
BIOGRAPHICAL SKETCH

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NAME: Reynold A. Panettieri, Jr., M.D.

eRA COMMONS USER NAME: PANETTIERI

POSITION TITLE: Professor of Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
St. Joseph's University, Philadelphia, PA	B.S.	05/1979	Biology
University of Pennsylvania, Philadelphia, PA	M.D.	05/1983	Medicine
University of Pennsylvania, Philadelphia, PA	M.A. (Hon.)	05/1998	Medicine

A. Personal Statement

I am Professor of Medicine at RWJMS and serve as Program Director for our CTSA Hub entitled: the New Jersey Alliance for Clinical and Translational Science (NJ ACTS). In December 2015, I transitioned to Rutgers University from the University of Pennsylvania, to serve as the inaugural Director of the Rutgers Institute for Translational Medicine and Science, and Vice Chancellor for Translational Medicine and Science. This Institute fosters translational studies in health and disease, and integrates the expertise of the disciplines of epidemiology, pharmacology, cell biology, genetics, biochemistry, and health economics and informatics across the Rutgers Biomedical and Health Sciences (RBHS) network. My basic translational science interests use state-of-the-art cellular and molecular techniques to characterize airway smooth muscle as an immunomodulatory cell, and in the study of cell signaling mechanisms inducing glucocorticoid insensitivity and excitation-contraction coupling. My fundamental studies also focus on translational targets for new therapeutics and bench-to- bedside testing of novel approaches in the treatment of severe asthma and COPD, and on proteomic and genomic studies to identify unique proteomic signatures in COPD and asthma. Relevant to CTS and NJ ACTS, I am also an accomplished clinical trialist who has published on real-world evidence to improve healthcare delivery in asthma and COPD, and have served as Chairperson on Data Safety and Monitoring Boards of numerous NIH Clinical Networks. I have published over 540 peer-reviewed articles and am currently the principal investigator or co-investigator of several NIH and extramural grants, including a program project grant. As Vice Chancellor, my responsibilities include: developing and implementing a clinical and translational science infrastructure at RBHS; leading initiatives to expand independent clinical research funding by collaborating with the deans, department chairs, and faculty to conduct clinical and translational research across the schools, centers, institutes, and clinical research units of RBHS, and; encouraging the formation of new translational research teams. During the pandemic, I was responsible for establishing a rapid response team that not only launched cohort studies and trials in March 2020 but that also procured PPE, conducted training, assembled an 'army' of graduate and post-graduate volunteers to complement staff, and pioneered e-consenting and widespread use of REDCap for data collection. In addition to these accomplishments, I have trained over 45 postdoctoral fellows and physician scientists, and I serve on several NIH study sections. Further, I am an MPI for the NIH REACH Award (Research Evaluation and Commercialization Hub) to accelerate commercialization of academic assets. Interaction with our REACH Hub will provide a platform for training in entrepreneurship.

Ongoing projects that I would like to highlight include:

NIH/NCATS UL1TR003017

Panettieri, PI

3/11/19-2/29/24

New Jersey Alliance for Clinical and Translational Science: NJ ACTS

1P01HL114471

Panettieri, PI, Program Director, Leader of Project 1, Program Director, Leader Core B, Program Director, Leader Core C

