

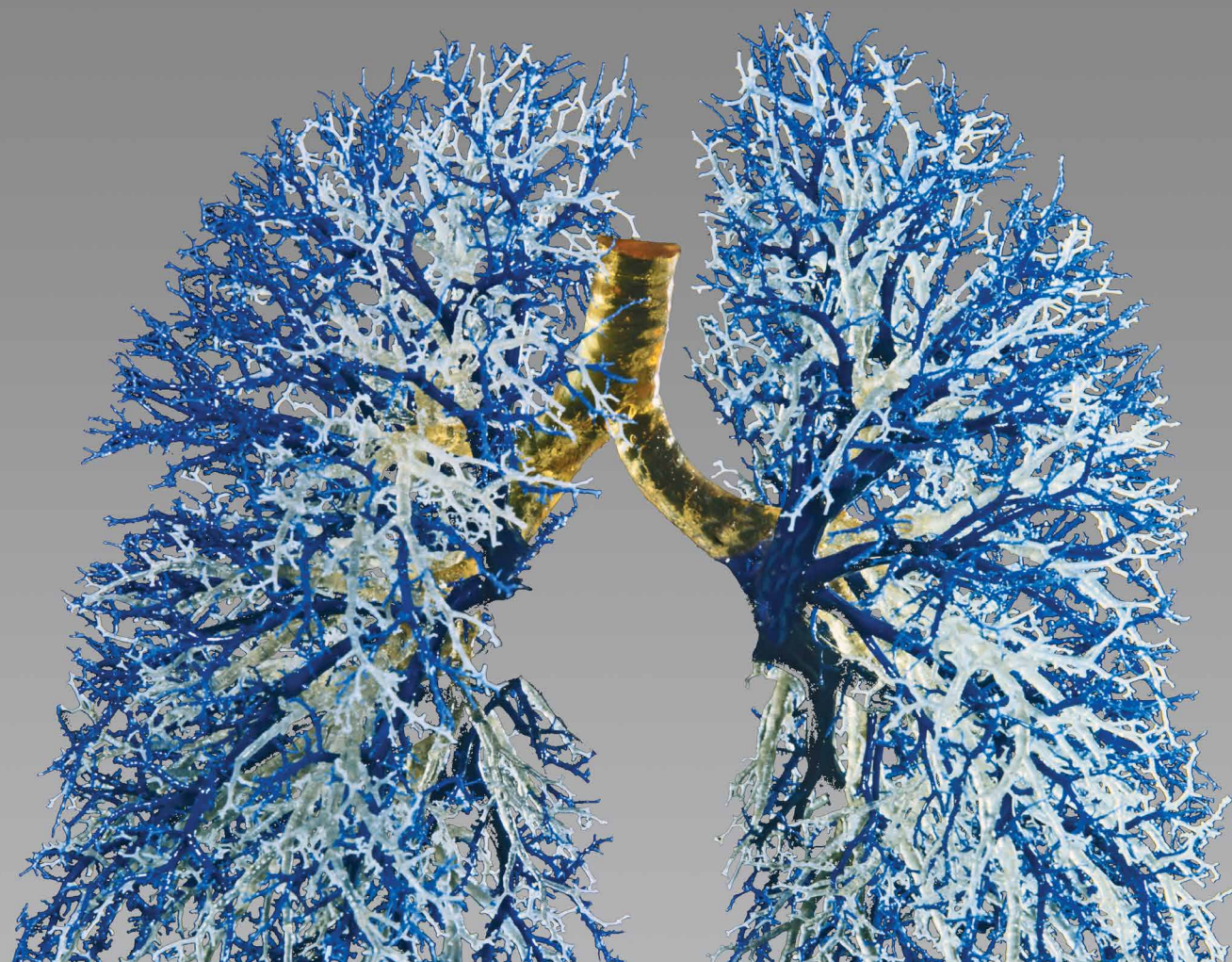


**National Jewish
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Breathing Science is Life.[™]



PULMONARY HIGHLIGHTS 2016



INSIDE

Clinical Expertise • Frontiers of Pulmonary Science • Leadership



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Dear Colleague,

With pleasure and pride, we present “National Jewish Health Pulmonary Highlights 2016,” our compilation of clinical, research and educational activities and capabilities in pulmonary medicine at National Jewish Health. As an academic medical institution focused for more than 118 years on respiratory and related diseases, and with one of the largest pulmonary divisions in the nation, we believe that our work helps advance pulmonary medicine and the options available to help your patients today and tomorrow.

Patients come to National Jewish Health from around the nation and the world seeking answers for their respiratory problems. Our team of expert pulmonologists conducts intensive evaluations in collaboration with cardiologists, gastroenterologists, allergists, oncologists, rheumatologists and others on the National Jewish Health staff. Once we develop a diagnosis and treatment plan, we then work with patients’ hometown physicians to implement the plan and adjust care as necessary.

We have a robust research program seeking answers to the many questions and challenges that remain in pulmonary medicine. Ranging from basic discovery to translational research and hundreds of clinical trials, we are finding new pathways, new biomarkers and new therapies. Our faculty, recognized national leaders in their fields, train medical students, residents and postgraduate fellows in affiliation with the University of Colorado School of Medicine. They also share their expertise with established physicians at conferences and continuing medical education programs across the country.

We hope you will take a few minutes to look through this publication and learn more about what is happening at the forefront of pulmonary medicine and how it can benefit your patients.

Irina Petrache, MD
Chief, Division of Pulmonary,
Critical Care and Sleep Medicine
National Jewish Health

Richard J. Martin, MD
Chair, Department of Medicine
National Jewish Health

CLINICAL EXPERTISE

National Jewish Health provides unparalleled care for complex, symptomatic pulmonary patients. People come from around the nation and the world for comprehensive evaluations, diagnoses and treatment plans from our expert pulmonary subspecialists and their colleagues in cardiology, gastroenterology, oncology, immunology, rheumatology and radiology. When needed, patients can transfer seamlessly to nearby Saint Joseph Hospital, our excellent local partner, where care can continue to be managed by National Jewish Health physicians. Our physicians and staff work with each patient's hometown physicians to implement, monitor and adjust care as needed.

Asthma

Thorough upper and lower airway evaluations in our multi-day adult and pediatric asthma programs help us phenotype patients and tease out complicating factors from aspiration to allergies, vocal cord dysfunction and inhaler technique. Our faculty members lead numerous National Institutes of Health (NIH) studies and industry-sponsored clinical trials.

Cardiology

Our cardiologists are experts in the heart-lung interface. They work closely with pulmonologists to diagnose and treat the cardiac causes and consequences of lung disease, including pulmonary hypertension, cardiac sarcoidosis and other rare diseases.

COPD

A complete medical and nonmedical evaluation allows our team of physicians and therapists to address not only COPD medications, but also education, compliance, nutrition and rehabilitation. Personalized management plans and education optimize care and quality of life. Our faculty is advancing pulmonary medicine with

COPD Gene and other studies to diagnose and phenotype COPD.

NTM

Mycobacterial disease is part of our DNA, with our origins as a hospital for destitute tuberculosis patients. The longevity of our program and our experience with thousands of complex mycobacterial infections have given us a deep knowledge of antibiotic regimens and surgical options. In addition to our intensive outpatient program, we provide inpatient care and surgical support through our collaborative relationship locally with Saint Joseph Hospital.

Chronic Beryllium Disease

National Jewish Health has more experience with the diagnosis and treatment of chronic beryllium disease than any other group in the world. We emphasize early disease detection and intervention to halt or slow disease progression. We have published extensively on exposures, genetic factors and immune responses associated with chronic beryllium disease.

