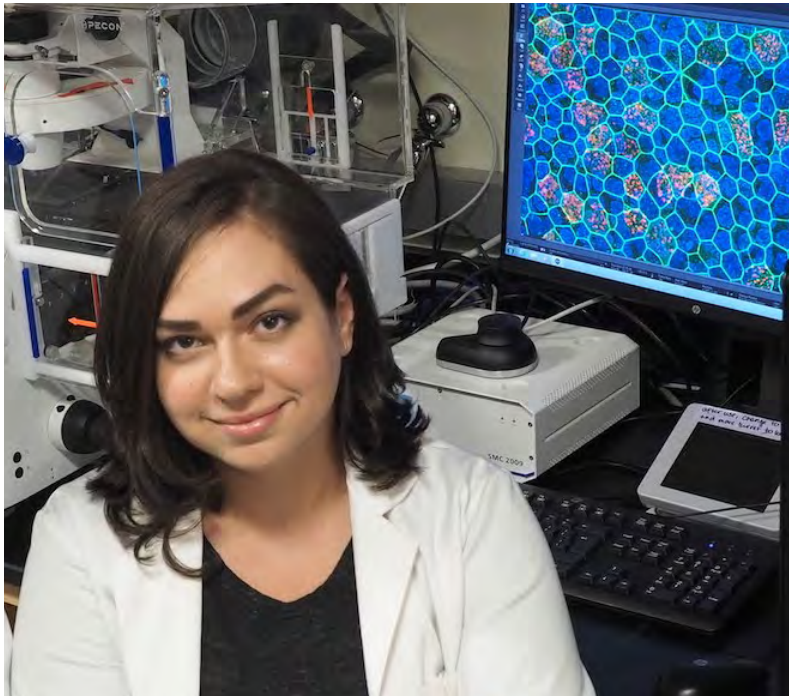


ATS 2019 Highlights

Respiratory Structure and Function Early Career Professionals

Get to know members of the RSF Assembly



Jennifer Mitchel, PhD

Research Associate

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Is your research clinical, basic science or translational?

Basic Science

Tell us about your research?

In the lab of Dr. Jin-Ah Park, I focus on the response of the airway epithelium to the mechanical forces which occur as a result of asthmatic bronchoconstriction. As the airway narrows it can buckle and compress the epithelium. In response to this mechanical perturbation, the airway epithelium initiates a program which appears to promote asthma pathogenesis, including goblet cell hyperplasia, sub-epithelial fibrosis, and airway smooth muscle hyperresponsiveness. In addition, mechanical compression provokes emergence of a striking collectively migratory phenotype through a process known as an unjamming transition. Recently, we have shown that these airway epithelial cells become migratory without invoking the well-known EMT program.

Where do you see yourself in 5 years?

In five years, I hope to be teaching and running a research lab as an independent PI at a research institution.

What do you find is the major benefit of RSF Assembly Membership?

As a member of the RSF Assembly, I have access to a network of researchers who are the world leaders in respiratory physiology. Members of this Assembly have a track record of leading research at the intersection of basic molecular and cellular biology with clinical medicine.

