

## Postdoctoral Research Enhancement Program



Dr. Kimberly Dunsmore

Dr. Ariel Gomez, Vice-President for Research and Graduate Studies has begun an initiative to organize and develop Post-Graduate Enhancement Programs at the University. This comes after much

discussion both nationally and at the University of Virginia concerning the postdoctoral community and its unique needs. The University's Research Policy Advisory Committee (URPAC) has spent a great deal of time over the past several years discussing postdoc and research associate issues at the University. The Faculty Forum on Scientific Research requested this topic be included on the URPAC agenda and supported the request with a thoughtful set of recommendations developed by the American Association of Universities (AAU). From discussions with UVA postdocs, faculty and administrators as well as a review of programs at other universities, it became clear that a central University individual was

needed to help coordinate postdoc activity across grounds. The Post-Graduate Enhancement Program will help coordinate postdoc activity and Dr. Kimberly Dunsmore will be the central UVA contact person. She can be reached by e-mail at [KPD6U@hscmail.mcc.virginia.edu](mailto:KPD6U@hscmail.mcc.virginia.edu)

The new program is designed to review policies concerning postdocs and to recommend changes to improve and enhance their postdoctoral experience at the University. The program will provide an office to act as a clearinghouse for information and aid. The office will facilitate and act as a liaison for postdocs with the appropriate University offices as needed. It will assist with postdoc administrative issues such as compensation, health insurance and benefits, issues concerning immigration visas, employment duration, job

opportunities and networking, research funding sources and grievance resolution. There are also plans to develop a comprehensive website and seminar series to further aid postdocs in their endeavors at the University.

The office is identifying the postdoc population as well as their concerns and is beginning to tackle some of the primary obstacles that postdocs face. Some of the primary issues being addressed include disparities in compensation, health insurance and benefits and visa issues. Enhancing the post-doctoral experience at the University will help to improve overall quality of research at the University and provide assistance to a very important component of our research effort. We are excited to get this program under way. ■

### Patent Foundation Announces New Software License

CircuSoft Instrumentation, LLC, (<http://www.circusoft.com>) a company focused on instrumentation for biomedical research, has recently licensed the rights to distribute Fluorescence Resonance Energy Transfer (FRET) data analysis software developed by Dr. Ammasi Periasamy and colleagues at UVA's W.M. Keck Center for Cellular Imaging. Since 1996, Periasamy has been the Director of the Keck Center which provides state-of-the-art optical imaging facilities to the University. Their FRET data analysis software allows the user to more easily see the dynamic behavior of specific proteins inside living cells and tissue by removing certain image artifacts. The result is a much more accurate determination of the energy transfer efficiency and distance between donor and acceptor molecules, two crucial measurements made by FRET microscopy. Periasamy and colleagues will host the 2003 Workshop on FRET Microscopy at the University of Virginia on March 5 – 9 ([www.cci.virginia.edu/FRET2003/index.php](http://www.cci.virginia.edu/FRET2003/index.php)). ■



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# Animal Research News: Mouse Hepatitis Virus

By Patricia Foley, DVM

In January of 2003, during routine health assessment of sentinel mice, viral antibodies to Mouse Hepatitis Virus (MHV) were detected in their serum. These mice were located in several rodent barrier colonies in different buildings and disparate room locations. This concerned the entire mouse research community

tremendously, because initially the Center for Comparative Medicine (CCM) did not know the source of the infection nor the extent of the outbreak. After extensive testing of mice in the breeding colonies themselves, and other sentinel mice, Dr. Feldman, Director of CCM, now believes that these mice came from one of the vendors, Hilltop Laboratories, already seroconverted and beyond their contagious period, as no seropositive mice other



Andrew Shurtleff

Patricia Foley

than sentinels have yet been found. The Advisory Committee to CCM reviewed the results of testing and concurred with Dr. Feldman. This committee mandated that shipments from the offending vendor be discontinued immediately. In light of this event and concern for a potentially devastating outbreak of MHV in our animal facilities, I am devoting this month's column to an overview of this virus and why it is of such concern to animal researchers.

