



Research Newsletter

Medicine Grand Rounds

“Chair’s Lecture Series” and Phillip Liverman Lectureship, March 13, 2006

Dr. Lifton uses genetic approaches to identify the genes and pathways that contribute to common human disease, including cardiovascular, renal and bone diseases. Dr. Lifton’s studies have led to identification of several genetic variants affecting blood pressure in humans. 1) One of these mutations is a chimeric gene duplication arising from unequal crossing over that leads to ectopic production of the key hormone determining salt and water homeostasis. The result is a severe form of hypertension characterized by a high incidence of early death from cerebral hemorrhage. 2) The second variant is in angiotensinogen and results in increased activity of the renin-angiotensin system. This causes modest effects on blood pressure in millions of individuals. 3) Mutations in two different subunits of the renal sodium channel, which regulates net renal sodium reabsorption, also cause a severe form of hypertension. The mutations delete the normal cytoplasmic carboxy termini from the sodium channel subunits, resulting in constitutive activation of channel activity leading to hypertension. 4) Pseudohypoaldosteronism type II (PHAII) is an autosomal-dominant disease featuring hypertension with hyperkalemia and renal tubular acidosis, despite otherwise normal renal function. By positional cloning, Dr. Lifton identified mutations in two novel serine-threonine kinases, WNK1 and WNK4, as the cause of this disease.

Dr. Richard P. Lifton



Sterling Professor of Genetics and Professor of Medicine and Molecular Biophysics and Biochemistry at Yale University School of Medicine, will be giving Grand Rounds on **March 13, 2006**.

Dr. Lifton is the Chairman of Genetics at Yale, a Howard Hughes Medical Institute Investigator, a member of the National Academy of Sciences, and the Institute of Medicine.

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Upcoming Grand Rounds in the Chair’s Series include:

Michael Thorner, April 10th

Jens S. Christiansen, Aarhus University Hospital, Denmark, April 24th

Raghu Mirmira, May 1st

[Lalouel JM](#). A chimeric 11 beta-hydroxylase/aldosterone synthase gene causes glucocorticoid-remediable aldosteronism and human hypertension. [Nature](#). 1992 Jan 16;355(6357):262-5.

[Hansson JH](#)...[Lifton RP](#). Hypertension caused by a truncated epithelial sodium channel gamma subunit: genetic heterogeneity of Liddle syndrome. [Nat Genet](#). 1995 Sep;11(1):6-9.

[Simon DB](#)...[Lifton RP](#). Gitelman’s variant of Bartter’s syndrome, inherited hypokalaemic alkalosis, is caused by mutations in the thiazide-sensitive Na-Cl cotransporter. [Nat Genet](#). 1996 Jan;12(1):24-30

[Chang SS](#)...[Lifton RP](#). Mutations in subunits of the epithelial sodium channel cause salt wasting with hyperkalaemic acidosis, pseudohypoaldosteronism type 1. [Nat Genet](#). 1996 Mar;12(3):248-53.

[Simon DB](#)...[Lifton RP](#). Bartter’s syndrome, hypokalaemic alkalosis with hypercalciuria, is caused by mutations in the Na-K-2Cl cotransporter NKCC2. [Nat Genet](#). 1996 Jun;13(2):183-8.

[Kahle KT](#)...[Lifton RP](#). WNK4 regulates the balance between renal NaCl [Proc Natl Acad Sci U S A](#). 2004;101(7):2064-9.



Research Day

Medicine Research Day, May 1st 2006

Please mark your calendars and plan to attend our annual research day. Raghu Mirmira from the Division of Endocrinology will give Grand Rounds at Noon. The rest of the program will include oral presentations selected from submitted abstracts, and a poster session/reception. Abstracts may be submitted by residents, postdoctoral fellows (M.D. or Ph.D.), students (medical or graduate), and other laboratory personnel.

Please submit your abstracts as a Microsoft word attachment using font Times, size 11 to: Camilla Curnow CMT4J@hscmail.mcc.virginia.edu by **Friday, March 24**.



Funding Opportunities

NIH

NIH is offering an important new “Pathway to Independence Award Program”. This award is designed to help new investigators (post-docs and new faculty) obtain an R01 award earlier in their research career. The primary, long-term goal of the PI Award Program is to increase and maintain a strong cohort of new and talented, NIH-supported independent investigators.

This combined funding mechanism includes a two-year segment for the mentored post-doc, and a three-year segment for that person after she or he obtains an independent research position. An applicant must have no more than five years of postdoctoral training at the time of the initial application. Unlike most NIH training mechanisms, PIs do not have to be US citizens. **The first due date will be April 7, 2006**; thereafter, the program will follow the standard March/July/November deadline cycle.

For complete details of this award check:

<http://grants.nih.gov/grants/guide/pa-files/PA-06-133.html>.



