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Kidney ischemia-reperfusion induces lung injury and lung cell cilia disruption via oxidative stress

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Objectives:

Acute kidney injury (AKI) causes remote lung injury. However, its molecular mechanisms remain to be defined. Recent studies have demonstrated that cilia injury and oxidative stress are associated with the progression of diseases. Here, we investigated the role of oxidative stress and cilia in AKI-induced lung injury.

Methods: Bilateral kidney ischemia reperfusion (IR) was induced in isocitrate dehydrogenase 2 (IDH2, a mitochondrial antioxidant enzyme)-deleted (*IDH2*$^{-/-}$) and wild-type (*IDH2*$^{+/+}$) mice. Some mice were treated with Mito-TEMPO, a mitochondrial-specific antioxidant. Lung injury was evaluated by lung histological analysis and cell numbers, protein concentration and IL-6 concentration in BALF. Superoxide level, DNA oxidation and lipid peroxidation were determined in the lung tissue and BALF. Ciliary protein expression was evaluated in lung and BALF by immunofluorescence staining and western blot analysis.

Results: Kidney IR caused lung injury, including inflammation and oxidative stress. In addition, kidney IR resulted in fragmentation of lung cell cilia and release of them into BALF. Kidney IR also increased the production of superoxide, lipid peroxidation, and mitochondrial and nuclei DNA oxidation in lungs, and decreased IDH2 expression. IDH2 deletion exacerbated kidney IR-induced lung injury. Treatment with Mito-TEMPO attenuated kidney IR-induced lung injuries, with greater attenuation in *IDH2*$^{-/-}$ *than IDH2*$^{+/+}$ *mice.*

Conclusions: Data indicate that acute kidney injury causes lung injury and disruption of cilia by increased oxidative stress in the lungs and releases ciliary protein into the BALF.