7/15/13 – 7/31/24

Novel Molecular Mechanisms Promote GPCR-Induced Bronchodilation in Asthma

U01HL150852

Panettieri, MPI

9/23/19-8/31/23

Rutgers Optimizes Innovation (ROI) Program

1. GebSKI E.B., Anaspure O, **Panettieri RA Jr.**, Koziol-White C.J. Airway smooth muscle and airway hyperresponsiveness in asthma - mechanisms of airway smooth muscle dysfunction. *Minerva Med.* 2021 Jan 26. Online ahead of print. PMID: 33496164. DOI: 10.23736/S0026-4806.21.07283-9.
2. Jo MH, Kim BC, Sung K, **Panettieri RA Jr**, An SS, Liu J, Ha T. Molecular Nanomechanical Mapping of Histamine-Induced Smooth Muscle Cell Contraction and Shortening. *ACS Nano.* 2021 Jul 1. Doi: 10.1021/acsnano.1c01782. Online ahead of print. PMID: 34197709.
3. Cao G, Lam H, Jude JA, Karmacharya N, Kan M, Jester W, Koziol-White C, Himes BE, Chupp GL, An SS, **Panettieri RA Jr.** Inhibition of ABCC1 Decreases cAMP Egress and Promotes Human Airway Smooth Muscle Cell Relaxation. *Am J Respir Cell Mol Biol* 2021 Oct 14. Online ahead of print. doi: 10.1165/rcmb.2021-0345OC.PMID: 34648729.
4. Johnson MT, Xin P, Benson JC, Pathak T, Walter V, Emrich SM, Yoast RE, Zhang X, Cao G, **Panettieri RA Jr.**, Trebak M. Revision: STIM1 is a Core Trigger of Airway Smooth Muscle Remodeling and Hyperresponsiveness in Asthma. *PNAS* 2022 Jan 4;119(1):e2114557118. DOI: 10.1073/pnas.2114557118. PMID: 34949717.

B. Positions Scientific Appointments, and Honors

2015- Chancellor Scholar, Rutgers University

2015- Vice Chancellor for Translational Medicine and Science, Rutgers University

2015- Director, Rutgers Institute for Translational Medicine and Science

2009-15 Director, Human Exposure Laboratory, CEET, University of Pennsylvania

2009-15 Director, Integrative Health Sciences Facility Core, CEET, University of Pennsylvania

2009-15 Deputy Director, Center of Excellence in Environmental Toxicology (CEET), University of Pennsylvania

2005-15 Associate Program Director, General Clinical Research Center, University of Pennsylvania

2002-15 Adjunct Professor, Wistar Institute

2001-15 Professor of Medicine with Tenure (Mayock & Cooper Professor of Medicine), University of Pennsylvania

1996-01 Associate Professor of Medicine with Tenure, University of Pennsylvania

1990-96 Assistant Professor of Medicine, University of Pennsylvania

1986-90 Fellow, Pulmonary and Critical Care Division, Hospital of the University of Pennsylvania

1983-86 Intern, Resident in Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA

Honors and Awards

- 2022 Gilbert Friday Memorial Lecture, International Asthma Conference, Nemaconlin, PA
- 2015 Recognition Award for Scientific Accomplishments, American Thoracic Society
- 2013 Joseph R. Rodarte Award for Distinguished Achievement, American Thoracic Society
- 2007 Association of American Physicians
- 2005 The John E. Salvaggio Memorial Lectureship
- 2004-06 Chairman, LCMI Study Section, NIH
- 2003 LAM Foundation Excellence in Research Award
- 2000-04 Member, LBPA Study Section, NIH
- 2000 American Society for Clinical Investigation

C. Contributions to Science

For the past 26 years, I have obtained independent research support through R01s, Specialized Center of Research, and Program Project grants that generated 512 peer-reviewed publications. My contributions to science are in four thematic areas. As a translational researcher, my focus has been on understanding airway smooth muscle (ASM) function and other structural cells in modulating asthma and COPD diatheses.

1. Novel Models of Human Airway Function: Our laboratory was the first to fully characterize primary non-immortalized human ASM cells. These cells retain physiologic and pharmacologic responses identical to those found *in vivo*. Importantly, ASM cells derived from fatal asthma donors retain a hyperresponsive phenotype manifested by agonist-induced calcium mobilization, cell proliferation and migration. Over the past five years, we have also developed an integrated airways model using human precision cut lung slices (PCLS). These slices retain responsiveness to contractile agonists and bronchodilators and retain ciliary beat frequency.