UVa. Silvio O. Conte Digestive Health Research Center Pilot Feasibility Award Program-Call for Proposals

The *NIH-funded University of Virginia Digestive Health Research Center* offers a program to support new research initiatives in digestive diseases. The primary goal of the Pilot/Feasibility Award is to provide initial funds to develop new digestive health related research initiatives leading to submission of competitive grant applications to traditional funding agencies. Limited awards of up to \$25,000/year will be made to eligible applicants. **A letter of intent is due March 15, 2005 and the full proposal May 15, 2006.** Check out the 2005 recipients of this award in "Kudos section of this newsletter. For specific details and application procedures see the information included in this newsletter.

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Grants Corner

The new NIH salary cap for grant and cooperative agreement awards and extramural research and development contract awards is:

\$183,500 effective January 1, 2006 thru December 31, 2006

Additional information can be found at

<http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-06-031.html>

BE PREPARED! On-line submission of NIH applications is being phased in over 2006 and 2007. **June/July submissions of R21 and R03 applications must be submitted on line through Grants.gov.** Please note that timeline for R01 applications has been delayed a cycle and won't take affect until the Feb/March submissions. To see the complete new transition schedule:

http://era.nih.gov/ElectronicReceipt/strategy_timeline.htm

Learn more about electronic submission: <http://era.nih.gov/ElectronicReceipt/>

Looking for a piece of equipment or have equipment that you don't use anymore? The Office for Research is piloting a system by which older (but still useful) equipment can be advertised for transfer between School of Medicine units. The description of the system and a list of currently available equipment can be found at

<http://www.healthsystem.virginia.edu/internet/research/surplus.cfm>.

This can also be accessed via the Office for Research Web site, clicking on "Find research resources" and then on the first item on that next page.



UVa Silvio O. Conte Digestive Health Research Center Pilot Feasibility Award Program-Call for Proposals

Intent of Pilot Feasibility Awards:

The NIH-funded University of Virginia Digestive Health Research Center announces a program to support new research initiatives in digestive diseases. The primary goal of the Pilot/Feasibility Award is to provide the Awardee with initial funds to develop new digestive health related research initiatives leading to submission of competitive grant applications to traditional funding agencies.

Limited awards of up to \$25,000/year will be made to eligible applicants. Awards are intended to support preliminary data collection, which will be used in applications for future independent research grants in areas related to digestive diseases. A second year of funding may be requested and requires submission of a competing renewal application to the Digestive Health Research Center with demonstration of satisfactory progress and justification for a second year of funding.

Eligibility for Pilot Feasibility Awards:

Investigators who meet one of the three following criteria are eligible to apply:

- 1 New investigators without current or past NIH research project support (RO1 or PO1) as a principal investigator (current or past support from other sources should be modest).*
- 2 Established, funded investigators with no previous work in digestive diseases or digestive disease-related areas who wish to test the applicability of their expertise to a digestive disease-related problem.
- 3 Established investigators in digestive diseases or digestive disease-related areas who wish to test the feasibility of a new or innovative idea, which constitutes a significant departure from their funded research.

*Trainees who are recipients of an NRSA individual award (F32) or are supported by an institutional training grant (T32) are eligible for funds, but only if they are in their last year of training, have had at least one year of clinical or laboratory research experience, and have suitable expertise and independence to design and carry out the planned experiments. Trainees should have a commitment from a senior scientist to sponsor the project. Funds may not be used to supplement NRSA stipends, but may be used for supplies, technical support, special services, etc.

Application Procedure:

Interested investigators should submit a Letter of Intent by **March 15th, 2006** that includes the following:

- 1 1-2 page description of project aims and method of approach
- 2 NIH-format biographical sketch

Eligible candidates will then be notified and asked to submit a full written proposal in the general format of NIH research project applications (RO3), and including the following:

- 1 Eligibility category of the investigator
- 2 Abstract
- 3 NIH-format biosketch
- 4 Budget with brief budget justification (Salary support for the principal investigator and indirect costs are not allowed).
- 5 Facilities and resources available for performance of the proposed research
- 6 Research proposal (no more than ten pages), including the following:



UVa Silvio O. Conte Digestive Health Research Center

is proud to announce the

Pilot Feasibility Awardees

For

2005-2006:

Eric R. Houpt, Assistant Professor, Internal Medicine (ID)

“Source of Protective IL-10 in Innate Intestinal Inflammation”

William McIntire, Research Assistant Professor, Pharmacology

“The Effect of G Protein α , β and γ Subunit Composition on Adenosine A2b Receptor Signaling in Intestinal Epithelial Cells”

Margo R. Roberts, Associate Professor, Microbiology and Medicine

“Role of β -Adrenergic Receptors in Modulation of Intestinal Injury and Inflammation”