Cystic Fibrosis

We have the largest and most experienced adult cystic fibrosis

program in the nation. Our team of pulmonary specialists, nurse coordinators, respiratory therapists, registered dietitians, psychologists and social workers provides treatment for more than 400 adults from around the nation. We have more than two dozen ongoing clinical trials to evaluate new cystic fibrosis therapies.

Environmental Health

In step with increasing recognition that environmental pollutants cause disease, our multidisciplinary team has helped define, diagnose and treat patients with a broad range of occupational, environmental and granulomatous lung diseases. Our thorough evaluations have uncovered previously unknown causes of pulmonary disease.

Interstitial Lung Disease

We have vast experience with interstitial lung disease (ILD). Our detailed evaluation, diagnosis and plan of care are based on the most current information about ILD, much of which has been discovered at National Jewish Health. We have ongoing trials of approved and experimental medications. We seek to broaden

CLINICAL EXPERTISE

knowledge of ILD causes and develop new treatments.

Oncology

Expert pulmonologists, thoracic radiologists, gastroenterologists and surgeons help us diagnose and treat cancers of the lungs, head and neck, and digestive system. Lung cancer screening and our tumor registry help us screen and monitor patients at high risk for lung cancer.

Pediatrics

For decades, we have helped shape the evolving knowledge about diagnosis and treatment of asthma, vocal cord dysfunction and other pediatric pulmonary diseases. Our Severe Asthma Clinic and Pediatric Day Program offer multi-day medical and psychological evaluations, education and management plans for children with pulmonary and atopic diseases.

Pulmonary Hypertension

Cardiologists and pulmonologists work as a team to provide comprehensive and sophisticated diagnostic, outpatient and inpatient services for pulmonary hypertension.

Sarcoidosis

Support from our expert cardiologists, neurologists and network of providers positions National Jewish Health to address the multi-organ nature of sarcoidosis. Our experience with thousands of sarcoidosis patients has helped us better define the disease and gain insight into its causes.

Sleep

The oldest and most comprehensive sleep center in the region relies on a full complement of pulmonologists, sleep medicine specialists, psychologists, respiratory therapists and polysomnographic technologists to address the full spectrum of sleep disorders.

Diagnostic Laboratories

Our Advanced Diagnostic Laboratories have CAP15189 accreditation and decades of experience developing immunology, complement, infectious disease and molecular diagnostic tests. We help clients from around the world select, customize and interpret laboratory tests.

Pulmonary Physiology Services

Our state-of-the-art laboratory offers many unique tests, including exercise-induced bronchoconstriction; cardiopulmonary exercise test with full metabolic testing, arterial line, lactate levels and cardiac data; and continuous laryngoscopy with exercise tolerance.

Interventional Pulmonology

Our minimally invasive diagnostic, therapeutic and palliative procedures include identification, diagnosis and treatment of pulmonary nodules; early detection of lung cancer; diagnosis and treatment of airway obstructions; pleural procedures; implantation and removal of airway stents; and bronchial thermoplasty.

MOUNT SINAI – NATIONAL JEWISH HEALTH RESPIRATORY INSTITUTE

The Icahn School of Medicine at Mount Sinai, a leading academic medical center in New York City, and National Jewish Health have partnered to create the **Mount Sinai – National Jewish Health Respiratory Institute** in New York City. The Respiratory Institute brings together leading experts in diagnosing and treating respiratory disease and offers a model for multidisciplinary, personalized care for patients with respiratory disease.

MOUNT SINAI - NATIONAL JEWISH HEALTH

Respiratory Institute



CLINICAL RESEARCH

National Jewish Health is constantly searching for new, more effective treatments and medications for our patients and for patients around the world. Today, we have more than 300 active clinical trials that offer cutting-edge, experimental treatments for a wide range of respiratory and related diseases. We collaborate with the National Institutes of Health, industry and leading research institutions across the nation as members of numerous research networks and consortiums.

SELECTED 2016 CLINICAL RESEARCH RESULTS

Acetaminophen for Children with Asthma

Previous research has raised concerns about the link between asthma and acetaminophen.

Ronina Covar, MD; Michael Wechsler, MD; Tod Olin, MD; and their colleagues in the AsthmaNet national research network reported that children with asthma who take acetaminophen for fever and pain relief suffer no more exacerbations than those taking ibuprofen. *N Engl J Med.* 2016 Aug 18;375(7):619-30.

Black Lung on the Rise

After declining for several decades, black lung disease is on the rise again. **Cecile Rose, MD, MPH,** and her colleagues recently reported that rapidly progressive lung disease in U.S coal miners is linked to silica and silicates in coal mine dust. This could be the result of mining thinner seams of coal, which requires cutting through surrounding rock containing silica and silicates. *Am J Respir Crit Care Med.* 2016 Mar 15;193(6):673-80.

Reducing Radiation

Shawn Teague, MD, and his colleagues report a successful quality improvement project

aimed at reducing radiation doses in thoracic imaging. Using an iterative reconstruction technique and reduced voltage, they were able to reduce the effective radiation dose by 44 percent with no perceived difference in diagnostic quality. *J Digit Imaging.* 2016 Oct;29(5):622-6.

Pirfenidone for Idiopathic Pulmonary Fibrosis

Evaluating treatment response for idiopathic pulmonary fibrosis can be difficult due to variable clinical course with periods of decline interspersed by stretches of stability. **Jeffrey Swigris, DO,** and his colleagues found that patients whose disease progressed during treatment with pirfenidone benefited from continued

treatment with lower risk of subsequent FVC decline compared to patients taking placebo. *Thorax.* 2016 May;71(5):429-35.

β -blockers and COPD exacerbations

James Crapo, MD, and his colleagues in the COPDGene network reported that moderate to severe COPD patients taking β -blocker medications experienced one-quarter fewer exacerbations and one-third fewer severe exacerbations than comparable patients not taking the medications. *Thorax.* 2016 Jan;71(1):8-14.



CLINICAL RESEARCH

SELECTED OPEN CLINICAL TRIALS

Asthma

Airway and Gut Microbiome in Allergy and Asthma: Relationships to Immune and Clinical Phenotype

Richard Martin, MD

Best African American Response to Asthma Drugs (BARD)

Michael Wechsler, MD

COPD

COPDGene — Genetic Epidemiology of COPD

James Crapo, MD

Beta Blockers for the Prevention of Acute Exacerbations of COPD

Barry J. Make, MD

Critical Care

Inflammatory and Antiviral Markers in Adults with Respiratory Distress Syndrome

Kenneth C. Malcolm, PhD

National Trends in Critical Care

Anuj Mehta, MD

Interstitial Lung Disease

Functional Status in Connective Tissue Disease-Associated Interstitial Lung Disease

Amy L. Olson, MD

Optimizing Management of IPF through Effective Health Care Provider-Patient Communication

Jeffrey Swigris, DO

Cystic Fibrosis

Continuous Glucose Monitoring as a Predictor of Lung Function and BMI Decline in Adults with CF

Jennifer L. Taylor-Cousar, MD

TEACH Trial: Testing the Effect of Adding Chronic Azithromycin to Inhaled Tobramycin

Jerry A. Nick, MD

Ivacaftor Therapy Expanded Access Program for Patients 2 Years of Age and Older with Selected Residual Function Mutations on a CFTR Allele

Jerry A. Nick, MD



ASTHMA INSTITUTE ADVANCES TOWARD A CURE

Asthma care has improved tremendously in recent years. However, we still do not know what causes asthma. We can neither prevent asthma nor cure it. For patients with severe disease, asthma remains a deadly disease, causing an average of 10 deaths in the United States every day.

