



Center for Lung Biology Pulmonary NewsLetter

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What's New in Pulmonary Science?

Our group possesses a strong expertise in pulmonary vascular biology. Two of our scientists, Drs. Songwei Wu and Mary Townsley, have been studying the expression and function of endothelial cell calcium channels. Dr. Wu's work has demonstrated that lung capillary endothelial cells express a T-type calcium channel that is not found in either pre- or post-capillary vascular segments. Dr. Townsley has discovered that expression of a different calcium channel, the transient receptor potential protein in the vanilloid family (TRPV4), is also enriched in capillaries. By



Drs. Songwei Wu (left) and Mary Townsley (right) work together to examine how different calcium channels control lung vascular function.

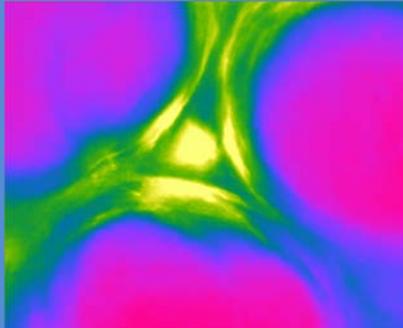
working together, these investigators demonstrate that activation of the T-type calcium channel is essential for P-selectin membrane translocation, but does not regulate endothelial cell barrier function. In contrast, activation of the TRPV4 channel increases lung capillary permeability, but has no effect on P-selectin membrane translocation. This exciting work illustrates the high fidelity in calcium signaling that regulates pulmonary endothelial cell physiology. Look for their forthcoming publications, available from PubMed.

What's New in Research Training?

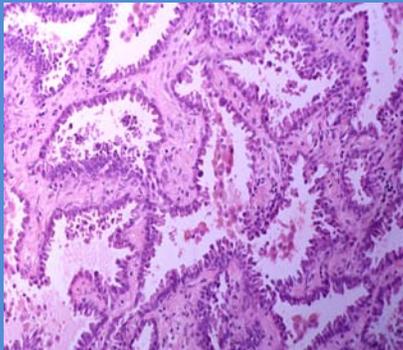
Our T32 training program in "Cell signaling and lung pathobiology" has just received the award notice for our second cycle of funding (2009-2014) from NHLBI. The program draws together a diverse group of well-funded and nationally-recognized training faculty with research interests in the biology and pathobiology germane to pulmonary hypertension, acute lung injury, airways disease and lung endothelial cell heterogeneity. In its inception, this program was designed to provide a state-of-the-art training program for pre-doctoral students, building on the interdisciplinary core curriculum in the Basic Medical Sciences PhD program. In this second cycle, we have added short-term training for graduate students in engineering or rising second-year medical students who are interested in Research Honors. This program has been effective, as evidenced by the success of our trainees in publication, accrual of individual extramural fellowships, recruitment of under-represented minorities, and progression of graduates to biomedical research positions in academia, industry and the government. Trainees in the Center for Lung Biology serve as an editorial board for a quarterly on-line publication entitled "Did you Know...". The goal of this initiative is to provide trainees the opportunity to author an historical perspective on influential discoveries that led to the modern understanding of pulmonary and critical care medicine, and further gain experience in the **peer review and editorial processes**. The program is directed by Dr. Mary Townsley

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The Art in Science Program was developed to increase community awareness about biomedical research performed at USA and provides an opportunity for scientists to present aesthetic aspects of their data to the public. The primary purpose of this program is best defined by its title, PERCIPIO, which means "to learn through the senses".



Peace - Dr. Abu-Bakr Al-Mehdi



Paisley - Dr. Judy King



Liquid - Clayton Campbell

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What's New in Pulmonary & Critical Care?

The Pulmonary and Critical Care Division of the Department of Medicine at USA provides all ICU and adult Pulmonary Medicine care to patients in the USA Health System including the USA Medical Center, Infirmiry West Medical Center, and Children's and Women's Hospital. There are a total of seven clinical faculty, most of whom are also scientists in the Center for Lung Biology, and six Fellows training in Pulmonary and Critical Care Medicine.

