Center for Lung Biology Pulmonary NewsLetter

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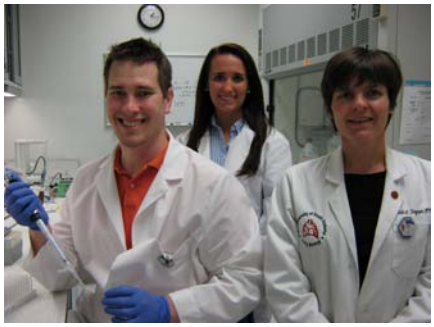
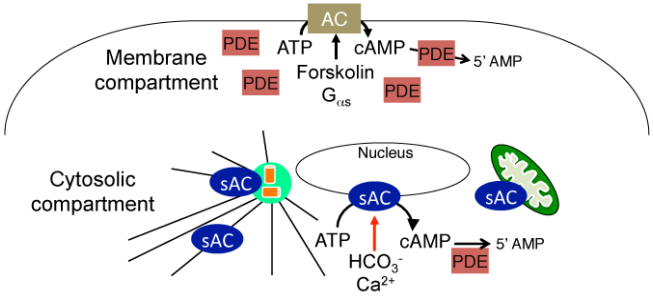
What's New in Pulmonary Science?



The Sayner Lab: Jonathan Daigle (Left), Jessica Nix (Middle), and Dr. Sarah Sayner (Right)

Cells sense and respond to diverse environmental cues, including mechanical and chemical stimuli, essential for maintaining homeostasis. Chemical signals bind to membrane receptors, which in turn activate other intracellular molecular signals to convey a message. Adenosine 3,5 cyclic monophosphate (cAMP) is one such intracellular cue that acts like a switch to control cell behavior. cAMP is synthesized by a family of transmembrane enzymes called adenylyl cyclases. In endothelial cells, the activation of transmembrane adenylyl cyclase strengthens barrier function, and is anti-inflammatory. In contrast, bacteria and other unicellular organisms produce a cytosolic version of adenylyl cyclase, and now investigators have discovered an eukaryotic cytosolic adenylyl cyclase. This enzyme, called soluble adenylyl cyclase (sAC or AC10), was first found in germ cells, including sperm, where it was thought to play a role in control of motility. We now recognize the sAC is expressed in nearly all mammalian cells. Dr. Sarah Sayner in the Department of Cell Biology and Neuroscience and the Center for Lung Biology has demonstrated that pulmonary endothelial cells express AC10, although not all endothelial cells express equal amounts of the enzyme; microvascular endothelial cells express a higher abundance than do conduit endothelial cells. Bicarbonate activates AC10. Exposure of endothelial cells to extracellular bicarbonate increases cAMP, and this bicarbonate-responsive signal seems to disrupt the endothelial cell barrier. Although the clinical relevance of this observation remains untested, these findings from the Sayner lab suggest that correcting acidosis with bicarbonate may cause pulmonary edema – due at least in part to the actions of AC10. Look for forthcoming publications from the Sayner lab on pubmed.



Transmembrane adenylyl cyclases are stimulated by forskolin or $G_{\alpha s}$ to generate cAMP in the membrane compartment. Phosphodiesterases (PDE), located at the periphery of the compartment, hydrolyze cAMP to 5'AMP. In contrast, mammalian soluble adenylyl cyclase 10 (sAC) lacks transmembrane domains and localizes to the centrosome, microtubules, nucleus and mitochondria. When stimulated by bicarbonate and calcium, sAC generates a phosphodiesterase sensitive cAMP pool in the cytosolic compartment of pulmonary endothelium. Am J Physiol Lung Cell Mol Physiol. 2011 Feb 18

Recognize these faces?

Charlene Jordan

Jennifer Collins

If you have visited the Center for Lung Biology, Charlene Jordan and Jennifer Collins will be familiar to you. Charlene and Jennifer staff the Center's administrative office, and ensure that our research and educational programs operate efficiently.

Charlene joined the CLB in 2002, its inaugural year. She served as the Center's coordinator until 2007, at which time she was named the financial operations specialist and director of PERCIPIO, the Art and Science program sponsored by the CLB. Most recently Charlene has completed the Certification Examination for Research Administrators. This designation indicates she has met the Research Administrators Certification Council's eligibility requirements as a sponsored programs administrator. Charlene has processed over 200 grant applications in her capacity as CLB financial operations specialist. Of these applications, approximately 35% have been awarded.

Jennifer joined the CLB family in 2008. She works closely with Charlene in the office, coordinates educational activities, including all CLB classes and schedules, research-in-progress seminars, the combined CLB and Pulmonary and Critical Care Research seminar, and CLB guest schedules. In the summer months, Jennifer ensures proper placement of our summer research students.

We are fortunate to have two outstanding professional staff operating our Center's administrative unit. Thanks to Charlene and Jennifer.

What's New in Research Training?

Predoctoral training in the Center for Lung Biology (CLB) is organized around the Lung Biology track in the Basic Medical Sciences PhD program. Trainees must have successfully completed the first year interdisciplinary core curriculum prior to affiliation with the track. The track curriculum includes 2 semesters of advanced coursework in lung biology and pathobiology, along with our hands-on skills course, a research-in-progress series and pulmonary conferences. The latter are held in collaboration with the Department of Medicine's Division of Pulmonary and Critical Care. The lung biology and pathobiology courses combine a didactic component with a writing component focused on some historical perspective related to the student's interest.

