



Cold and Warm Ischemia Result in Different Histological Characteristics of Reperfusion Injury After Lung Transplantation in Mice

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Background

Ischemia-reperfusion (I/R) injury is a major cause of morbidity and mortality after lung transplantation. In clinical scenario, the donor lungs often experience both cold and warm ischemia to different degrees. It is generally accepted that metabolic rate is the only difference. Orthotopic lung transplantation in mice is an ideal model to study the characteristics of pathology. We hypothesized that cold and warm ischemia cause different pattern of tissue damage.

Methods

Syngeneic left lung transplants (B6→B6) were performed after cold/ warm preservation, and the grafted lungs were sampled for histology at 24 h after reperfusion. In Group 1, donor lungs were stored at 0°C (ice box) for 24h, 48h, 72h and 96h (n≥3). In group 2, donor lungs were stored at 37°C (digital water bath) for 1h, 2h, 3h and 4h (n≥3).

Results

Results: All recipients survived. 1) Less than 72h cold ischemia resulted in sporadic epithelium damage and mild infiltration around small airways at 24h after reperfusion. In the grafts experienced 96h CI + 24h reperfusion, epithelial cells swelled to an enormous size, became translucent or even broke, and infiltration increased dramatically. No obvious change was found in alveoli and blood vessels. 2) Warm I/R was featured by diffuse alveolar damage and infiltration. Epithelium wasn't affected significantly. 3) Both extended cold (96h) and warm (4h) I/R injury recovered on POD7. 4) Western Blot analysis revealed that necroptosis was activated, consistent with the pathology in "96h CI+24h R".

Figure 1. Histology of **COLD** Ischemia-reperfusion injury.

