptor 2 (CMKLR2). We recently reported that respiratory system elastance (E_{stat}) was significantly greater in mice genetically deficient in CMKLR1 as compared to wild-type C57BL/6N mice (Johnston *et al*., *Physiol Rep*, 2024). Because chemerin is a ligand for CMKLR1, and because, at present, most of the biological effects attributed to chemerin are mediated *via* CMKLR1, we hypothesized that E_{stat} would be greater in mice genetically deficient in chemerin (chemerin-deficient mice) as compared to wild-type mice. **METHODS:** Wild-type C57BL/6J and chemerin-deficient mice were exposed to filtered room air for three hours and twenty-four hours following cessation of exposure, mice were anesthetized, and quasi-static respiratory system pressure-volume (P-V) curves were generated with the assistance of a specialized ventilator (*flexiVent*). From each P-V curve, E_{stat}; A, an estimate of inspiratory capacity; K, curvature of the upper portion of the expiratory limb of the P-V curve; and Area, respiratory system hysteresis, were determined. A separate cohort of wild-type and chemerin-deficient mice were euthanized twenty-four hours following cessation of exposure to filtered room air to collect bronchoalveolar lavage fluid and lungs, which were analyzed for the presence of chemerin protein or messenger ribonucleic acid (mRNA). **RESULTS:** Chemerin protein was detectable in bronchoalveolar lavage fluid and lung tissue *via* an enzyme-linked immunosorbent assay or a Western immunoblot, respectively. Chemerin mRNA was also detectable in lung tissue *via* reverse transcription-quantitative real-time polymerase chain reaction. P-V curves of chemerin-deficient mice were shifted downward and to the right of P-V curves generated from wild-type mice. In addition, E_{stat} was significantly greater while A was significantly lower in chemerin-deficient as compared to wild-type mice. No genotype-related differences were observed for either K or Area. **CONCLUSIONS:** In the absence of any inciting stimulus, chemerin is required to conserve the orderly quasi-static elastic properties of the respiratory system, and it is probable that these effects of chemerin are mediated *via* CMKLR1. Based on these results, we speculate that if chemerin-CMKLR1 signaling is attenuated in restrictive lung diseases, including idiopathic pulmonary fibrosis and silicosis, this may contribute to the pathogenesis of these diseases.

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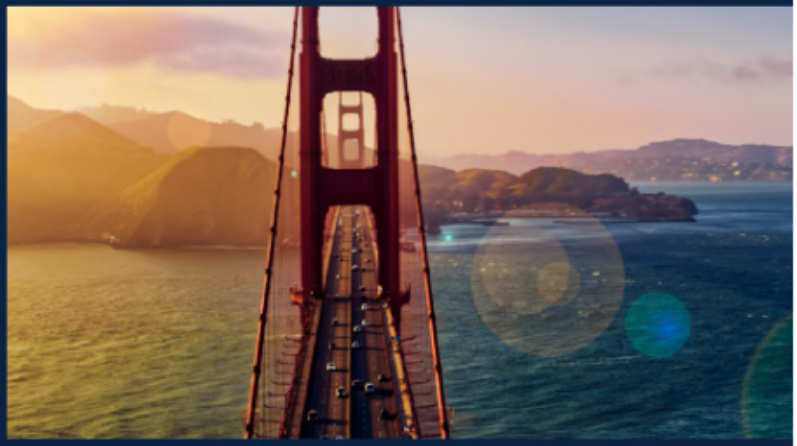

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