Thanks to a \$5 million gift from Martin and Michele Cohen, National Jewish Health has launched the Cohen Family Asthma Institute to focus on the causes, treatments and prevention of asthma. The institute builds on historic strengths at National Jewish Health in asthma, allergy and immunology, bringing together a broad coalition of researchers, physicians, patients and health care organizations to seek a cure for asthma. The Cohen Family Asthma Institute is led by Co-Directors **Michael Wechsler, MD**; and **Rohit Katial, MD**; and Associate Director **Ronina Covar, MD**.

Sleep

The Evaluation of the Astral IVAPS Auto-EPAP Treatment Algorithm

Sheila Tsai, MD

Therapist-Directed vs. Online Therapy for Insomnia Co-Occurring with Sleep Apnea.

Jack D. Edinger, PhD

Laboratory scientists at National Jewish Health are advancing the frontiers of pulmonary science. Working closely with physicians, who bring crucial insights and questions from the clinic, our scientists are delving deeply into the genetics and epigenetics of lung disease, the fundamental mechanisms of lung injury and repair and the immunological function of the lungs. The answers they find will inspire the therapies of tomorrow.

SELECTED 2016 RESEARCH REPORTS

Antioxidant Protects Against Mustard Gas

Brian Day, PhD, and his colleagues reported that the catalytic antioxidant AEOL 10150 reduced biomarkers of lung damage and improved survival by more than 50 percent in rats exposed to sulfur mustard, a powerful chemical warfare agent. *Toxicol Sci.* 2016 Sep 7. [Epub ahead of print]

Enhanced Defense Against TB

Xiyuan Bai, PhD, and **Ed Chan, MD**, showed that curcumin, an organic chemical that gives the spice turmeric its yellow color, protects against tuberculosis infections in cell culture. Curcumin enhanced immune defense, increasing death of infected cells and destruction of the bacteria inside infected cells. Since *M. tuberculosis* inevitably develops resistance to antibiotics that attack the organism directly, enhancing the body's own defenses against tuberculosis may be a strategy less prone to the development of resistance. *Respirology.* 2016 Jul;21(5):951-7.

What Do Endothelial Microparticles Do?

Vesicles released from the plasma membrane of endothelial cells, known as endothelial microparticles, are emerging as biomarkers of COPD. **Irina Petrache, MD; Karina Serban, MD**, and their colleagues found that cigarette smoke exposure releases endothelial microparticles with distinct microRNA cargo within. Therefore, the endothelial microparticles in smokers and COPD patients may not only be biomarkers, but also can have biological activities important in development of disease. The engulfment of the particles by circulating macrophages reduced their ability to clear dying cells, which may contribute to increased inflammation. *Sci Rep.* 2016 Aug 17;6:31596.

Alternative Splicing in Chronic Asthma

Max Seibold, PhD, and his colleagues discovered that an unconventional form of the cytokine IL-33 appears important

in chronic asthma. Alternative splicing of IL-33, lacking exons 3 and 4, causes it to be secreted from epithelial cells. Once in circulation, IL-33 binds to receptors on mast cells and basophils, which then release cytokines that drive Type 2 inflammation in chronic asthma. *Proc Natl Acad Sci U S A.* 2016 Aug 2;113(31):8765-70.

Cell-Based Therapy for Lung Injury

Moumita Ghosh, PhD, and her colleagues reported that transplantation of both tissue stem cells and stem-cell-derived progenitors, rather than stem cells alone, could be an effective therapy for repair of damaged airways. That mixture actively contributed to epithelial repair. Two weeks after transplantation, the mixture of cells differentiated into basal, secretory and ciliated epithelial cells that persisted for at least 43 days. *Am J Respir Cell Mol Biol.* 2016 Sep 15. [Epub ahead of print]

FRONTIERS OF PULMONARY SCIENCE

NOTEWORTHY ONGOING RESEARCH

Mechanisms of Lung Macrophage Programming by MUC5B During Health and Disease

William Janssen, MD

Macrophage Endocytosis in Resolving Lung Inflammation

Peter M. Henson, PhD

Epigenetic Regulation of Altered T Cell Immunity in Sarcoidosis

Nabeel Y. Hamzeh, MD

Lung Stem Cells and Their Niches

Stijn De Langhe, PhD

Mechanisms of Repair of the Alveolar Epithelium after Lung Injury

Rachel L. Zemans, MD

Asthma Susceptibility Due to Environmental Programming of Innate Immunity in Utero

Magdalena M. Gorska, MD, PhD

DUSP1 as a Therapeutic Target in Fibroproliferative Acute Lung Injury

David W. Riches, PhD

Novel Function of MUC18: Amplification of Inflammation in Allergic Lungs

Hong W. Chu, MD

RECENT PATENTS

Methods and Composition for the Disruption of Biofilms (Pat. # 9314479)

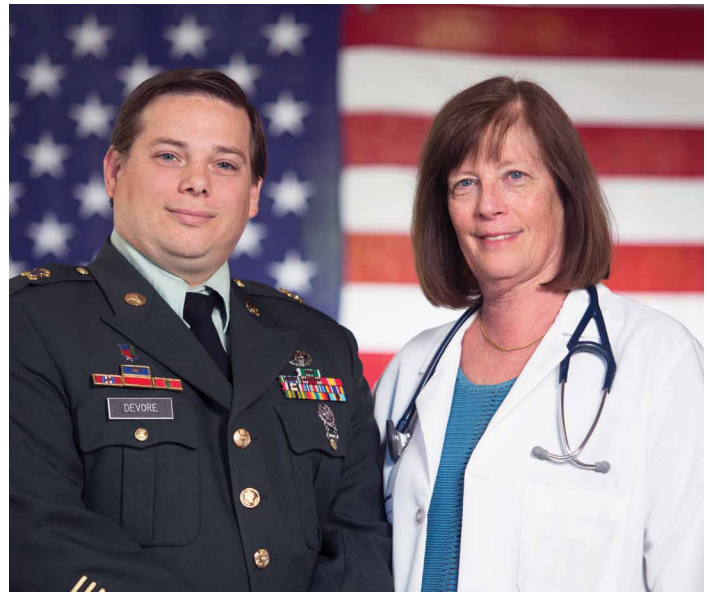
Inventors: Jerry Nick, MD, and Quinn Parks, PhD

Methods of inhibiting biofilm formation or reducing biofilms in a subject or on a device or surface by administering a charged compound such as a polyamino acid to a subject, device or surface.

Methods to Determine Susceptibility to Treatment with Leukotriene Modifiers (Pat. # 9383374)

Inventors: Nathan Rabinovitch, MD, and Erwin Gelfand, MD

A method of determining the susceptibility of a subject to treatment with a leukotriene modifier by identifying a subject with a high ratio of CysLT levels to eosinophilic airway inflammation as susceptible to treatment with the leukotriene modifier.



RESEARCH SEEKS ANSWERS TO WARFIGHTERS' PULMONARY DISEASE

National Jewish Health researchers are studying why warfighters deployed to Southwest Asia suffer increased rates of respiratory disease, and will test potential treatments thanks to \$11.5 million in grants from the U.S. Department of Defense. The grants take advantage of a unique cohort of previously deployed veterans with lung disease and leverage National Jewish Health expertise in lung injury and repair.