**Epizootiology:** MHV is a pleomorphic, positive sense single stranded RNA coronavirus. *Mus musculus* is the natural host. There are many MHV strains, which differ in their tropism, tendency to disseminate, and virulence. Enterotropic strains replicate initially in the intestinal epithelium, tend not to disseminate, and usually are weakly virulent. "Polytropic" strains replicate initially in the respiratory tract, tend to disseminate to liver, brain, lymph nodes, etc., and are usually more virulent. MHV is extremely contagious, is prevalent among conventionally-housed mice, and outbreaks are not uncommon in "barrier maintained" mice, especially in multipurpose user facilities. Mice with active infection shed virus in feces and oral and nasal secretions. Transmission is by several routes, including contact, aerosol, fomites, and airborne particles of feces, bedding, etc. MHV is also a common contaminant of transplantable tumors and cell lines.

**Pathogenesis and Clinical Signs:** Adult immunocompetent mice with MHV infection rarely show clinical signs. Enzoitic subclinical infection is typical of conventional breeding colonies,

in which adults are immune, sucklings are passively protected, and infection perpetuated in weanlings that are partially protected by residual maternal antibody. Epizootic infection can cause diarrhea and death in neonates, and a wasting disease is typically seen in immunodeficient mice, such as athymic or SCID mice. In such mice, infection with virulent MHV strains can be rapidly fatal, while less virulent strains can cause chronic hepatic or intestinal disease. Factors, such as age, genotype, concurrent infections, and immune status all affect the course of the infection. For example, in suckling BALB/c and ICR mice, enteric strains such as MHV-Y can cause encephalitis. MHV infections induce strong immune responses in immunocompetent mice, which confers immunity to the infecting strain, but not necessarily to other viral strains.

**Diagnosis and Control:** Serology using ELISA with confirmation of positive results by IFA is the method most commonly used. One problem in acute outbreaks is that affected mice may not develop detectable antibodies for up to 10 days, or perhaps more, after initial exposure. In such cases, a direct detection method (reverse transcription PCR) can be very beneficial. A good health monitoring program is critical to detect the inevitable breaks. For barrier maintenance to work, technique must follow strict protocol. Coronaviruses are very susceptible to disinfectants, which disrupt the viral envelope, especially those with detergent activity. If infection occurs, the most effective option is elimination of affected colonies, and thorough decontamination of equipment and facilities. This highlights the importance of cryopreservation of valuable lines, or having known additional sources such as at another institution. Alternatively, immunocompetent mice only shed virus for 2 or 3 weeks, so infection can be eliminated by not introducing new susceptible mice for several weeks (i.e., stop breeding or purchasing). However, in this booming age of genetically modified mice, it is now impossible to tell which lines of mice will effectively shed infection permanently, from those that can remain latent carriers. Extreme care must also be taken to test all transplantable tumor and cell cells for the presence of rodent pathogens prior to use.

**Significance:** MHV is the single most important and common infectious agent of mice, at least in regard to their use as research subjects. More complications of research are known for MHV than any other agent. There are numerous studies documenting its impact in oncology, infectious disease, immunology, and physiology research. For a list of references on the impact of MHV in research, please contact Patricia Foley at [pfoley@virginia.edu](mailto:pfoley@virginia.edu).

An overview of the health surveillance program at University of Virginia can be found at <http://hsc.virginia.edu/research/ccm/docs/sentinel.htm>. Response to this latest incident at UVA included removing Hilltop from the list of approved vendors, use of wildtype immune competent mice generated from in-house breeding colonies as sentinel mice, and use of mice purchased from Taconic Farms (and pre-tested for presence of viral antibodies) in other mouse rooms. ■

## Cephalon and MDS Proteomics Announce Research Collaboration

Cephalon Inc. and MDS Proteomics Inc., a subsidiary of MDS Inc., located in the University's North Fork Research Park, have announced that they have entered into a five-year agreement that will utilize MDS Proteomics' technologies to further enhance Cephalon's drug discovery efforts. The collaboration covers a range of initiatives using MDS Proteomics' technologies with the objectives of accelerating the clinical development of Cephalon's pipeline of small molecule compounds.