- a. Jo MH, Kim BC, Sung K, **Panettieri RA Jr**, An SS, Liu J, Ha T. Molecular Nanomechanical Mapping of Histamine-Induced Smooth Muscle Cell Contraction and Shortening. *ACS Nano*. 2021 Jul 1. Doi: 10.1021/acsnano.1c01782. Online ahead of print. PMID: 34197709.
- b. Cao G, Lam H, Jude JA, Karmacharya N, Kan M, Jester W, Koziol-White C, Himes BE, Chupp GL, An SS, **Panettieri RA Jr**. Inhibition of ABCC1 Decreases cAMP Egress and Promotes Human Airway Smooth Muscle Cell Relaxation. *Am J Respir Cell Mol Biol* 2021 Oct 14. Online ahead of print. doi: 10.1165/rcmb.2021-0345OC. PMID: 34648729.
- c. Johnson MT, Xin P, Benson JC, Pathak T, Walter V, Emrich SM, Yeast RE, Zhang X, Cao G, **Panettieri RA Jr**, Trebak M. Revision: STIM1 is a Core Trigger of Airway Smooth Muscle Remodeling and Hyperresponsiveness in Asthma. *PNAS* 2022 Jan 4;119(1):e2114557118. DOI: 10.1073/pnas.2114557118. PMID: 34949717.
- d. Wang S, Xie Y, Huo YW, Li Y, Abdel PW, Jiang H, Zou X, Jiao HZ, Kuang X, Wolff DW, Huang YG, Casale TB, **Panettieri RA Jr**, Wei T, Cao Z, Tu Y. Airway Relaxation Mechanisms and Structural Basis of Osthole to Improve Lung Function in Asthma. *Sci Signal*. 2020 Nov 24;13(659):eaax0273. doi: 10.1126/scisignal.aax0273. PMID: 33234690

2. The Immunobiology of ASM Cells: Research in trafficking leukocytes mediating airway inflammation has led to new therapeutic approaches in asthma. Our laboratory has pioneered the concept that structural cells, ASM and epithelium may also orchestrate and perpetuate airway inflammation. Additionally, we have described novel mechanisms for studying glucocorticoid insensitivity and have identified targets in remediating glucocorticoid resistance. We have shown that ASM expresses cell adhesion molecules and secretes chemokines and cytokines that modulate leukocyte function. Further, our work has shown that T cells directly modulate human ASM cell proliferation.

- a. **Panettieri RA**, Schaafsma D, Amrani Y, Koziol-White C, Ostrom R, Tliba O. Non-genomic Effects of Glucocorticoids: An Updated View. *Trends Pharmacol Sci*. 2019 Jan;40(1):38-49. doi: 10.1016/j.tips.2018.11.002. Epub 2018 Nov 26. PMID: 30497693; PMCID: PMC7106476.
- b. Madigan LA, Wong GS, Gordon EM, Chen WS, Balenga N, Koziol-White CJ, **Panettieri RA Jr**, Levine SJ, Druey KM. RGS4 Overexpression in Lung Attenuates Airway Hyperresponsiveness in Mice. *Am J Respir Cell Mol Biol*. 2018 Jan;58(1):89-98. Doi: 10.1165/rcmb.2017-019OC. PMID: 28853915
- c. Guidi R, Xu D, Choy DF, Ramalingam TR, Lee WP, Modrusan Z, Liang Y, Marsters S, Ashkenazi A, Huynh A, Mills J, Flanagan S, Hambro S, Nunez V, Leong L, Cook A, Tran TH, Austin CD, Cao Y, Clarke C, **Panettieri RA Jr**, Koziol-White C, Jester WF Jr, Wang F, Wilson MS. Steroid-induced fibroblast growth factors drive an epithelial-mesenchymal inflammatory axis in severe asthma. *Sci Transl Med*. 2022 Apr 20;14(641):eabl8146. doi: 10.1126/scitranslmed.abl8146. Epub 2022 Apr 20. PMID: 35442706.
- d. Koziol-White CJ, Jia Y, Baltus GA, Cooper PR, Zaller DM, Crackower MA, Sirkowski EE, Smock S, Northrup AB, Himes BE, Alves SE, **Panettieri RA Jr**. Inhibition of spleen tyrosine kinase attenuates IgE-mediated airway contraction and mediator release in human precision cut lung slices. *Br J Pharmacol*. 2016 Nov;173(21):3080-3087. Doi: 10.1111/bph.13550. Epub 2016 Oct 5. PMID: 27417329

3. Cytokines Amplify Agonist-Induced Excitation-Contraction Coupling: The link between airway inflammation and airway hyperresponsiveness (AHR) remains unknown. Our work has demonstrated that cytokines such as IL-13, TNF and IL-1 β enhance non-specific AHR through a variety of molecular mechanisms. We have shown that TNF and IL-13 enhance CD38 expression, and these cytokines also enhance agonist-induced calcium mobilization in human ASM. Further, our studies have shown that glucocorticoids enhance β -agonist-induced bronchodilation without increasing β_2 -adrenergic receptor

number. The aforementioned studies have identified novel targets for the development of new therapeutics.