For more than five years, warfighters with respiratory symptoms have come to the Center of Excellence on Deployment-Related Lung Disease led by **Cecile Rose, MD**, an expert in occupational lung disease. Dr. Rose has collected extensive clinical and epidemiological information as well as biological samples from the ill warfighters. **Gregory Downey, MD**, an expert on the molecular mechanisms of lung injury and repair, will combine forces with Dr. Rose and her group for this groundbreaking study. In addition to laboratory studies, the researchers will evaluate experimental medications that target the WNT/ β -catenin and matrix metalloproteinase pathways.

EDUCATION

ACADEMIC TRAINING

National Jewish Health physicians and scientists are thought leaders in their fields who elevate the standard of patient care and teach the next generation of health professionals with fellowships, training and continuing medical education. National Jewish Health is an accredited teaching affiliate of the University of Colorado School of Medicine, where our physicians and scientists have faculty appointments.



Based at National Jewish Health:

- Adult Sleep Medicine
- Pediatric Allergy and Immunology
- Adult Allergy and Immunology
- Mycobacterial Disease

Based at University of Colorado School of Medicine with rotations at National Jewish Health:

- Adult Pulmonary and Critical Care Medicine
- Infectious Disease
- Pediatric Pulmonary Medicine
- Rheumatology
- Cardiothoracic Radiology

In collaboration with the Colorado School of Public Health, National Jewish Health also offers fellowships in:

- Occupational and Environmental Medicine
- Pediatric Sleep Medicine

Postdoctoral Fellowships

National Jewish Health has a robust discovery and translation research enterprise, placing National Jewish Health in the top 6 percent of institutions funded by the National Institutes of Health. Numerous opportunities exist for postdoctoral training in laboratories in the Department of Biomedical Research, the Division of Cell Biology and the Basic Science Section of the Department of Medicine.

Graduate Education

Students enrolled in one of the PhD programs offered by the Graduate School of the University of Colorado Denver have the opportunity to perform their thesis research in the laboratories of the faculty at National Jewish Health.

Residents and Medical Students

Residents and medical students at the University of Colorado School of Medicine have rotations at National Jewish Health in a variety of specialties including pulmonary medicine, cardiology, allergy and gastroenterology. In addition, our faculty train residents in family medicine at National Jewish Health — Saint Joseph Hospital.



CONTINUING MEDICAL EDUCATION

The Office of Professional Education at National Jewish Health is an award-winning provider of accredited education. Professional Education produces innovative educational activities that assist physicians, pharmacists, nurses and other health care providers in developing and enhancing their clinical knowledge, competency and performance to improve the quality of patient care. Educational programs that are offered focus on the disease states that National Jewish Health researches and treats.

In support of improving patient care, National Jewish Health is accredited with commendation by:

- The Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians
- The Accreditation Council for Pharmacy Education (ACPE), and the California Board of Registered Nursing (CBRN) to provide continuing education for the health care team.

Upcoming programs include:

39th Annual National Jewish Health Pulmonary and Allergy Update

February 1-4, 2017, Keystone Conference Center, Keystone, CO

The Pulmonary and Allergy Update highlights insights and recent advances in pulmonary medicine, asthma, allergy and immunology, and is presented by expert faculty from National Jewish Health. The conference features lectures, case workshops and hands-on sessions. Certified for CME and nursing contact hours.

54th Annual Denver TB Course

April 5-8, 2017, National Jewish Health, Denver, CO

The Denver TB Course is the most cutting-edge, comprehensive and longest running tuberculosis course in the United States. Topics include epidemiology of tuberculosis, transmission and pathogenesis and diagnosis and treatment of tuberculosis, emphasizing vulnerable populations such as pediatric and HIV co-infection. Certified for CME and nursing contact hours.



Online Course — Learn about emerging therapies for severe asthma

Changing Paradigms in the Treatment of Severe Asthma: The Role of Biologic Therapies (CME)

For more information about our courses, visit njhealth.org/CME or call 800.844.2305.

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Gregory Downey, MD



Debra S. Dyer, MD



Pamela Zeitlin, MD, PhD



Philippa Marrack, PhD



Stephen K. Frankel, MD

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Brian J. Day, PhD,

Vice Chair of Research

Jeffrey A. Kern, MD,

Vice Chair of Finance

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Nabeel Hamzeh, MD, FCCP
Silpa Krefft, MD
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Karin A. Pacheco, MD, MSPH
Clara Restrepo, MD, MPH
Cecile S. Rose, MD, MPH

Mycobacterial and Respiratory Infections Division

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Wendi Drummond, DO, MPH
Gwen A. Huitt, MD, MS
Shannon H. Kasperbauer, MD

PAMELA ZEITLIN, MD, NEW CHAIR OF PEDIATRICS



Pamela Zeitlin, MD, PhD

In December 2016, nationally renowned pediatric pulmonologist **Pamela Zeitlin, MD, PhD**, was named Chair of the Silverstein Family Department of Pediatrics at National Jewish Health. Dr. Zeitlin comes to National Jewish Health from Johns Hopkins University School of Medicine, where she served as Professor of Pediatrics and Deputy Director for the Institute for Clinical and Translational Research. She was also director of the Eudowood Division of Pediatric Respiratory Sciences and co-director of the Pediatric Cystic Fibrosis Clinical Center.

Dr. Zeitlin received her medical degree and her doctorate in cell biology at Yale University. She completed her residency and fellowship at The Johns Hopkins Hospital. Following her education, Dr. Zeitlin spent 28 years at Johns Hopkins, where she built and oversaw many successful pediatric pulmonary, research and faculty education programs.



Erwin Gelfand, MD

Erwin Gelfand, MD, retired from the Pediatrics Chair position after serving for 29 years and is continuing to see patients and conduct research at National Jewish Health. Under Dr. Gelfand's leadership, the Pediatrics Department became a world leader in the treatment and research of pediatric allergies, asthma and atopic dermatitis. Innovative clinical programs, such as the Pediatric Day Program and the Severe Asthma Program, were introduced during Dr. Gelfand's tenure and continue to provide unparalleled care to children from around the world. During Dr. Gelfand's tenure, more than 75 clinical fellows graduated from the National Jewish Health Fellows Program. He trained more than 100 post-doctoral students in his laboratory, and clinical and basic research programs have thrived.

NATIONAL JEWISH HEALTH FACULTY HONORED BY AMERICAN THORACIC SOCIETY



Charles Daley, MD

Charles Daley, MD, chief of the Division of Respiratory and Mycobacterial Infections at National Jewish Health, received the 2016 World Lung Health Award for his efforts around the world to improve diagnosis and treatment of patients with tuberculosis, the world's most deadly infectious disease. For

more than two decades, Dr. Daley has worked with physicians, hospitals, health ministers and others to stop the spread of tuberculosis in countries around the world, from Russia to China, India to South Africa. He currently holds leadership positions in the World Health Organization and the Stop TB Partnership.

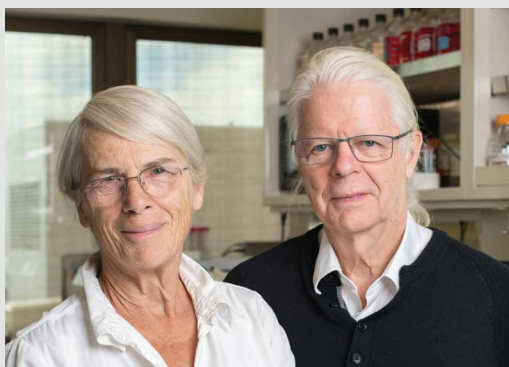


Irina Petrache, MD

Irina Petrache, MD, chief of the Division of Pulmonary, Critical Care and Sleep Medicine at National Jewish Health, received the 2016 Elizabeth A. Rich, MD, Award, given each year to a woman who has made significant achievements in pulmonary medicine, demonstrated

leadership and shown dedication to mentoring. Before leading one of the largest pulmonary divisions in the nation at National Jewish Health, Dr. Petrache was Vice Chair of Research at Indiana University. She also chaired the ATS International Conference for three years. She has provided training and mentoring to predoctoral and postdoctoral students, fellows, residents, and junior faculty at Johns Hopkins University, Indiana University and now National Jewish Health and University of Colorado.