An active group of 16 predoctoral trainees are currently affiliated with the Lung Biology track in the CLB. Of this number, 6 trainees are supported by the CLB's predoctoral T32 grant, 3 trainees hold individual predoctoral fellowships from the American Heart Association, and 1 trainee was just awarded an individual predoctoral fellowship (F31) from the NIH.

Cristhiaan Ochoa authored the latest on-line article in the Center for Lung Biology's "Did you know..." series, focused on development of an artificial lung. The complete text of Cristhiaan's article is included in this issue of the newsletter.

What's New in Pulmonary & Critical Care?

Great News! The Division of Pulmonary and Critical Care Medicine in the Department of Medicine at the University of South Alabama was recently reaccredited by the Accreditation Council for Graduate Medical Education for the next 5 years! This is even a bigger accomplishment given that the program transitioned from a 2-year Pulmonary Medicine training program to a 3-year Pulmonary and Critical Care Medicine combined program just 3 years ago. This clearly recognizes the efforts of the entire faculty, especially the Fellowship Director, Dr. Brian Fouty, in the creation of a quality training program and as we enter the recruiting season for new fellows will make USA even more attractive to highly qualified trainees.

Clinical services continue to expand with the introduction of endobronchial ultrasound (EBUS) capabilities to USA and the Northern Gulf Coast. Indeed, USA is the first facility in the region to offer the capability to use EBUS and will likely have an important impact in our community. Dr. Casey Schaphorst recently completed advanced training in the use of EBUS and will soon be performing these procedures in the newly remodeled Endoscopy Suites at the USA Medical Center. EBUS allows for visualization of structures (usually lymph nodes) outside the trachea and bronchi allowing for directed needle biopsies of these previously hidden areas. This technology may spare patients the need for surgical procedures to stage lung cancers or make other diagnoses such as sarcoid.

Overall, the Division continues to provide outstanding pulmonary and critical care to patients in the northern Gulf Coast with active, productive research and educational programs for the region. We look forward to being the major resource for expert clinical care and research in Pulmonary and Critical Care Medicine in the area.

Did You Know...

...Did you know that scientists are in the final stages of developing a fully artificial lung[1]? An implantable artificial lung would allow a patient with advanced respiratory failure to move freely and to live at home. Consequently, an artificial lung – in a similar fashion to what dialysis does for the kidneys – could be a bridge to lung transplantation (Figure 1).

The primary role of the lungs is the extraction of oxygen from the environment and the elimination of carbon dioxide. This occurs when the lungs inflate and deflate, respectively; and ever since the Greek physician Galen (A.D. 175) used bellows to inflate the lungs of dead animals[2], scientists have attempted to replace the lung function with non-living, inert materials.

Figure 1. Dr. Robert Bartlett, Professor Emeritus of Surgery at the University of Michigan holds the artificial lung. Dr. Bartlett's research on artificial lung systems has been funded by the National Institutes of Health for over thirty years.

The first to report the successful inflation of the lungs by artificial means, which sustained life, was the Dutch physician Andreas Vesalius (1514-1564). He blew air into a tube of cane that had been implanted in an animal's trachea. By doing so, Vesalius was able to sustain the animal's life and observe the motions of the heart directly[2]. Two centuries later, the British surgeon John Hunter (1728-1793) – building upon Vesalius' work – invented the first device for artificially assisted respiration. He built an apparatus with double-chambered bellows (one chamber inflated the lungs, the other deflated them) and used it successfully in dogs[3].

The Scottish physician John Dalziel is credited with the first effort to develop a fully automated respirator in 1832[3]. The principle behind this device was to cause subatmospheric pressures to be exerted outside of the thorax, thus allowing the more positive pressure of the atmosphere to inflate the lungs. A pair of bellows operated by a piston rod created the subatmospheric pressure[4]. Over the next century, different variations of this apparatus were developed including the famous "iron lung"[5, 6].

These advances eventually evolved into the modern mechanical ventilator, a device that is now routinely used in intensive care units around the world. But since patients on mechanical ventilation have to be bedridden, intubated, and sedated – it follows that a mechanical ventilator is not an ideal artificial lung.

The concept behind an implantable lung stems from the first heart-lung machines developed for open heart surgery[7]. It was proposed by Bodell et al. in 1965 as an implantable "third lung"[8]. It consisted of a 20-inch-long polytetrafluoroethylene graft and was successfully tested in dogs and sheep. Since then, scientists have improved its design, its gas exchange capabilities, its biocompatibility, and the implantation techniques[9]. Scientific collaborations eventually yielded a consortium formed by the University of Michigan and MC3 Corporation, which conceived the BioLung ® (Figure 2). This prototype has sustained a sheep's life for 30 days[10], and more recently, it allowed animals to engage in moderate exercise[1]. These studies have moved the artificial lung closer to clinical trials.

Figure 2. Schematic representation of the implantable artificial lung, BioLung ®.

This is important, because the only alternative available to treat non-reversible chronic lung disease is lung transplantation. But a significant percent of patients waiting for lung transplants die while waiting for a donor[9]. The artificial lung is expected to improve and extend the life of those patients waiting to be transplanted. In consequence, an artificial lung is urgently needed; and with continued advances, it is expected to be available soon.

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