- a. Xu S, **Panettieri RA Jr**, Jude J. Metabolomics in asthma: A platform for discovery. *Mol Aspects Med.* 2022 Jun;85:100990. doi: 10.1016/j.mam.2021.100990. Epub 2021 Jul 17. PMID: 34281719; PMCID: PMC9088882.
- b. Deeney BT, Cao G, Orfanos S, Lee J, Kan M, Himes BE, Parikh V, Koziol-White CJ, An SS, **Panettieri RA Jr**. Epinephrine evokes shortening of human airway smooth muscle cells following β_2 adrenergic receptor desensitization. *Am J Physiol Lung Cell Mol Physiol.* 2022 Aug 1;323(2):L142-L151. doi: 10.1152/ajplung.00444.2021. Epub 2022 Jul 5. PMID: 35787178; PMCID: PMC9359643.
- c. Hashem T, Kammala AK, Thaxton K, Griffin RM, Mullany K, **Panettieri RA Jr**, Subramanian H, Das R. CD2 Regulates pathogenesis of Asthma Induced by House Dust Mice Extract. *Front Immunol.* 2020 May 12;11:881. Doi: 10.3389/fimmu.2020.00881. eCollection 2020. PMID: 32477356.
- d. Yon C, Thompson DA, Jude JA, **Panettieri RA Jr**, Rastogi D. Crosstalk Between CD4+ T Cells and Airway Smooth Muscle in Pediatric Obesity-related Asthma. *Am J Respir Crit Care Med.* 2022 Oct 4. doi: 10.1164/rccm.202205-0985OC. Epub ahead of print. PMID: 36194662

4. Environmental Toxicants Induce Airway Hyperresponsiveness (AHR): A major component of AHR in asthma and COPD is in part mediated by inhaled toxicants. Our laboratory demonstrated that ozone mediates AHR through airway epithelial generation of mediators that induce AHR without inflammation. After the acute airway injury, inflammation plays an important role in mediating secondary AHR. The uncoupling of airway inflammation and AHR is important and has identified novel approaches in mitigating ozone-induced AHR. Further, our studies in co-cultures of primary airway epithelial cells and smooth muscle have discovered novel mechanisms by which toxicants such as ozone induce AHR.

- a. Xu S, Karmacharya N, Woo J, Cao G, Guo C, Gow A, **Panettieri RA Jr**, Jude JA. Starving a Cell Promotes Airway Smooth Muscle Relaxation: Inhibition of Glycolysis Attenuates Excitation-Contraction Coupling. *Am J Respir Cell Mol Biol.* 2023 Jan;68(1):39-48. doi: 10.1165/rcmb.2021-0495OC. PMID: 36227725.
- b. Xu S, Karmacharya N, Cao G, Guo C, Gow A, **Panettieri RA Jr**, Jude JA. Obesity elicits a unique metabolomic signature in human airway smooth muscle cells. *Am J Physiol Lung Cell Mol Physiol.* 2022 Sep 1;323(3):L297-L307. doi: 10.1152/ajplung.00132.2022. Epub 2022 Jul 5. PMID: 35787188; PMCID: PMC9514806.
- c. Huang J, Lam H, Koziol-White C, Limjunyawong N, Kim D, Kim N, Karmacharya N, Rajkumar P, Firer D, Dalesio NM, Jude J, Kurten RC, Pluznick JL, Deshpande DA, Penn RB, Liggett SB, **Panettieri RA Jr**, Dong X, An SS. The odorant receptor OR2W3 on airway smooth muscle evokes bronchodilation via a cooperative chemosensory tradeoff between TMEM16A and CFTR. *Proc Natl Acad Sci U S A.* 2020 Nov 10;117(45):28485-28495. doi: 10.1073/pnas.2003111117. Epub 2020 Oct 23. PMID: 33097666; PMCID: PMC7668088.
- d. Jude J, Koziol-White CJ, Scala J, Yoo E, Jester W, Maute C, Dalton P, **Panettieri RA Jr**. Formaldehyde Induces Rho-Associated Kinase Activity to Evoke Airway Hyperresponsiveness. *Am J Respir Cell Mol Biol.* 2016 Oct;55(4):542-553. PMID: 27149505

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/reynold.panettieri.1/bibliography/47889063/public/?sort=date&direction=ascending>