Introduction
Mechanical ventilation is the mainstay of intensive care medicine and an essential tool of post-surgical care. Ventilator-Induced Lung Injury (VILI) is an adverse consequence of mechanical ventilation. Hypercapnic Acidosis (HCA) may occur when protective lung ventilatory strategies are employed, and this “therapeutic hypercapnia” has been demonstrated to be protective in multiple lung injury models. Our group wish to determine the potential for the protective effects of HCA in VILI to be mediated via inhibition of nuclear factor kappa B (NF-κB), a transcription factor central to inflammation and repair that is a key therapeutic target in ALI/ARDS.

Materials and Methods
Human alveolar A549 cells are cultured and subjected to cyclical stretch of 20% elongation for a series of specific timepoints in either normocapnic or HCA atmospheric conditions. We use the Flexcell Tension Plus FX-4000T to simulate experimental VILI. This is a computer-driven instrument that simulates biological strain conditions using vacuum pressure to deform cells cultured on flexible, matrix-bonded growth surfaces of specially-designed culture plates. Control wells are compared with stretched wells. The cells are then harvested. Viability assays to check membrane integrity, and Western Blots to determine NF-κB activation are performed. ELISA is performed on the medium to quantify interleukin 8 (IL-8) chemokine secretion. Statistical significance is determined by t-test.

Results
High lung stretch induced a pulmonary epithelial inflammatory response, as evidenced by raised IL-8 concentrations and activation of NF-κB. (Panel A). HCA attenuated stretch induced inflammation and reduced activation of NF-κB (Panel B).

Discussion and Conclusions
From this preliminary data, we can further explore the role of the NF-κB pathway in the pathogenesis of VILI and the potential therapeutic role of HCA.

References

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Disclosures
Authors have nothing to disclose.