THE Flexner DISCOVERY LECTURE SERIES

Upcoming Discovery Lecture:

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January 4, 2018

208 Light Hall / 4:00 P.M.

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SALLY E. WENZEL, M.D.

PRECISION MEDICINE AND ASTHMA:
IS THE VISION MEETING THE REALITY?

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4:00 P.M.

208 LIGHT HALL

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PRECISION MEDICINE AND ASTHMA: IS THE VISION MEETING THE REALITY?

Asthma has long been recognized as a heterogeneous disease. However, only recently has the intersection of pathobiology and targeted biologic therapies begun to unveil the differing yet overlapping phenotypes which make up asthma, and in particular severe asthma. For many years, asthma, as defined by bronchodilator responsiveness and appropriate symptoms, was considered a disease of childhood onset with allergic reactions contributing heavily to disease. This promoted drugs, including anti-IgE, which targeted these allergic pathways. However, large scale epidemiologic studies, including genetic studies, failed to identify a critical importance of allergic pathways to more severe disease. In contrast, evidence from pathologic studies suggested that Type-2 immuno-inflammation (i.e. activated by IL-4, 5 and 13) persisted, even in the absence of allergy, despite the use of even high doses of inhaled and systemic corticosteroids. These studies were then complemented by studies of biologic therapies targeted to these pathways, which showed efficacy above that of corticosteroids and long acting beta agonists, in patients with elevations in appropriate biomarkers. Thus, the concept of a molecular phenotype of Type-2 Hi asthma arose. However, subsequent studies suggest that Type-2 Hi asthma itself is likely to be heterogeneous, with some patients presenting with an IL-4/13 prominent disease and others with an IL-5 prominent disease. The biomarkers for each of these remain unknown. Others may have a disease which goes beyond T2 inflammation alone, and thus will only partially respond to T2 targeted therapies. Finally, much less is understood regarding those patients without obvious Type-2 inflammatory signatures. No clear molecular phenotypes or targeted therapies yet exist. However, studies are showing that some T2 targeted therapies may show efficacy even in patients with low levels of current T2 biomarkers, suggesting that better biomarkers are also needed. Despite these uncertainties, many patients can now be precisely targeted for treatment with considerable impact on the overall morbidity of the disease, particularly in those with severe asthma.

SALLY E. WENZEL, M.D.

PROFESSOR OF MEDICINE, UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE

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Dr. Sally Wenzel completed her MD degree at the University of Florida. Following her residency in internal medicine at Wake Forest University and her fellowship in pulmonary and critical care medicine at Virginia Commonwealth University, she spent 19 years at National Jewish Health and the University of Colorado before moving to the University of Pittsburgh. She received the Elizabeth Rich Award for her role in promoting women in science, the ATS Award for Scientific Achievement, the ATS Foundation Breathing for Life Award, and the ERS President's Award. She is currently Director of the University of Pittsburgh Asthma Institute at UPMC, holds the UPMC chair in Translational Airway Biology and is Subsection Chief of Allergy. Dr. Wenzel has served as Deputy Editor for the American Journal of Respiratory and Critical Care Medicine and is a frequent reviewer for the New England Journal of Medicine and other publications.

Dr. Wenzel has a passion for understanding and improving the treatment of asthma, in particular severe asthma. She has promoted severe asthma as a complex disease and her studies of asthma phenotypes have led the field in understanding these complexities. Dr. Wenzel has developed a strong translational program to study the pathobiology of severe asthma and its phenotypes, modeling ex vivo findings in vitro, using primary human airway cells from patients and controls.