Patients with acute respiratory failure often require mechanical ventilation (MV). Unfortunately, ventilator induced lung injury (VILI) is a common condition that occurs during MV where high mechanical forces exacerbate lung injury via the release of pro-inflammatory cytokines and blood-air barrier disruption. Alveolar macrophages (AMs) are the primary regulators of the innate immune response and likely contribute to the pro-inflammatory response seen during VILI. The mechanotransduction mechanisms by which AMs contribute to VILI are unknown. In this work, we hypothesized that human AMs directly respond to mechanical forces and will increase secretion of pro-inflammatory markers. Our results indicate that AMs play an important role in the mechanotransduction processes responsible for VILI and that miR-146a can regulate these mechanotransduction events. Therefore, this anti-inflammatory miRNA may provide a point of therapeutic intervention in mitigating the pro-inflammatory cytokine secretion that occurs during VILI. Ongoing in vitro studies are investigating the molecular mechanisms of miR-146a regulation in AMs and in vivo studies are using miR-146a knock out mice to further demonstrate the important role miR-146a plays in regulating VILI.