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Title: Importance of the receptor for advanced glycation end products in the respiratory mechanics

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Body: Background: There is an increasing clinical interest in studying the receptor for advanced glycation end products (RAGE) and its soluble forms in pulmonary diseases. Interestingly, RAGE and its soluble forms are preferentially expressed in alveoli thereby challenging the pathophysiological role of RAGE. As we have already shown the importance of RAGE as an adhesion molecule in alveolar cells, this study aimed to investigate the age-dependent physiological significance of RAGE in respiratory mechanics. Methods: Lungs of young (<6 month), adult (6-9) and old (>24) RAGE knock out (k.o.) and wild-type mice were analyzed ex vivo using the perfused isolated lung system with negative-pressure ventilation at weight-matched constant tidal volume. Elastin expression was assessed by gene array and histochemistry. Results: Dynamic lung compliance increased gradually with the age in RAGE k.o. as well as in wild-type mice. Independent of age, the lungs of RAGE k.o. mice showed higher compliance than that of the wild-type. In this context, old wild-type and young-adult RAGE k.o. mice had similar lung dynamic compliance. According to the effect of RAGE deficiency on lung compliance, we determined a reduced elastin mRNA and protein expression in the lung tissue of RAGE k.o. mice. However, lack of RAGE had no significant effect on airway resistance and epithelial layer permeability. Conclusion: Our study suggests the physiological importance of RAGE and/or its soluble forms in mediating an appropriate lung compliance in which its/their impact on the elastin expression might play a critical role.