SCIENTISTS RECOGNIZED FOR FUNDAMENTAL DISCOVERIES



Philippa Marrack, PhD, and **John Kappler, PhD**, received the 2016 Novartis Prize for Immunology for discoveries about the basic biology of the immune system. Drs. Marrack and Kappler and their colleague, Harald von Boehmer, PhD, discovered how the immune system distinguishes "self" from "non-self," which helps it determine what should be tolerated in the human body and what should be attacked as an external threat. The researchers demonstrated that the ability is acquired in the thymus through a process of positive and negative selection of T cells with different receptors.

Drs. Marrack and Kappler, both distinguished professors in the Department of Biomedical Research at National Jewish Health, have received numerous international awards and prizes for their discoveries about the immune system, especially T cells. Today, their research continues to reveal how the immune system develops, functions and malfunctions in autoimmune disease, vaccines and aging.

SELECTED 2016 PUBLICATIONS

National Jewish Health faculty members publish more than 400 articles each year in peer-reviewed scientific journals. Below is a selection of leading articles from the past year.

Asthma

Patterns of Growth and Decline in Lung Function in Persistent Childhood Asthma.

McGeachie MJ, Yates KP, Zhou X, Guo F, Sternberg AL, Van Natta ML, Wise RA, Szeffler SJ, Sharma S, Kho AT, Cho MH, Croteau-Chonka DC, Castaldi PJ, Jain G, Sanyal A, Zhan Y, Lajoie BR, Dekker J, Stamatoyannopoulos J, Covar RA, Zeiger RS, Adkinson NF, Williams PV, Kelly HW, Grasemann H, Vonk JM, Koppelman GH, Postma DS, Raby BA, Houston I, Lu Q, Fuhlbrigge AL, Tantisira KG, Silverman EK, Tonascia J, Weiss ST, Strunk RC; CAMP Research Group. *N Engl J Med*. 2016 May 12;374(19):1842-52. doi: 10.1056/NEJMoa1513737. PubMed PMID: 27168434; PubMed Central PMCID: PMC5032024.

Acetaminophen versus Ibuprofen in Young Children with Mild Persistent Asthma.

Sheehan WJ, Mauger DT, Paul IM, Moy JN, Boehmer SJ, Szeffler SJ, Fitzpatrick AM, Jackson DJ, Bacharier LB, Cabana MD, Covar R, Holguin F, Lemanske RF Jr, Martinez FD, Pongratic JA, Beigelman A, Baxi SN, Benson M, Blake K, Chmiel JF, Daines CL, Daines MO, Gaffin JM, Gentile DA, Gower WA, Israel E, Kumar HV, Lang JE, Lazarus SC, Lima JJ, Ly N, Marbin J, Morgan WJ, Myers RE, Olin JT, Peters SP, Raissy HH, Robison RG, Ross K, Sorkness CA, Thyne SM, Wechsler ME, Phipatanakul W; NIH/NHLBI AsthmaNet. *N Engl J Med*. 2016 Aug 18;375(7):619-30. doi: 10.1056/NEJMoa1515990. PubMed PMID: 27532828; PubMed Central PMCID: PMC5085065.

Maternal age and asthma in Latino populations.

Abid Z, Oh SS, Hu D, Sen S, Huntsman S, Eng C, Farber HJ, Rodriguez-Cintron W, Rodriguez-Santana JR, Serebrisky D, Avila PC, Thyne SM, Kim KA, Borrell LN, Williams LK, Seibold MA, Burchard EG, Kumar R. *Clin Exp Allergy*. 2016 Nov;46(11):1398-1406. doi: 10.1111/cea.12765. PubMed PMID: 27238356.

The nasal methylole and childhood atopic asthma.

Yang IV, Pedersen BS, Liu AH, O'Connor GT, Pillai D, Kattan M, Misiak RT, Gruchalla R, Szeffler SJ, Khurana Hershey GK, Kercsmar C, Richards A, Stevens AD, Kolakowski CA, Makhija M, Sorkness CA, Krouse RZ, Visness C, Davidson EJ, Hennessy CE, Martin RJ, Togias A, Busse WW, Schwartz DA. *J Allergy Clin Immunol*. 2016 Oct 13. pii: S0091-6749(16)30955-1. doi: 10.1016/j.jaci.2016.07.036. [Epub ahead of print] PubMed PMID: 27745942.

Within-microenvironment exposure to particulate matter and health effects in children with asthma: A pilot study utilizing real-time personal monitoring with GPS interface.

Rabinovitch N, Adams CD, Strand M, Koehler K, Volckens J. *Environ Health*. 2016 Oct 10;15(1):96. PubMed PMID: 27724963; PubMed Central PMCID: PMC5057244.

Distinguishing characteristics of difficult-to-control asthma in inner-city children and adolescents.

Pongratic JA, Krouse RZ, Babineau DC, Zoratti EM, Cohen RT, Wood RA, Khurana Hershey GK, Kercsmar CM, Gruchalla RS, Kattan M, Teach SJ, Johnson CC, Bacharier LB, Gern JE, Sigelman SM, Gergen PJ, Togias A, Visness CM, Busse WW, Liu AH. *J Allergy Clin Immunol*. 2016 Oct;138(4):1030-1041. doi:10.1016/j.jaci.2016.06.059. PubMed PMID: 27720017.

Leveraging Partnerships: Families, Schools, and Providers Working Together to Improve Asthma Management.

Gleason M, Cicutto L, Haas-Howard C, Raleigh BM, Szeffler SJ. *Curr Allergy Asthma Rep*. 2016 Oct;16(10):74. Review. PubMed PMID:27709456.

Mechanism of Th2/Th17-predominant and Neutrophilic, Th2/Th17-low Subtypes of Asthma.

Liu W, Liu S, Verma M, Zafar I, Good JT, Rollins D, Groshong S, Gorska MM, Martin RJ, Alam R. *J Allergy Clin Immunol*. 2016 Oct 1. pii: S0091-6749(16)31056-9. doi: 10.1016/j.jaci.2016.08.032. [Epub ahead of print] PubMed PMID: 27702673.

IL1RL1 asthma risk variants regulate airway type 2 inflammation.

Gordon ED, Palandra J, Wesolowska-Andersen A, Ringel L, Rios CL, Lachowicz-Scroggins ME, Sharp LZ, Everman JL, MacLeod HJ, Lee JW, Mason RJ, Matthey MA, Sheldon RT, Peters MC, Nocka KH, Fahy JV, Seibold MA. *JCI Insight*. 2016 Sep 8;1(14):e87871. PubMed PMID: 27699235; PubMed Central PMCID: PMC5033813.

Reslizumab in the management of poorly controlled asthma: The data so far.

Maselli DJ, Velez MI, Rogers L. *J Asthma Allergy*. 2016 Aug 31;9:155-62. doi: 10.2147/JAA.S94164. Review. PubMed PMID: 27621657; PubMed Central PMCID: PMC5012840.

Association of a PAI-1 Gene Polymorphism and Early Life Infections with Asthma Risk, Exacerbations, and Reduced Lung Function.