Currently, most drugs act by binding directly to proteins or drug targets that are associated with a particular disease, thereby modifying both the activities of the proteins and their cellular pathways. MDS Proteomics' proprietary technology enables observation of proteins and interactions not only to understand the underlying causes of disease but also to develop new drugs and diagnostic products.

The companies will collaborate and use MDS Proteomics' technologies including the application of differential analysis, chemiproteomics, phosphorylation fingerprinting (PhosMapT) and protein interaction mapping (PathMapT) to expand the potential disease indications for Cephalon's development compounds, maximizing the potential of Cephalon's proprietary chemical library, and identifying novel targets implicated in and critical for the pathogenesis of

diseases of the central nervous system.

"We believe this collaboration has the potential to significantly enhance Cephalon's drug discovery efforts, particularly in the neurosciences," said Jeffrey Vaught, Senior Vice President and President of Research and Development at Cephalon. "Working with MDS Proteomics will enhance our

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Jeffrey Vaught  
Senior Vice President  
and President of Research and  
Development at Cephalon.

technological base for identifying and validating disease relevant therapeutic targets."

MDS Proteomics employs over 175 people in its next-generation proteomics facilities in Europe and North America. The company focuses on antibody and small molecule therapeutics and presently has a number of candidate targets in pre-clinical discovery. ■

## New Ultrasound Device Licensed by Carilion Biomedical Institute

The Carilion Biomedical Institute (CBI) has recently licensed intellectual property covering a new low-cost ultrasound device being developed by the Virginia Medical Ultrasound Technology Group. This device, which the team has named the "Sonic Window," will be smaller than a deck of cards, cheaper than most PCs, and simple enough that a child can use it. The Sonic Window is intended to open the application of ultrasound to routine tasks such as the introduction of intravenous lines. The team, including William F. Walker and John A. Hossack of Biomedical Engineering and Travis N. Blalock of Electrical and Computer Engineering, has fabricated prototype integrated circuits and intends to demonstrate a full system prototype by the summer. CBI is currently assessing commercialization options including partnering with an existing corporation or forming a new venture. ■

## Teachers For A New Era Award from Carnegie Foundation

A \$5M grant has been awarded for the Teachers for a New Era program by the Carnegie Foundation. Dean David Breneman, Dean Edward Ayres and a team of faculty were involved. It will be a collaborative effort between the Curry School of Education and the School of Arts and Sciences. U.Va. is one of five universities selected to participate in this award. Victor Luftig, director of the Center for the Liberal Arts, is the PI. ■

**Cost Accounting Standards (CAS)**

In most basic terms, federal cost accounting standards, or CAS, are a series of federal regulations that stipulate how educational institutions must administer the financial aspects of grants they receive.

The Federal Office of Management and Budget (OMB) Circular A-21 is the governing federal document that specifies the expectations and restrictions of the cost accounting standards, and this can be viewed at [www.whitehouse.gov/omb/circulars/a021/a021.html](http://www.whitehouse.gov/omb/circulars/a021/a021.html)

Contact Vonda Durrer (924.4031) if you have questions concerning Cost Accounting Standards, and contact Carole Wagonhurst (924.6346) if you want to request training on CAS in your area or department.

**Gifts**

These are defined as a unilateral transfer of money, property, or other assets to the recipient for the recipient's ownership and use, by a donor who makes no claims on the recipient in connection with the gift. Gifts normally have the following characteristics:

- *The statement of work allows the project director significant freedom to change emphases within the general area of work as the project progresses.*
- *No deliverables are involved.*
- *Separate accounting procedures are not required.*
- *Benefits of the project are to accrue to the nation or the world.*
- *The sponsor or donor has no rights to audit the use of the gift.*
- *No regulatory issues are involved, such as human subjects or animal care.*

Contact Gerry Kane (924.6142) for additional information.

