Adipose-derived stem cells weigh in as novel therapeutics for acute lung injury

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Acute lung injury is characterized by intense neutrophilic lung inflammation and increased alveolar-capillary barrier permeability leading to severe hypoxemia, and is associated with high mortality despite improvements in supportive care. There is an urgent need for effective therapies for acute lung injury. Zhang and colleagues tested the efficacy of adipose-derived stem cells in acute lung injury in mice. When adipose-derived stem cells were delivered to mice that had been challenged with lipopolysaccharide, they potently limited acute lung inflammation and injury in the mice, indicating that adipose-derived stem cells have therapeutic potential in acute lung injury in humans. Herein, we discuss the advantages and potential limitations of using adipose-derived stem cells as therapeutics for human acute lung injury.
that induces robust neutrophilic lung inflammation. Additionally, the authors compared the therapeutic efficacy of human versus murine ASCs. While both hASCs and mASCs attenuated ALI, it is noteworthy that for most ALI parameters examined, mASCs were more potent than hASCs. However, it is possible that hASCs have greater potency at restraining acute lung inflammation in human subjects.

The study of Zhang and colleagues has several limitations that need to be addressed before ASCs can be advanced to human clinical trials. First, no single ALI animal model can completely reproduce all the pathologic features of human ALI/ARDS. While the LPS model studied by Zhang and coworkers induces robust neutrophilic lung inflammation, it causes only modest alveolar-capillary barrier injury, which is a hallmark of ALI/ARDS. Thus, it will be important to test the efficacy of ASCs in ALI models associated with severe ALI (such as hyperoxia and acid-induced ALI) and to assess the effects of ASCs on physiologic readouts of ALI, including lung compliance and hypoxemia. Second, ALI/ARDS in humans is often initiated by bacterial infections, but the model chosen (LPS-mediated ALI) causes sterile lung inflammation. Given that ASCs suppress immune responses, it will be important to assess their effects on host responses to pathogens that can cause ALI/ARDS. Third, the mechanisms by which ASCs produce their beneficial effects in this model were not addressed. Fourth, given that ARDS patients are often not treated within the first 4 hours of illness (the single time-point when ASCs were delivered to mice in this study), future studies should determine how late in the disease course ASCs can be delivered and still induce a protective effect and for how long this protective effect is sustained. Moreover, the long-term safety of delivering ASCs was also not assessed in this study. It is noteworthy in this respect that hASCs promote the growth of tumor cells [12]. Therefore, before ASCs can be used to treat human subjects, it will be necessary to investigate their long-term safety in animals.

Conclusion
The study by Zhang and colleagues provides evidence that ASCs have potential as novel cell-based therapeutics for ALI/ARDS. The next logical step towards advancing ASCs into human clinical trials for ALI/ARDS will be to further test ASCs for their efficacy and safety in additional small and large animal models of ALI, including models more clinically relevant than the LPS-mediated ALI model studied by Zhang and colleagues.

Abbreviations
ALI, acute lung injury; ARDS, acute respiratory distress syndrome; ASC, adipose-derived stem cell; BMSC, bone marrow-derived stem cell; hASC, human adipose-derived stem cell; LPS, lipopolysaccharide; mASC, mouse adipose-derived stem cell; MSC, mesenchymal stem cell.

Competing interests
KG, AH, and CAO have no financial or non-financial competing interests to declare in relation to this manuscript.

Author’s contributions
KG, AH, and CAO all contributed to the writing of this manuscript.

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