Cho SH, Min JY, Kim DY, Oh SS, Torgerson DR, Pino-Yanes M, Hu D, Sen S, Huntsman S, Eng C, Farber HJ, Rodriguez-Cintron W, Rodriguez-Santana JR, Serebrisky D, Thyne SM, Borrell LN, Williams LK, DuPont W, Seibold MA, Burchard EG, Avila PC, Kumar R. *PLoS One*. 2016 Aug 24;11(8):e0157848. doi: 10.1371/journal.pone.0157848. PubMed PMID: 27556405; PubMed Central PMCID: PMC4996454.

Psychosocial Factors in Severe Pediatric Asthma.

Booster GD, Oland AA, Bender BG. *Immunol Allergy Clin North Am*. 2016 Aug;36(3):449-60. doi: 10.1016/j.iac.2016.03.012. Review. PubMed PMID: 27401618.

Developing, Implementing, and Evaluating a School-Centered Asthma Program: Step-Up Asthma Program.

Liptzin DR, Gleason MC, Cicutto LC, Cleveland CL, Shocks DJ, White MK, Faino AV, Szeffler SJ. *J Allergy Clin Immunol Pract*. 2016 Sep-Oct;4(5):972-979.e1. doi: 10.1016/j.jaip.2016.04.016. PubMed PMID: 27283054.

Analysis of Asthma-Chronic Obstructive Pulmonary Disease Overlap Syndrome Defined on the Basis of Bronchodilator Response and Degree of Emphysema.

Cosentino J, Zhao H, Hardin M, Hersh CP, Crapo J, Kim V, Criner GJ; COPD Gene Investigators. *Ann Am Thorac Soc*. 2016 Sep;13(9):1483-9. doi: 10.1513/AnnalsATS.201511-7610C. PubMed PMID: 27268723.

Personalized asthma therapy in blacks - the role of genetic ancestry.

Dunn RM, Wechsler ME. *J Allergy Clin Immunol*. 2016 May;137(5):1370-2. doi: 10.1016/j.jaci.2016.03.004. PubMed PMID: 27155033.

MiR-3162-3p Is a Novel MicroRNA That Exacerbates Asthma by Regulating β -Catenin.

Fang C, Lu W, Li C, Peng X, Wang Y, Huang X, Yao Z, Cai N, Huang Y, Zhang X, Tan J. *PLoS One*. 2016 Mar 9;11(3):e0149257. doi: 10.1371/journal.pone.0149257. Erratum in: *PLoS One*. 2016;11(4):e0153734. PubMed PMID: 26959414; PubMed Central PMCID: PMC4784915.

Is the Road to Precision Medicine in Chronic Lung Disease Paved with Degraded Chitin?

Wesolowska-Andersen A, Seibold MA. *Am J Respir Crit Care Med*. 2016 Jan 15;193(2):107-8. doi: 10.1164/rccm.201510-1925ED. PubMed PMID: 26771411.

1,25D3 prevents CD8(+)/Tc2 skewing and asthma development through VDR binding changes to the Cyp11a1 promoter.

Schedel M, Jia Y, Michel S, Takeda K, Domenico J, Joetham A, Ning F, Strand M, Han J, Wang M, Lucas JJ, Vogelberg C, Kabesch M, O'Connor BP, Gelfand EW. *Nat Commun*. 2016 Jan 11;7:10213. doi: 10.1038/ncomms10213. PubMed PMID: 26750596; PubMed Central PMCID: PMC4712703.

Effects of omalizumab on T lymphocyte function in inner-city children with asthma.

Gruchalla RS, Sampson HA, Liu AH, Shreffler W, Wallace PK, Togias A, David G, Calatroni A, LeBeau P; Inner-city Asthma Consortium. *Pediatr Allergy Immunol*. 2016 May;27(3):328-31. doi: 10.1111/pai.12508. PubMed PMID: 26573086; PubMed Central PMCID: PMC4888877.

Vitamin D Supplementation and the Risk of Colds in Patients with Asthma.

Denlinger LC, King TS, Cardet JC, Craig T, Holguin F, Jackson DJ, Kraft M, Peters SP, Ross K, Sumino K, Boushey HA, Jarjour NN, Wechsler ME, Wenzel SE, Castro M, Avila PC; NHLBI AsthmaNet Investigators. *Am J Respir Crit Care Med*. 2016 Mar 15;193(6):634-41. doi: 10.1164/rccm.201506-11690C. PubMed PMID: 26540136; PubMed Central PMCID: PMC4824938.

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Cystic Fibrosis

Nontuberculous mycobacterial infections in cystic fibrosis: To treat or not to treat?

Nick JA, Pohl K, Martiniano SL. *Curr Opin Pulm Med*. 2011 Nov;22(6):629-36. doi: 10.1097/MCP.0000000000000317. PubMed PMID: 27583673.

Nontuberculous Mycobacterial Infections in Cystic Fibrosis.

Martiniano SL, Nick JA, Daley CL. *Clin Chest Med*. 2016 Mar;37(1):83-96. doi: 10.1016/j.ccm.2015.11.001. Review. PubMed PMID: 26857770.

Diagnosis of Adult Patients with Cystic Fibrosis.

Nick JA, Nichols DP. *Clin Chest Med*. 2016 Mar;37(1):47-57. doi: 10.1016/j.ccm.2015.11.006. Review. PubMed PMID: 26857770.

US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of nontuberculous mycobacteria in individuals with cystic fibrosis.

Floto RA, Olivier KN, Saiman L, Daley CL, Herrmann JL, Nick JA, Noone PG, Bilton D, Corris P, Gibson RL, Hempstead SE, Koetz K, Sabadosa KA, Sermet-Gaudelus I, Smyth AR, van Ingen J, Wallace RJ, Winthrop KL, Marshall BC, Haworth CS; US Cystic Fibrosis Foundation and European Cystic Fibrosis Society. *Thorax*. 2016 Jan;71 Suppl 1:i1-22. doi: 10.1136/thoraxjnl-2015-207360. PubMed PMID: 26666259; PubMed Central PMCID: PMC4717371.

Inhaled alpha1-proteinase inhibitor therapy in patients with cystic fibrosis.

Gaggar A, Chen J, Chmiel JF, Dorkin HL, Flume PA, Griffin R, Nichols D, Donaldson SH. *J Cyst Fibros*. 2016 Mar;15(2):227-33. doi: 10.1016/j.jcf.2015.07.009. PubMed PMID: 26321218; PubMed Central PMCID: PMC4993024.

Effect of ivacaftor in patients with advanced cystic fibrosis and a G551D-CFTR mutation: Safety and efficacy in an expanded access program in the United States.

Taylor-Cousar J, Niknian M, Gilmartin G, Pilewski JM; VX11-770-901 investigators. *J Cyst Fibros*. 2016 Jan;15(1):116-22. doi:10.1016/j.jcf.2015.01.008. PubMed PMID: 25682022.

COPD

Pulmonary Predictors of Incident Diabetes in Smokers.

Kinney GL, Baker EH, Klein OL, Black-Shinn JL, Wan ES, Make B, Regan E, Bowler RP, Lutz SM, Young KA, Duca LM, Washko GR, Silverman EK, Crapo JD, Hokanson JE. *Chronic Obstr Pulm Dis*. 2016;3(4):739-747. PubMed PMID: 27795984; PubMed Central PMCID: PMC5084840.

A New Approach for Identifying Patients with Undiagnosed Chronic Obstructive Pulmonary Disease.