## Virginia's Center for Innovative Technology (CIT) Announces the FAST Partnership Program

If you are seeking SBIR/STTR federal funding to support your company's development and commercialization plans, then CIT's FAST Program may be able to help you. The FAST Program provides proposal assistance, business advisory services, training, and financial awards to assist you with successful SBIR and STTR grant proposals. Resources include:

- **Business Advisory Services** - Awards up to \$2,500 for business advisory services including commercialization plans, product development strategy, financial statement analysis, market/competitive analysis.
- **SBIR/STTR Proposal Assistance Awards** - Awards up to \$2,500 for assistance with SBIR and STTR proposal reviews by experienced and successful grant writing consultants.
- **Proposal Writing Software** - Discounts off of proposal preparation software & solutions that help ensure compliant proposals.
- **Innovation Award** - Award up to \$30,000 for use in project support for final phase of technology development life-cycle.
- **Business Plan Development** - Offering NxLevel Training, a 10-12 session course providing practical, hands-on approaches to developing a small business. Combines education,

*counseling, and networking to help potential entrepreneurs plan for their next level of success. Course fee reimbursed for companies considering SBIR funding.*

- **TechStart Bootcamp** - One-day course providing valuable overview in important topics including: How to grow your tech business, acquire R&D money, develop business connections, licensing your product, intellectual property protection, financing an early-stage tech company, business planning, and much more! Check out [www.cit.org](http://www.cit.org) for complete event schedules.
- **Mentoring and Guidance Support** - Engage with SBIR/STTR experienced companies in mentoring relationships to enhance your chance of successful commercialization of SBIR/STTR-funded technologies.

For more information about CIT's FAST Program and assistance with SBIR and STTR funding opportunities, please contact CIT's FAST Partnership Program Managers or CIT Regional Director:

Joe Schmidt, Central Virginia  
434-982-3756  
[joeschmidt@virginia.edu](mailto:joeschmidt@virginia.edu)

For CIT Regional Directors –call 1-800-3TECHVA or go to [http://www.cit.org/award\\_assist.asp#fast](http://www.cit.org/award_assist.asp#fast)

# New Regulations on Possession, Use, and Transfer of Biological Agents and Toxins

On December 13, 2002, the Centers for Disease Control and Prevention (“CDC”) and the Animal and Plant Health Inspection Service (“APHIS”) published regulations required by the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 and Agricultural Bioterrorism Act of 2002. These regulations govern the use, handling, and transfer of certain biologically hazardous bacteria, viruses, toxins, and nucleic acids. The full list can be found on the Centers for Disease Control web site at [www.cdc.gov/od/sap/docs/salist.pdf](http://www.cdc.gov/od/sap/docs/salist.pdf)

The regulations apply primarily to select agents in isolated form. Naturally occurring select agents, such as soil samples, infected animals and plants, and infected tissue samples, are exempt until they have been isolated. If tests reveal select agents in such contexts, they must be reported to the CDC or APHIS, and the samples either transferred to a registered facility or destroyed.

All facilities handling select agents must register with and be certified by CDC or APHIS. Under the prior select agent regulations, registration was required to transfer a select agent. The new regulations implement the Act’s direction that possession and use also be controlled

## Safety and Emergency Plans

Each facility must complete and implement safety and emergency plans, based largely on existing law, such as NIH’s Recombinant DNA Guidelines and the CDC/NIH publication, Biosafety in Microbiological and Biomedical Laboratories.

