



## **Elizabeth Nash Memorial Fellowship Program**

**This fellowship program supports CF research at the post-doctoral level. One year terms may be extended to a second year of funding, based on the reviews of progress-to-date. Post-doctoral researchers and their Principal Investigators meet at semi-annual colloquia held in the Bay Area.**

***The following are research projects funded by CFRI that will be concluding June/July 2009.***

- 1) University of California San Diego is investigating how bicarbonate affects mucous secretion. (Ruth Muchekehu, PhD & Paul Quinton, PhD at UC San Diego)
- 2) At University of California San Francisco, researchers are studying *Pseudomonas*, the most common destructive bacteria in the CF airway, binding to glycoreceptors expressed on epithelial cells. (Iwona Bucior, PhD & Joanne Engel MD at UC San Francisco)
- 3) At University of California Davis, therapeutic strategies are being explored to combat oxidative stress in the CF respiratory tract. (Vihas Vasu, PhD & Jason Eiserich, PhD at UC Davis)
- 4) Research at Stanford/UCSF questions how airway mucous gland secretions are altered in cystic fibrosis. (Monal Sonecha, MD & Jeffrey Wine, PhD at Stanford University)

***The following are research projects approved by CFRI membership for July 2009 start date.***

- 1) At University of California San Francisco, researchers will be studying the relationship between CF Airway Microbiome and Pulmonary Health. (Michael Cox, PhD & Susan Lynch, PhD)
- 2) At University of California San Francisco, researchers will be exploring EX VIVO Surrogate Assays to Assess Efficacy of Ion Channel-Targeted CF Drugs. (Nico Derichs, MD & Dennis Nielsen, MD, PhD)
- 3) At University of California Davis, researchers are studying a New Therapeutic Strategy Focusing on Anti-Inflammatory Therapies for Cystic Fibrosis-Related Lung Disease: Preliminary Data Toward Consideration of Therapy with Soluble Epoxide Hydrolase Inhibitor (*sEHI*). (Jun Yang, PhD & Bruce Hammock, PhD)
- 4) At University of California San Diego, researchers will be exploring how bicarbonate helps with mucus release in Cystic Fibrosis. (Ning Yang, PhD & Paul Quinton, PhD)



## **New Horizons Research Campaign**

**This program supports Cystic Fibrosis research of Principal Investigators at a higher level of funding. One year terms may be extended to a second year of funding, based on the reviews, progress-to-date and availability of funds.**

*The following projects are currently being funded through this program:*

**1) University of California at Berkeley - Terry Machen, PhD:**

The flagellin-stimulated inflammatory response includes activation of a slow increase in transepithelial chloride secretion that appears to result from activation of CFTR. Absence of this chloride secretion in CF might reduce bacterial clearance in the lungs of CF patients compared to non-CF patients. An inhibitor of JNK reduced IL8 secretion and increased chloride secretion.

Dr. Machen hypothesizes that flagellin activates CFTR-dependent chloride secretion by activating CFTR or related ion transport pathways, and that JNK inhibits this response. The specific aims of Dr. Machen's research are: (i) identify ion transport pathways involved in CFTR-dependent chloride secretion and (ii) test the role of JNK in regulating both the inflammatory response and chloride secretion. Inflamed airways in CF may benefit from treatment with JNK blockers because these should reduce inflammation and increase chloride secretion in CF patients with the G551D deletion who express CFTR in the plasma membrane or in patients treated with correctors to increase delta F508 CFTR in the membrane.

**2) San Diego State University - Forest Rohwer, PhD:**

Metagenomics is a field of study investigating community genetic information obtained from a particular environment. For a CF airway infection, this means a metagenomic study would include the study of all the microbial, viral and fungal populations present in the airway of the patient and not just the species that the clinical lab can culture and identify. Identifying all members of these populations is important because the immune system mounts an inflammatory response to the entire community (i.e. microbial, viral and fungal) and not just *Pseudomonas* or *Staphylococcal* species that are typically cultured.

Dr. Rohwer's proposed work approaches the CF airway infection as a complex and dynamic ecosystem composed of interacting microbial populations competing in an environment of limited resources (i.e. oxygen, nutrients etc). The environment also poses challenges for these microbial communities because of the actions of the immune system and the effects of therapies such as antibiotics and chest physiotherapy.