ATS 2025 Highlights

Respiratory Structure and Function Early Career Professionals

Niyati A. Borkar, PhD

(she/her)
Research Fellow
Department of Anesthesiology
Mayo Clinic
@NiyatiBorkar
www.linkedin.com/in/niyati-borkar

Get to know members of the RSF Assembly

Is your research clinical, basic science or translational?

Basic science

Tell us about your research?

Emerging evidence, including our own, suggests that α7nAChRs directly impact airway smooth muscle (ASM) function. However, the precise mechanism underlying this influence remains unclear. My research focuses on elucidating how nicotine interacts with α7nAChRs and their associated chaperone proteins, RIC-3 and TMEM35, to modulate ASM function in the context of asthma.

Where do you see yourself in 5 years?

I hope to continue and contribute to the field of asthma research. My aim is to keep expanding my work and learn new skills through collaborations. Over the next five years, I hope to become an expert in my field of research and establish an independent laboratory to better understand asthma.

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

I value the RSF as an indispensable resource for researchers in my field. It provides a unique opportunity to connect with colleagues, peers, and mentors, enriching my professional network and fostering a strong sense of community within the airway research community.

ATS

Please follow us on LinkedIn and X @ATS_RSF

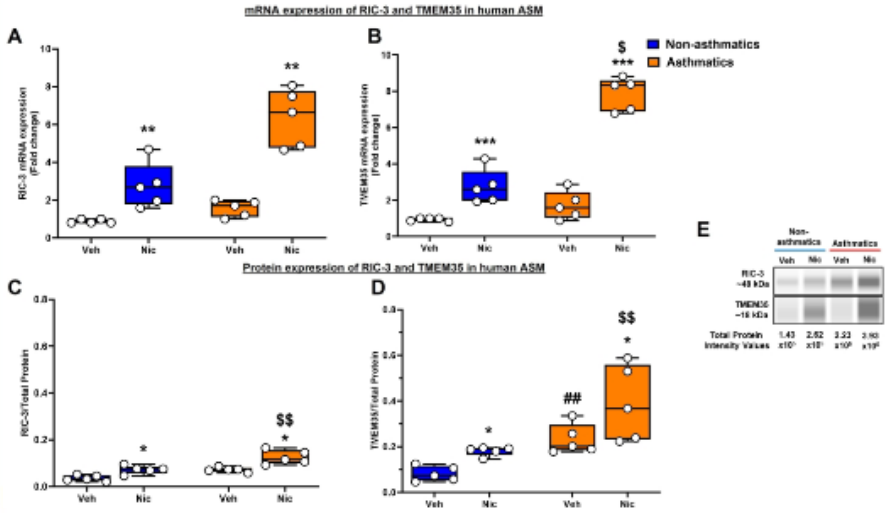
If you or someone you know would like to be featured as an ATS RSF ECP please email Carolyn Wang (carolyn.wang@hli.ubc.ca)

ATS 2025 Highlights

Respiratory Structure and Function Early Career Professionals

Niyati A. Borkar, PhD

(she/her)
Research Fellow
Department of Anesthesiology
Mayo Clinic



mRNA (top) and protein expression (bottom) of RIC-3 and TMEM35 in non-asthmatic vs. asthmatic human ASM. Representative electropherograms are shown in (E).

Nicotine-Induced ER Stress and ASM Cell Proliferation is Mediated by α7nAChR and Chaperones-RIC-3 and NACHO

Objective: The goal of the present study is to investigate how nicotine affects α7nAChR chaperones, RIC-3 and TMEM35 in regulating upstream mechanisms such as endoplasmic reticulum (ER) stress and influence mitochondrial energetics which may have further consequences on airway smooth muscle (ASM) cell proliferation and remodeling.

Methods: Primary human ASM cells originating from non-asthmatic and asthmatic individuals with no or very remote smoking history (>15 years) were obtained post-surgery from lung tissues after approval by the Mayo Clinic Institutional Review Board. ASM cells treated for 24-48hrs with nicotine (α7nAChR agonist), TNFα, IL-13, Tunicamycin (TM) and TUDCA were probed for expression of α7nAChR regulatory chaperones and ER stress response elements. α7nAChR siRNA and RIC-3/TMEM35 shRNA ASM were utilized to explore the role of α7nAChR-specific effects of nicotine on ASM cell proliferation and intracellular Ca^{2+}. To monitor whether nicotine induces ER stress response, the Green/Red Cell Stress Assay from Montana Molecular was used.

Results: We observed an increase in α7nAChR chaperones, RIC-3 and TMEM35 upon exposure to nicotine, TNFα and IL-13. Interestingly, α7nAChR-mediated increase in ASM cell proliferation was attenuated in the presence of α7nAChR, RIC-3/TMEM35 knockdown cells indicating the importance of α7nAChR chaperones in the assembly and functionality of α7nAChR in the ASM. Additionally, nicotine-induced increase in intracellular Ca^{2+} was abolished in the presence of RIC-3 and TMEM35 knockdown. Separately, nicotine and inflammation increased the expression of ER stress response elements, IRE1, PERK and ATF6, albeit more in the concurrent presence of TM, but not TUDCA suggesting the detrimental effects of nicotine and inflammation in the ASM.

Conclusion: There are links between nicotine, ER stress and inflammation resulting in modulation of α7nAChR and α7nAChR chaperones-RIC-3 and TMEM35. α7nAChR and its chaperones play a direct role in induction of nicotine-induced ER stress and proliferation in asthma.

ATS

Please follow us on LinkedIn and X @ATS_RSF

If you or someone you know would like to be featured as an ATS RSF ECP please email Carolyn Wang (carolyn.wang@hli.ubc.ca)