## Biocontainment and Security Plan

The plans must be developed commensurate with the risks (e.g., risks of escape, transmission, toxicity) of the select agents at the facility and must include the following elements, among others:

- *Physical security, including physical separation of areas in which select agents are located*
- *Cyber security*
- *Training for all employees, guests, and visitors, including verification systems*
- *Educational and experience criteria for employees*
- *Reporting requirements for a variety of problem situations*
- *Protocols for internal lab-to-lab transfers*
- *Inspection of packages on entrance/exit*
- *Inventory control of select agents*
- *Documentation of each person’s entry into and exit from select agent area*
- *Provisions for routine cleaning, maintenance, and repairs*
- *Provisions for reporting suspicious persons and activities*

## Key dates for Compliance:

### **2/7/03 for CDC/ 2/11/03 for APHIS:**

- *Name Responsible Official and any alternates*
- *Complete and implement Safety and Emergency Response Plans*
- *Develop and implement recordkeeping procedures, including list of approved individuals, current inventory, training records, and access and use documentation*
- *Begin HHS notifications for theft, loss, and release of select agents*
- *Safety/emergency response training begins (subject to grandfather certifications)*

### **3/12/03:**

- *Apply for registration under the new regulations. Registration under the previous law remains valid until November 12, 2003, provided that the March 12, 2003 deadline is met under the new regulations.*
- *Apply for DOJ approval for facility, responsible official, and any alternates*
- *Transfer requirements, including prior approval of transfers between facilities*

### **4/11/03 for APHIS/ 4/12/03 for CDC:**

- *Apply for DOJ approval for all employees*

### **6/12/03:**

- *Develop security plan*

### **9/12/03:**

- *Implement security plan*
- *Implement training for security plan*

### **11/12/03:**

- *Registration process to be complete and in full compliance. Failure to receive approval by this date means that possession of select agents is no longer permitted.*

These guidelines have been prepared with the assistance of the CDC web site and the National Association of College and University Attorneys. To discuss these new regulations or for further information, please contact the University’s Biological Safety Officer, David Easton at 982-4909 or [dne2a@virginia.edu](mailto:dne2a@virginia.edu) ■

# Major New Cancer Grant

A new type of research group called the Cancer Cube was formed 5 years ago by the NIH and has met twice yearly since then. Investigators from eighteen medical centers are involved in the Cancer Cube, and now an award of \$5,600,000 over four years has been made to determine the cause of breast cancer and to develop new means of prevention. Investigators from eighteen medical centers are involved. This grant is entitled *Estrogen induced depurination of DNA; a novel target for breast cancer prevention*. Cancer Cube investigators have now received funding under the Department of Defense Breast Cancer Centers of Excellence Program. The grant is shared by the Eppley Cancer Center in Omaha, the Fox Chase Cancer Center in Philadelphia, the University of Virginia Cancer Center, the Mayo Clinic, The Stehlin Institute in Houston, and the University of Memphis.

The key concept to be studied is that estrogens are metabolized to compounds that directly cause DNA damage and lead to genetic mutations. When a sufficient number of these mutations have developed, cancer results. By blocking the production of estrogens, this process is prevented. Various aspects of this hypothesis will be tested. Since the application was submitted, a large clinical trial has provided additional data that suggests that the estrogen-toxic



Andrew Shurleiff

**Dr. Richard Santen and his cancer research group:**

***l. to r.: Amanda Lynch, Robert Song, Zhenguang Zhang, Robert McPherson, Wei Yue, Dr. Richard J. Santen, Peggy Nees, Ji-Ping Wang, Ya Hua Li***

metabolite hypothesis may be correct. The PI for the grant at U.Va. is Dr. Richard Santen, who will work collaboratively with Drs. Wei Yue and Jiiping Wang. ■

## researchnews

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*Editor*

Prudence Thorne

*Contributors*

David Easton, Dr. Patricia Foley,  
Joe Schmidt, Carole Wagonhurst

*Photography*

Tom Cogill

*Graphic Design*

Richard Montoya Design



Office of the Vice President for  
Research and Graduate Studies  
UNIVERSITY OF VIRGINIA

P.O. Box 400301  
314 Madison Hall  
Charlottesville, VA 22904-4301  
(804) 924-3606

Web site:

[www.virginia.edu/researchandpublicservice/researchnews.html](http://www.virginia.edu/researchandpublicservice/researchnews.html)