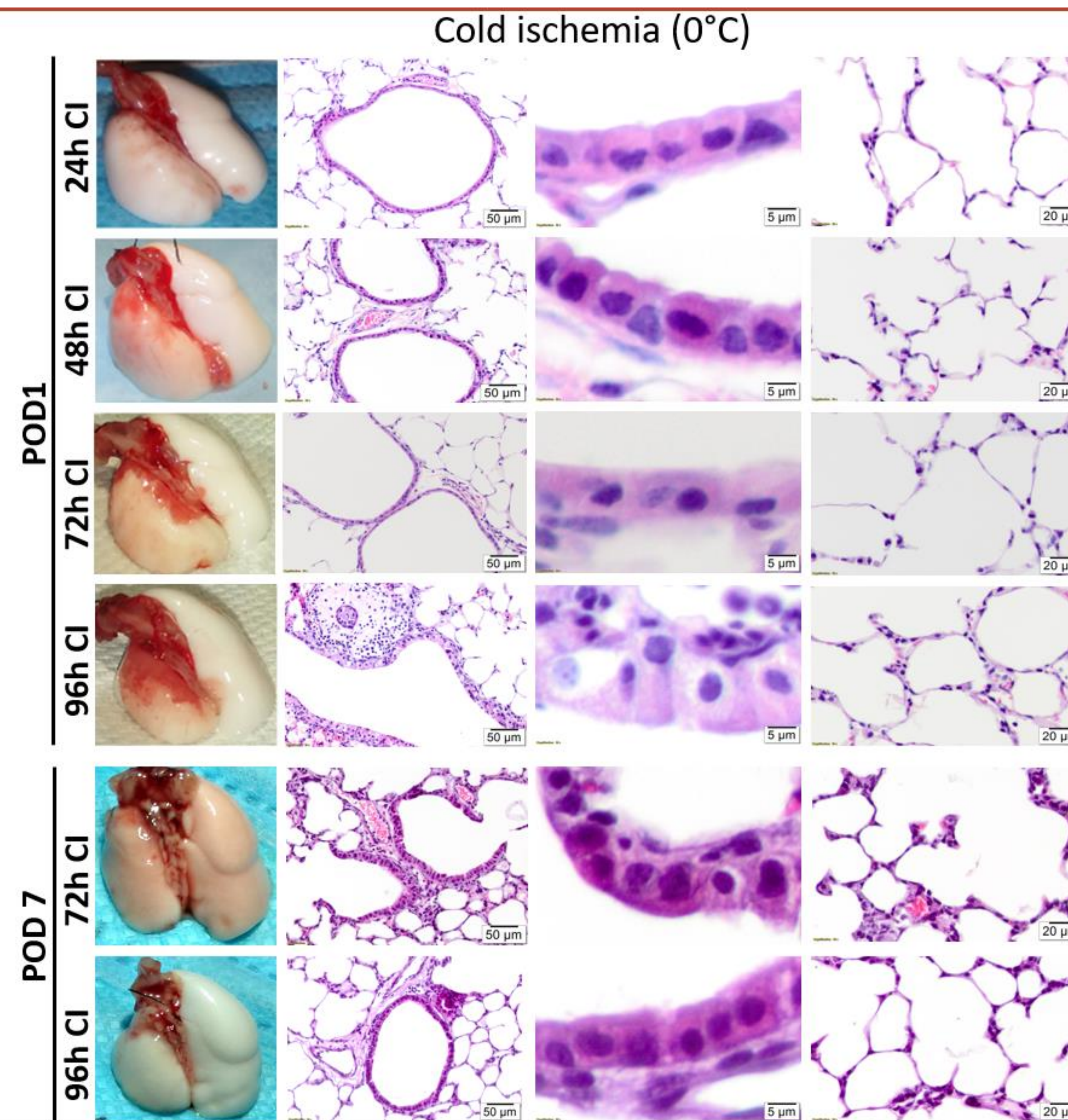
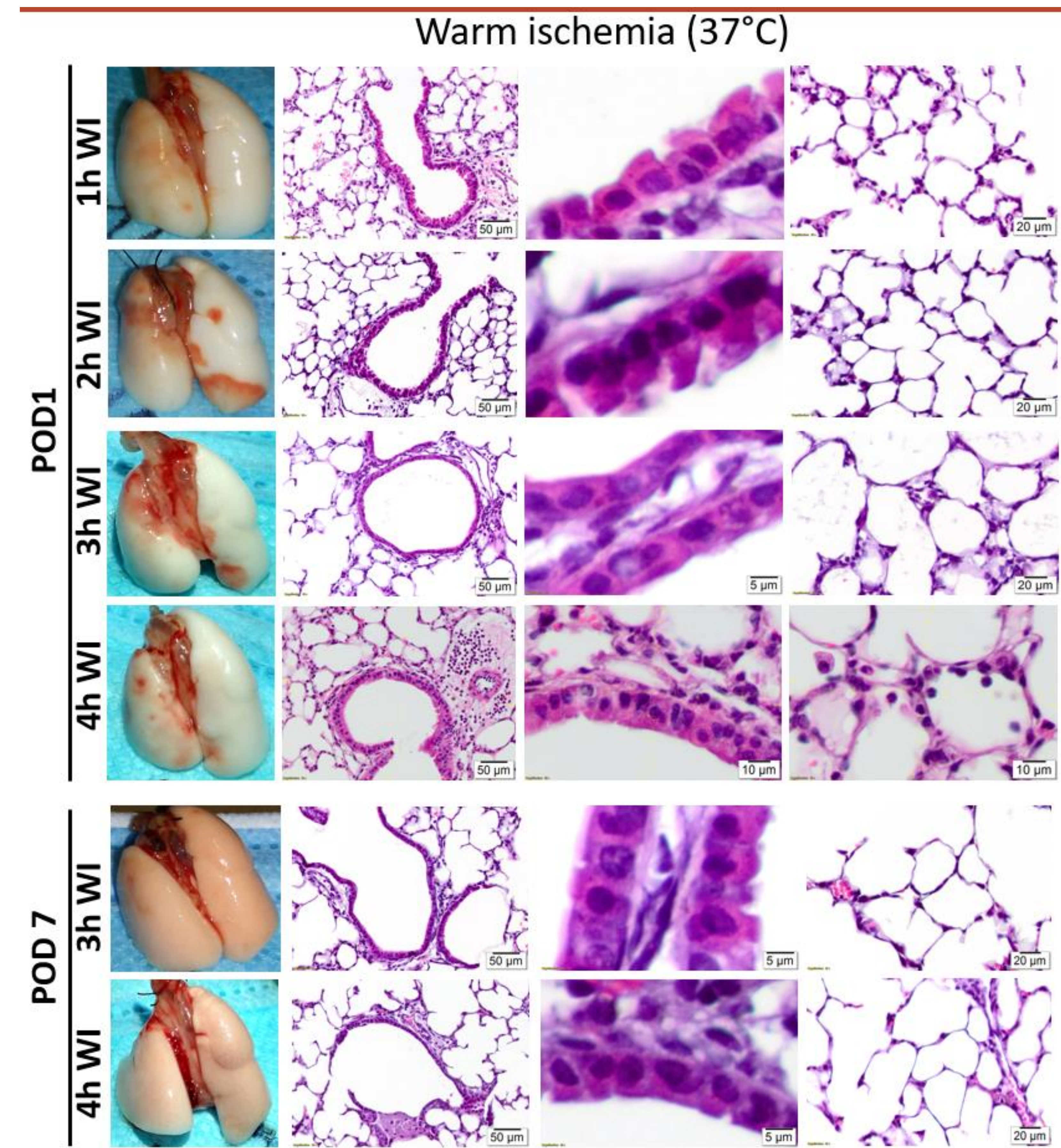


Figure 2. Histology of **WARM** Ischemia-reperfusion injury.



Conclusion

Cold I/R injury is featured by epithelium damage and infiltration, whereas warm I/R injury mainly causes diffused alveolar damage and infiltration.

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➤ Support: This work was supported by the Competitive Medical Research Fund (CMRF) of University of Pittsburgh and Samuel and Emma Winters Foundation.