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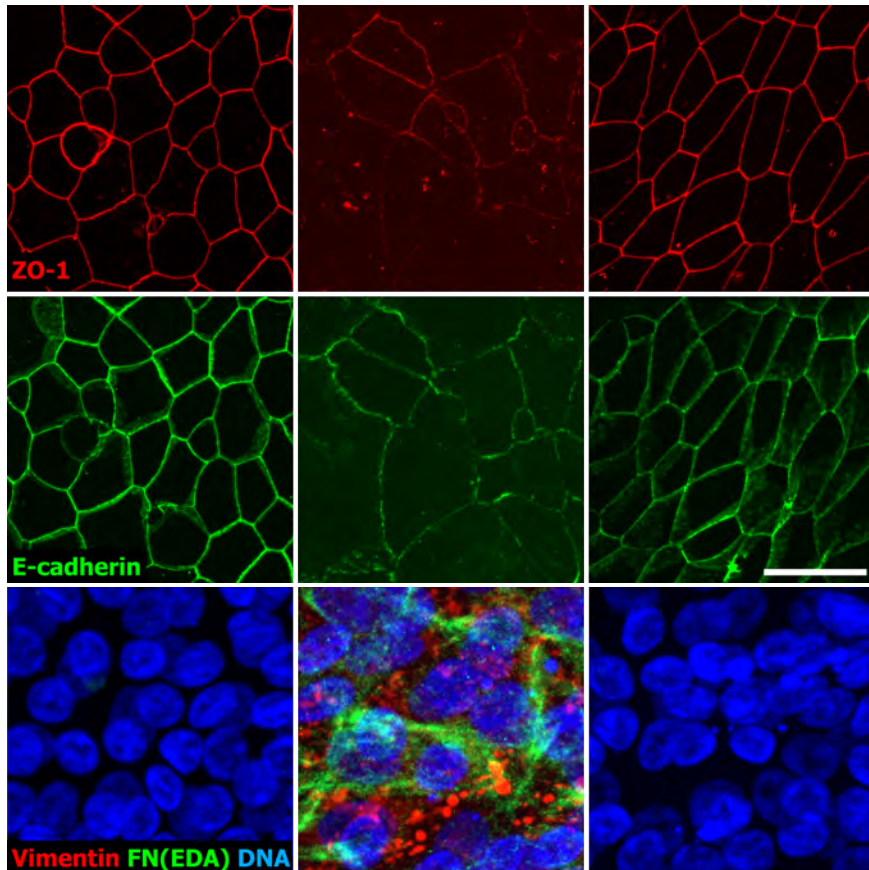
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Jammed (Control) TGF β -1 (pEMT) Compressed (UJT)



In primary airway epithelial cells, a mechanically induced unjamming transition is distinct from the epithelial-mesenchymal transition

Rationale: Despite a century-long emphasis on the immune system, recent experimental evidence places the structural cells of the airways, the epithelial and smooth muscle cells, at the center of asthma pathogenesis. Mechanical compression of airway epithelial cells by bronchospasm induces airway remodeling that is a hallmark of asthma^{1,2}. Further, such compression promotes the transition of these cells from a stationary, quiescent, jammed phase to a striking migratory unjammed phase via the newly discovered unjamming transition, UJT³. Migration of epithelial cells has long been believed to require destabilization of apico-basal polarity and junctional integrity in a well-known process called epithelial-to-mesenchymal transition, EMT. Here we assess the extent to which these mechanisms – EMT vs. UJT – overlap.

Methods: Primary human bronchial epithelial (HBE) cells were maintained in air-liquid interface culture for 14 days. To compare UJT vs EMT, well-differentiated HBE cells were subjected to mechanical compression to stimulate UJT, or to TGF β to stimulate EMT. Migration was evaluated from time-lapse images and while epithelial and mesenchymal marker proteins were evaluated by western blot and immunofluorescence.

Results: Both the UJT and the EMT resulted in migration of the well-differentiated HBE layer, but by distinct mechanisms. Through the UJT, the cell layer could initiate and sustain vigorous collective cellular migration while retaining expression of epithelial markers, apico-basal polarity, junctional integrity and intact barrier function, in the absence of acquiring mesenchymal characteristics.

Conclusions: We establish here that collective migration of epithelial cells can occur via an UJT that does not involve disruption of the epithelial cell layer as in EMT. This is the first report to show that the UJT and EMT share some similarities but are distinct. Accordingly, EMT is not a requirement for onset of epithelial cell migration. Together, these results clarify mechanisms through which the airway epithelium responds to mechanical compression and contributes to asthma pathogenesis.

References: ¹Tschumperlin et al., Nature, 2003; ²Grainge et al. NEJM, 2011; ³Park et al. Nat Mat, 2015

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