Martinez FJ, Mannino D, Leidy NK, Malley KG, Bacci ED, Barr RG, Bowler RP, Han MK, Houfek JF, Make B, Meldrum CA, Rennard S, Thomashow B, Walsh J, Yawn BP; High-Risk-COPD Screening Study Group. *Am J Respir Crit Care Med*. 2016 Oct 26. [Epub ahead of print] PubMed PMID: 27783539.

Obstructive sleep apnea and chronic obstructive pulmonary disease.

Borukhov I, Rizzolo D. Overlap syndrome: *JAAPA*. 2016 Nov;29(11):18-22. PubMed PMID: 27749401.

Quantitative computed tomography measurements to evaluate airway disease in chronic obstructive pulmonary disease: Relationship to physiological measurements, clinical index and visual assessment of airway disease.

Nambu A, Zach J, Schroeder J, Jin G, Kim SS, Kim Yi, Schnell C, Bowler R, Lynch DA. *Eur J Radiol*. 2016 Nov;85(11):2144-2151. doi: 10.1016/j.ejrad.2016.09.010. PubMed PMID: 27776670.

Hemizygous Deletion on Chromosome 3p26.1 Is Associated with Heavy Smoking among African American Subjects in the COPD Gene Study.

Begum F, Ruczinski I, Hokanson JE, Lutz SM, Parker MM, Cho MH, Hetmanski JB, Scharpf RB, Crapo JD, Silverman EK, Beaty TH. *PLoS One*. 2016 Oct 6;11(10):e0164134. doi: 10.1371/journal.pone.0164134. PubMed PMID: 27711239; PubMed Central PMCID: PMC5053531.

Biomarkers Predictive of Exacerbations in the SPIROMICS and COPD Gene Cohorts.

Keene JD, Jacobson S, Kechris K, Kinney GL, Foreman MG, Doerschuk CM, Make BJ, Curtis JL, Rennard SI, Barr RG, Bleecker ER, Kanner RE, Kleerup EC, Hansel NN, Woodruff PG, Han MK, Paine III R, Martinez FJ, Bowler RP, O'Neal WK; for COPD Gene and SPIROMICS Investigators. *Am J Respir Crit Care Med*. 2016 Aug 31. [Epub ahead of print] PubMed PMID: 27579823.

Acute Exacerbations and Lung Function Loss in Smokers With and Without COPD.

Dransfield MT, Kunisaki KM, Strand MJ, Anzueto A, Bhatt SP, Bowler RP, Criner GJ, Curtis JL, Hanania NA, Nath H, Putcha N, Roark SE, Wan ES, Washko GR, Wells JM, Wendt CH, Make BJ; COPD Gene Investigators. *Am J Respir Crit Care Med*. 2016 Aug 24. [Epub ahead of print] PubMed PMID: 27556408.

What is asthma-COPD overlap syndrome? Towards a consensus definition from a round table discussion.

Sin DD, Miravittles M, Mannino DM, Soriano JB, Price D, Celli BR, Leung JM, Nakano Y, Park HY, Wark PA, Wechsler ME. *Eur Respir J*. 2016 Sep;48(3):664-73. doi: 10.1183/13993003.00436-2016. PubMed PMID: 27338195.

Analysis of Asthma-Chronic Obstructive Pulmonary Disease Overlap Syndrome Defined on the Basis of Bronchodilator Response and Degree of Emphysema.

Cosentino J, Zhao H, Hardin M, Hersh CP, Crapo J, Kim V, Criner GJ; COPD Gene Investigators. *Ann Am Thorac Soc*. 2016 Sep;13(9):1483-9. doi: 10.1513/AnnalsATS.201511-761OC. PubMed PMID: 27268723.

Persistent and Newly Developed Chronic Bronchitis Are Associated with Worse Outcomes in Chronic Obstructive Pulmonary Disease.

Kim V, Zhao H, Boriek AM, Anzueto A, Soler X, Bhatt SP, Rennard SI, Wise R, Comellas A, Ramsdell JW, Kinney GL, Han MK, Martinez CH, Yen A, Black-Shinn J, Porszasz J, Criner GJ, Hanania NA, Sharafkhaneh A, Crapo JD, Make BJ, Silverman EK, Curtis JL; COPD Gene Investigators. *Ann Am Thorac Soc*. 2016 Jul;13(7):1016-25. doi: 10.1513/AnnalsATS.201512-800OC. PubMed PMID: 27158740; PubMed Central PMCID: PMC5015750.

Inflammatory triggers associated with exacerbations of COPD orchestrate plasticity of group 2 innate lymphoid cells in the lungs.

Silver JS, Kearley J, Copenhaver AM, Sanden C, Mori M, Yu L, Pritchard GH, Berlin AA, Hunter CA, Bowler R, Erjefalt JS, Kolbeck R, Humbles AA. *Nat Immunol*. 2016 Jun;17(6):626-35. doi: 10.1038/ni.3443. PubMed PMID: 27111143.

Understanding the impact of second-hand smoke exposure on clinical outcomes in participants with COPD in the SPIROMICS cohort.

Putcha N, Barr RG, Han MK, Woodruff PG, Bleecker ER, Kanner RE, Martinez FJ, Smith BM, Tashkin DP, Bowler RP, Eisner MD, Rennard SI, Wise RA, Hansel NN; SPIROMICS Investigators. *Thorax*. 2016 Mar 9. pii: thoraxjnl-2015-207487. doi: 10.1136/thoraxjnl-2015-207487. [Epub ahead of print] PubMed PMID: 26962015.

Early response to inhaled bronchodilators and corticosteroids as a predictor of 12-month treatment responder status and COPD exacerbations.

Calverley PM, Postma DS, Anzueto AR, Make BJ, Eriksson G, Peterson S, Jenkins CR. *Int J Chron Obstruct Pulmon Dis*. 2016 Feb 25;11:381-90. doi: 10.2147/COPD.S93303. PubMed PMID: 26952309; PubMed Central PMCID: PMC4772946.

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Bhatt SP, Terry NL, Nath H, Zach JA, Tschirren J, Bolding MS, Stinson DS, Wilson CG, Curran-Everett D, Lynch DA, Putcha N, Soler X, Wise RA, Washko GR, Hoffman EA, Foreman MG, Dransfield MT; Genetic Epidemiology of COPD (COPD Gene) Investigators. *JAMA*. 2016 Feb 2;315(5):498-505. doi: 10.1001/jama.2015.19431. PubMed PMID: 26836732.

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Bhatt SP, Soler X, Wang X, Murray S, Anzueto AR, Beaty TH, Boriek AM, Casaburi R, Criner GJ, Diaz AA, Dransfield MT, Curran-Everett D, Galbán CJ, Hoffman EA, Hogg JC, Kazerooni EA, Kim V, Kinney GL, Lagstein A, Lynch DA, Make BJ, Martinez FJ, Ramsdell JW, Reddy R, Ross BD, Rossiter HB, Steiner RM, Strand MJ, van Beek EJ, Wan ES, Washko GR, Wells JM, Wendt CH, Wise RA, Silverman EK, Crapo JD, Bowler RP, Han MK; COPD Gene Investigators. *Am J Respir Crit Care Med*. 2016 Jul 15;194(2):178-84. doi: 10.1164/rccm.201511-2219OC. PubMed PMID: 26808615; PubMed Central PMCID: PMC5003216.

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Chang Y, Glass K, Liu YY, Silverman EK, Crapo JD, Tal-Singer R, Bowler R, Dy J, Cho M, Castaldi P. *Genomics*. 2016 Mar;107(2-3):51-8. doi: 10.1016/j.ygeno.2016.01.004. PubMed PMID: 26773458; PubMed Central PMCID: PMC4761317.