The goal of the Division is to provide state-of-the-art care to patients, train outstanding young physicians in Pulmonary medicine, and promote research to find cures for a variety of lung diseases. Faculty and fellows see outpatients in the General Pulmonary as well as Sub-Specialty Clinics such as Pulmonary Hypertension, TB, Sleep Disorders, and Cystic Fibrosis. Divisional faculty have active clinical and translational research programs in the areas of Acute Lung Injury, Asthma, COPD, and Pulmonary Hypertension.

The Pulmonary/Critical Care Fellowship Program is a 3-year program designed to provide the fellow with the education, training, and clinical skills necessary to pursue an academic career in pulmonary and critical care medicine. Fellows have a broad exposure to a wide variety of patient experiences from the ICU setting to outpatient clinics. All fellows also participate in research during their 3-years of training with the intent to train academic physicians.

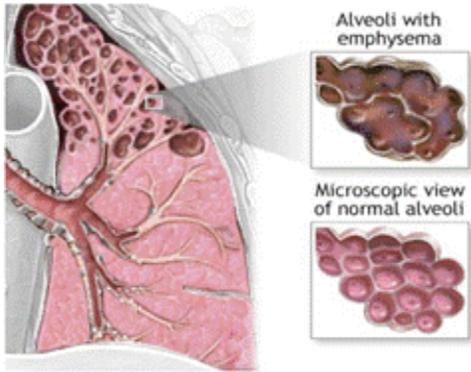
Art in Science!!!



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2006 Hypothetical Illustrations Exhibit

Did You Know...



Emphysema is a lung disease, involving permanent abnormal enlargement of airsacs (alveoli) and destruction of surrounding support tissue without fibrosis. The destruction of alveolar walls decreased elastic recoil resulting in air trapping and reduced oxygenation.⁷

...not all cases of emphysema are caused by smoking? The first comprehensive report describing emphysema was presented by Watson in 1764.¹ His 28 year-old patient complained of "chronic shortness of breath and productive cough" and died 10 days later. On autopsy, Watson observed, "greatly distended lungs, and large bladders filled with air, which no pressure on the surface of the lung could force back." On the right lung, he found "ruptured blebs filled with bloody fluid".¹ Today emphysema is characterized by enlargement of the respiratory airspaces without obvious fibrosis.² The accompanying destruction of alveolar walls and decreased elastic recoil, reduces exhalation capacity. While many cases of emphysema are related to cigarette smoking, a genetic risk factor has also been identified.^{2,3}

Indeed, in 1838 Louis reported the findings of a young pulmonologist, James Jackson Jr, who died of typhus in 1834. Jackson had observed a hereditary link to emphysema.⁴ Budd, in 1839, proposed that loss of pulmonary elasticity and dilation of air spaces in horses could have a hereditary component and be comparable to human emphysema.¹

However, it was not until 1963 that Laurel and Eriksson linked inherited alpha1-antitrypsin (AAT) deficiency to premature emphysema.³ AAT is a protease inhibitor, which blocks proteases such as neutrophil elastase, from proteolytically degrading elastin, the lung matrix component responsible for elastic recoil. In the 1960s, observations by Janoff and Scerer and others led to the development of the proteinase-antiproteinase imbalance hypothesis.⁵ This hypothesis is based on four observations: (1) elastin is degraded by elastase, (2) in an animal model, a protease can induce alveolar damage similar to emphysema in humans, (3) AAT is a specific inhibitor of neutrophil elastase, (4) deficiency of AAT is associated with the development of pulmonary emphysema in both smokers and nonsmokers.⁵ While neutrophil elastase has been implicated in alveolar destruction in pulmonary emphysema, it is still unclear whether other proteases are implicated in disease progression. However, the arena is set for development of therapies to counteract matrix degradation while promoting protection of the remaining pulmonary matrix, specifically elastin.

Although genetic predisposition plays a critical role in the development of emphysema, the single most *preventable* risk factor is smoking, accounting for 90% of emphysema cases in the U.S.⁶ Other preventable risk factors include air pollution, poor diet, and occupational hazards.³ While genetic predisposition alone can lead to early onset emphysema, genetic predisposition in association with preventable risk factors exacerbates disease progression. A greater understanding of the pathophysiology of pulmonary emphysema, whether related to genetic or preventable risk factors, will offer greater opportunities for targeted drug therapy and/or disease prevention.

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This article written by **Dr. Natavia Middleton**, Feb. 2009. **All Articles**