ATS 2025 Highlights

Respiratory Structure and Function Early Career Professionals

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Get to know members of the RSF Assembly

Is your research clinical, basic science or translational?

Basic Science

Tell us about your research?

Mitochondrial structure, motility, and tethering are highly dynamic processes that shape the subcellular organization and functional capacity of mitochondria. These properties are not fixed but vary by cell type and pathophysiological context. My research focuses on uncovering how mitochondrial dynamics and function are uniquely regulated in the airways—particularly in airway smooth muscle cells—under disease conditions. We aim to understand how mitochondrial morphology and function contributes to cellular adaptation in chronic airway diseases such as asthma.

Where do you see yourself in 5 years?

Over the next five years, I aim to establish myself as an independently funded academic researcher and contribute to the global knowledge of airway disease pathophysiology, with a primary focus in understanding mitochondrial dysfunction and mechanisms underlying fetal origins of adult airway disease. Beyond research, I am committed to advancing science communication and mentoring the next generation of scientists by fostering curiosity, resilience, and inclusion in biomedical research.

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

The RSF Assembly has been instrumental in connecting me with a supportive scientific community. It provides early career researchers like myself with unique opportunities to engage with leaders in the field, receive mentorship, and build collaborative networks. This assembly has fostered my growth as a researcher and as a member of a shared mission to advance respiratory health through science.

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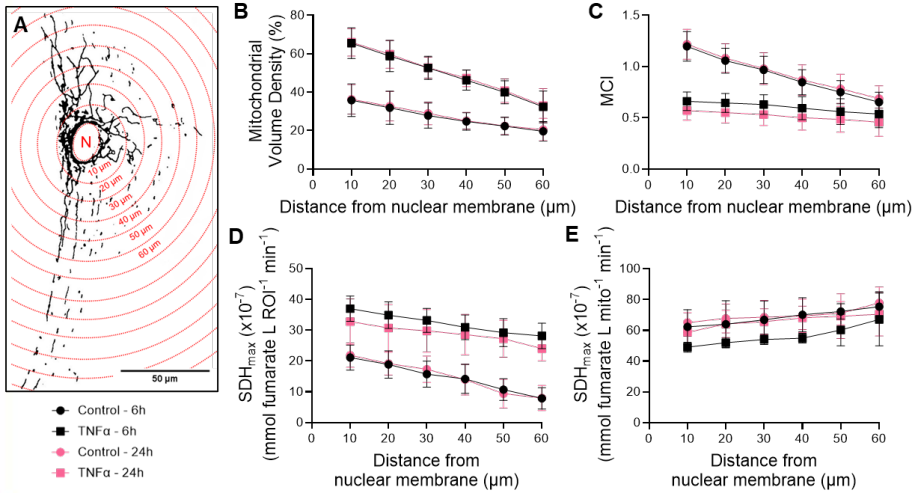

TNFα increases mitochondrial volume density and SDH_{max} per cell in the perinuclear compartment. However, MCI was relatively similar within different compartments, indicating mitochondria are homogenously fragmented throughout the cell. On normalizing to mitochondrial volume, SDH_{max} per mitochondrial volume increased relative to the distance from the nuclear membrane.

Mitochondria Are Functionally Heterogeneous Within Human Airway Smooth Muscle Cells

Objective: Mitochondria show cell and context-specific heterogeneity in their morphometry, determined by regulators of mitochondrial dynamics. Previously, we reported that TNFα increased maximum O_2 consumption rate (OCR) and mitochondrial volume density (MVD) in human airway smooth muscle (hASM) cells. However, when normalized to mitochondrial volume, maximum OCR per mitochondrion was reduced following TNFα exposure. TNFα exposure also altered mitochondrial distribution and motility within hASM cells relative to the nuclear membrane. Although high-resolution respirometry is a valuable tool for assessing mitochondrial function, it does not account for the presence of mitochondrial structural and functional heterogeneity within cells. Therefore, a direct measurement of cellular mitochondrial function provides valuable novel information and physiological insight. Previously, we developed a confocal-based quantitative histochemical technique to determine the maximum velocity of the succinate dehydrogenase (SDH) reaction (SDH_{max}) in single cells and observed that cellular SDH_{max} corresponds with MVD. Therefore, we hypothesize that SDH activity varies relative to the intracellular mitochondrial distribution within hASM cells.

Methods: Cells were dissociated from bronchiolar tissue samples collected from female and male patients with no history of smoking or respiratory disease. Isolated hASM cells were serum-deprived for 48 h and split into two treatment groups: 1) TNFα-treated (20 ng/mL, 6 h and 24 h) and 2) time-matched untreated control. Following treatments, CellLight GFP-labeled mitochondria were imaged in 3D (Z optical slice of 0.5 µm) on a Nikon Eclipse A1 laser scanning confocal system (oil-immersion ×60/1.4 NA objective). Using a concentric shell method for analysis, MVD, mitochondrial complexity index (MCI) and SDH_{max} were quantified relative to the nuclear membrane. SDH_{max} was measured using a solution containing 80 mM succinate (maximum substrate concentration) and 1.5 mM nitroblue tetrazolium (reaction indicator). As the reaction proceeded, the change in optical density (OD), was measured every 15 s over a 10-min period. Using the Beer-Lambert equation, the change in OD was used to determine SDH_{max} expressed as mmol fumarate/L cell/min.

Results: Within each shell, SDH_{max} and MVD peaked in the perinuclear region and decreased toward the distal compartments of the cell in all treatment groups. When normalized to mitochondrial volume, SDH_{max} decreased in the perinuclear region compared to the distal compartments of the cell. Compared to control, TNFα exposure caused a significant shift in mitochondrial morphometry and function relative to the nuclear membrane.

Conclusion: In summary, our data indicate that mitochondria within individual cells are morphologically heterogeneous with distinct functional properties, which is disrupted in disease.

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