Julie Sando, Research Professor, Department of Anesthesiology Research

“Regulations of Ghrelin Structure and Function by Protein Kinase C”

Costi David Sifri, Assistant Professor of Medicine, Internal Medicine (ID)

“Candida Virulence Gene Identification Using *C. elegans* and Human Esophageal Candidiasis Model Systems”

David Wotton, Assistant Professor, Biochemistry Molecular Genetics

“Regulation of PPAR Gamma Levels and Activity by TGIF”



- Specific Aims
 - Relevance to digestive diseases
 - Background
 - Preliminary Data (if this proposal seeks to build on previous results)
 - Research Plan. Include within the research plan a discussion of any anticipated difficulties in the proposed experiments and potential alternative approaches.
 - References
- 7 If the applicant is currently a trainee, a letter of commitment from a senior scientist to sponsor the project should be provided.

**Format:**

The proposal must be single spaced, printed on one side only, with one-inch margins using 12-point type. The general format of an NIH research project application (RO3) should be used, including a detailed budget page (not the modular budget page in the new NIH form).

Applications must be received no later than **May 15, 2006**. Send the completed original application and eight copies to:

The Digestive Health Research Center
Pilot/Feasibility Research Award
c/o Dr. Steven Cohn
UVa Health System, MSB Room 2091B
P.O. Box 800708
Charlottesville, VA 22908

Review Criteria and Procedures:

The DHRC Executive Committee and an external advisory board will review applications. Preference will be given to proposals in the area of IBD/mucosal immunology, intestinal epithelial cell biology and GI infections.

The merit of each application will be judged using the following criteria:

- Novelty of the proposed research
- Relevance to digestive health
- Potential of the pilot/feasibility study to lead to future independent support

Award Conditions & Reporting:

The monetary award will be provided beginning **September 2006** and can only be used to support laboratory personnel, supplies, and limited domestic travel as detailed in the approved budget. Indirect costs are not allowed for this award.

All presentations and/or publications arising from the research project funded through this award must acknowledge support from the University of Virginia Digestive Health Research Center. Copies of all manuscripts, accepted abstracts, or grants arising from research funded through this award should be sent to the University of Virginia Digestive Health Research Center.

At the conclusion of the award, the recipient is required to submit a written summary of the research conducted, as well as a description of all funded, pending, or planned grant submissions arising from this award.

Kudos

Harini Bagavant, (Rheum), was awarded an R01 entitled "Autoimmunity and Pathogenesis of Glomerulonephritis"

Mike Brown (Rheum) has received his competitive renewal of his R01 "Molecular study of mouse viral resistance mechanisms".

John Chirgwin, (Endo), has received a grant from the Prostate Cancer Foundation entitled "PSA Regulates Bone Metastases through PTHrP Proteolysis: Preclinical Assay Development."

Rebecca Dillingham, (ID), will be funded for her work international HIV/AIDS by the Harvard Partners in Health Program directed by Paul Farmer, as well as play a major role in her and Dick Guerrant's new NIH Fogarty Center "Framework Grant in Global Health"

Larisa Gubareva, (ID), has received an R01 entitled "Luciferase-encoded influenza virus for antiviral screening."

Dick Guerrant (ID), was awarded the competitive renewal of the ICIDR (International Collaborations in Infectious Diseases Research) grant entitled "Long Term Impact and Intervention for Diarrhea in Brazil," through April, 2010. This is the 3rd competing renewal of this ICIDR that began in 1989.

Fred Hayden, (ID), received an Honor Award Certificate from the National Center for Infectious Diseases "For adding substantially to the body of scientific and public health knowledge regarding avian influenza."

Eric Houtp, (ID), has received a 3 year Basic Research Career Development Award from the Crohns and Colitis Foundation on the topic of "Control of Innate Intestinal Inflammation in Mice" an NIH STTR "Real-time PCR diagnostic kit for Giardia and Cryptosporidium", and NIH R21 "Multiplex bead-PCR Diagnosis for AIDS diarrhea"

Dean Kedes, (ID), has renewed his NIH R01 grant entitled "Structure and Molecular Characterization of KSHV and RRV" for 5 years.

Chris Moore, (ID), has received his K08 entitled "The effects of A2A adenosine receptor agonists in sepsis"

Emilie Rissman, (Endo), is President-Elect of the Society for Behavioral Neuroendocrinology.

Michael Scheld, (ID), has been funded on an SBIR grant with Adenosine Therapeutics entitled "Safety of Adenosine A2A Agonists for Treatment of Sepsis"

Recent Publications

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J.Linden and M. D. Okusa. Adenosine A2A Receptor Activation Attenuates Inflammation and Injury in Diabetic Nephropathy. Am J Physiol Renal Physiol. 2005 Dec 6, In press 2006.

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J Clin Endocrinol Metabol, 90 (10): 5684-5691.

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