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Identifying a Deletion Affecting Total Lung Capacity Among Subjects in the COPD Gene Study Cohort.

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Interstitial Lung Disease

Plasma Leptin Is Elevated in Acute Exacerbation of Idiopathic Pulmonary Fibrosis.

Cao M, Swigris JJ, Wang X, Cao M, Qiu Y, Huang M, Xiao Y, Cai H. *Mediators Inflamm*. 2016;2016:6940480. doi: 10.1155/2016/6940480. PubMed PMID: 27642238; PubMed Central PMCID: PMC5014970.

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Evans CM, Fingerlin TE, Schwarz MI, Lynch D, Kurche J, Wang L, Yang IV, Schwartz DA. *Physiol Rev*. 2016 Oct;96(4):1567-91. doi: 10.1152/physrev.00004.2016. Review. PubMed PMID: 27630174.

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COUNTERPOINT: Should All Patients With Idiopathic Pulmonary Fibrosis, Even Those With More Than Moderate Impairment, Be Treated With Nintedanib or Pirfenidone? No.

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What's it like to live with idiopathic pulmonary fibrosis? Ask the experts.

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Desmoplakin Variants Are Associated with Idiopathic Pulmonary Fibrosis.

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RECOGNITION

National Jewish Health is the leading respiratory hospital in the nation and the only health care organization to be fully focused on respiratory and related illnesses. National Jewish Health has been recognized for this expertise through a variety of outside measurements and tangible achievements, including those listed below.



National Jewish Health has been ranked by *U.S. News & World Report* as #1 or #2 every year that the Pulmonology category has been included in the rankings (since 1997). Of those years, National Jewish Health was in the #1 spot for 15 years.



U.S. News & World Report recently added a new award category, "Best Hospitals for Common Care." This year, our COPD care and our Lung Cancer Surgery program were rated "high performing," the highest rating available.



National Jewish Health has more than 45 doctors named on various lists, including "America's Top Doctors" by Castle Connolly, and "Top Docs" in the *5280 magazine's* 2016 rankings of Denver-area physicians.

National Jewish Health is in the top 6 percent of institutions in the country funded by the NIH, in terms of absolute dollars. This is a tremendous achievement for a specialty hospital/research center.

BREAKTHROUGHS IN RESEARCH

National Jewish Health is responsible for many important scientific advances, including:

IgE, the molecule responsible for allergic reactions. This discovery has become the basis for many new treatments for asthma and allergies.

The T cell receptor gene, which plays a crucial role in recognizing foreign invaders and orchestrating an immune response. It opened the door to understanding how bodies fight viruses, bacteria and cancer.

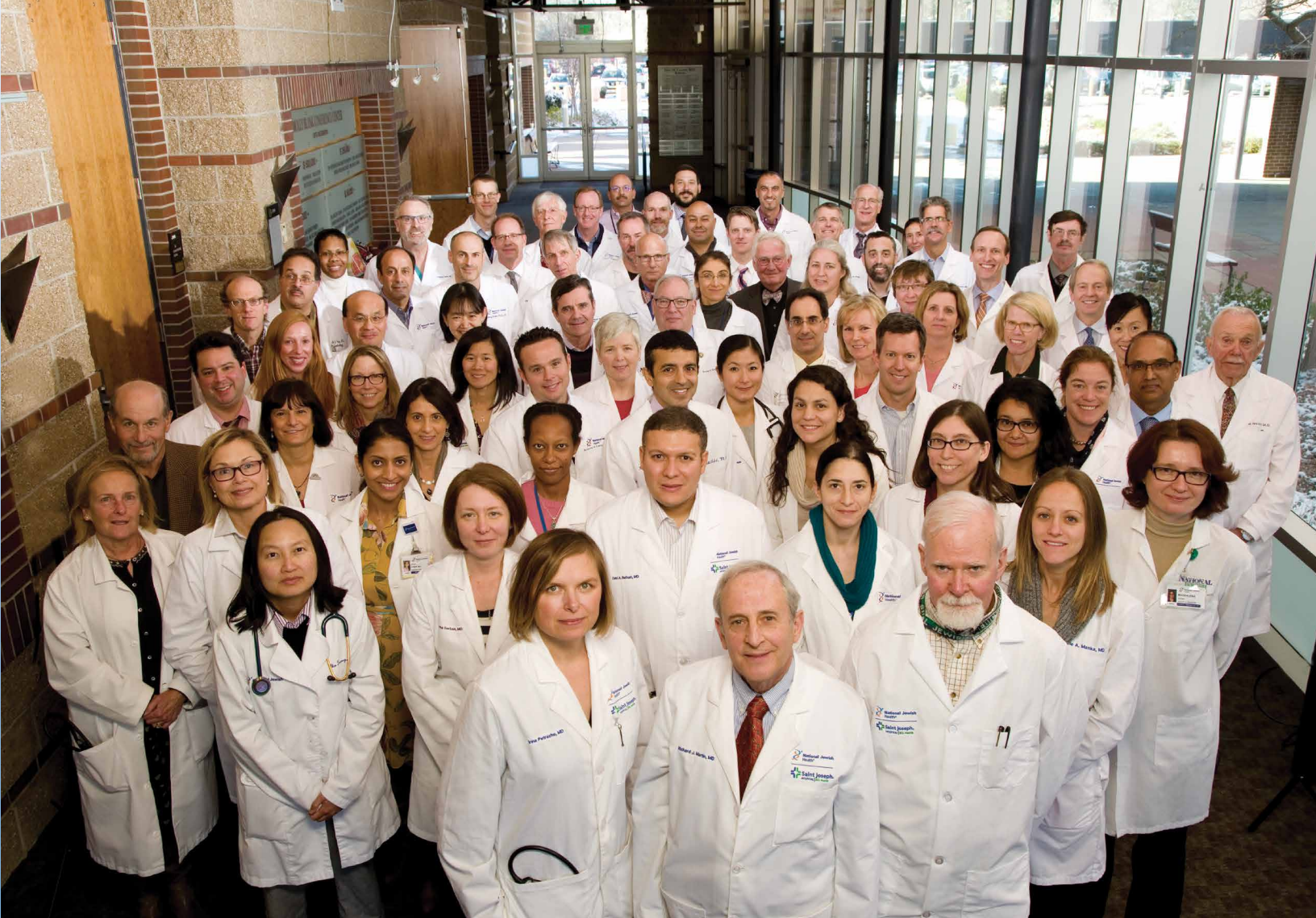
Superantigens, extremely powerful bacterial toxins associated with particularly virulent diseases, such as toxic shock syndrome and Legionnaire's disease.

Combined chemotherapy for tuberculosis. National Jewish Health physicians were among the leaders in developing this crucial tool for fighting tuberculosis.

Mechanisms of apoptosis. Pioneering efforts have helped doctors understand how the body effectively removes and recycles up to two billion cells a day and resolves inflammation in the lung.

Allergies to artificial joints. Researchers have developed a blood test that can detect allergy to nickel used in artificial joints, a common cause of failure.






FOCUS, EXPERIENCE, COLLABORATION

With a 118-year history of transformative medicine, National Jewish Health is the only health care organization in the world dedicated exclusively to respiratory and related diseases. Today, National Jewish Health has an unparalleled pulmonary expertise, with internationally recognized physician-scientists bringing their extensive experience and knowledge to many of the most challenging respiratory cases in the nation. Pulmonologists work closely with their colleagues in cardiology, gastroenterology, allergy, immunology, oncology and radiology to understand the whole person and find solutions for our patients and for patients around the world.

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