

## INSIDE THIS ISSUE

<i>From the Director</i>	1
<i>Biomedical Mass Spectrometry Laboratory: Exploring the Molecules of Life</i>	2
<i>NIH Announces First National Research Study Recruitment</i>	4
<i>The CTSI Web Portal: The Right Technology at the Right Time</i>	5
<i>Pilot Project Grants Awarded</i>	6
<i>NIH Student Internship Opportunity</i>	8
<i>The Last Page....</i>	9

## FROM THE DIRECTOR

**W**e have several holiday treats stuffed in this issue of the CTSI Newsletter, from molecular phenotyping through metabolomics to research opportunities at NIH for students. There's also a wonderful new resource, called Researchmatch, that connects investigators to patients interested in participating in clinical trials. An update on the CTSI's Research Portal fills the stocking. Last of all, we have specially gift-wrapped the announcement of awards from those who applied to our latest RFA for seed funds to jump-start new clinical and translational research initiatives.

The CTSI will be taking an extended holiday break next month, so the Newsletter will resume in February. In the meantime, all of us in the CTSI extend our very best wishes to you for a Holiday Season filled with health, happiness and peace.

Happy Reading!



Peter W. Stacpoole, PhD, MD  
Director, Clinical and Translational Science Institute  
Associate Dean for Clinical Research and Training

BIOMEDICAL MASS SPECTROMETRY LABORATORY:  
EXPLORING THE MOLECULES OF LIFE

BY PAULA RAUSCH

**S**uperman and Ironman have joined forces with UF researchers in the battle to unravel the chemical complexities of the human body.

They are the aptly nicknamed newest and oldest analytical instruments in the UF's Biomedical Mass Spectrometry Laboratory. Superman, the newest member of the lab's team, got its moniker because of its increased capacity, and better, faster and cheaper technology, while after a decade of demanding labor, Ironman is still churning out data about some of the body's most mysterious compounds and processes. The Mass Spectrometry lab is one of four facilities that comprise the CTSI's Metabolomic Core – which also includes existing the Chemistry and Analytical Toxicology labs and one planned in Nutrition – where scientists study the chemical processes involving the byproducts of metabolism in living organisms.

In conjunction with their human colleagues, Superman, Ironman and four other mass spectrometry instruments work to help increase understanding of the small molecules contained in blood and urine and the body's other biological fluids by determining their chemical compositions and structures. The purpose of the laboratory is to aid UF researchers in developing procedures for testing and measuring the activity of these molecular compounds, which ultimately will result in better care and treatments for patients with a variety of diseases and conditions, including cancer, Alzheimer's, and organ transplantation, said Dr. Tim Garrett, PhD, the laboratory's director.

“Mass spectrometry can't necessarily solve everything but it can solve a lot of puzzles, and so it's one of the more widely used analytical tools because of its high sensitivity and specificity,” he said. Part of the goal of the lab is to work with researchers to develop a way to analyze small molecules within a body fluid that would provide some measure of progression, status or other clinical marker of the disease being investigated, and then if it works in a research setting to move it into a clinical diagnostic application, he said.

Dr. Garrett and two senior doctoral-trained chemists who staff the Mass Spectrometry lab help to identify the molecular information that's contained in a fluid and the best approach for measuring it, and then analyze the samples collected through the study, and quantify the data. Once they know the concept a researcher is interested in investigating, the chemists conduct research and literature reviews to see if it has been measured previously, and what has and hasn't worked. If it hasn't been measured before, they try to figure out a way to do it. This method development stage is the most difficult and time consuming, and depending on how difficult the procedure is, how many chemical components are involved, and the problems that may come up along the way, it sometimes can take several months even for the lab's molecular experts.

One project with which Dr. Garrett and the Mass Spectrometry lab are currently involved is a pediatric liver transplantation study, in collaboration with Dr. Vikas Dharnidharka, investigating the amino acid tryptophan, and one of its metabolites called kynurenine in blood and urine. These compounds measure the activity of the immune system, but have also been linked to changes in the brain associated with Alzheimer's and Parkinson's diseases. How the tryptophan is broken down by the body can determine whether the byproducts – or metabolites – of these compounds are beneficial or toxic, and understanding those processes is important for the clinical care of patients.

“In this organ transplantation project, if a patient's immune system is activated [as measured the by ratio of kynurenine to tryptophan] that means they may be rejecting the organ,” he said. “We want to know before rejection occurs,” so what we're trying to figure out is a technique – or assay – that can be used in clinical situations to monitor and measure a patient over time before a rejection occurs so it can be predicted, prevented or handled more effectively.

“It's just preliminary right now so we don't know, but hopefully that will be a measure of success or failure of the organ transplantation” that would eventually be a diag-

## BIOMEDICAL MASS SPECTROMETRY LABORATORY: EXPLORING THE MOLECULES OF LIFE

nostic measure for all transplant patients, Dr. Garrett said. “There are some studies that seem to suggest that it will be useful, but we don’t know right now.”

He and the Mass Spectrometry lab also are involved in a joint UF-Moffitt Cancer Center project investigating tryptophan and kynurenine with respect to breast cancer prognosis, through a similar approach, he said. The study is looking at whether the assay can be used to determine if the immune system plays a critical role in cancer prognosis and treatment using banked human blood samples. Dr. Garrett expects to examine other metabolites of tryptophan as well, including quinolinic acid, which has been found in elevated concentrations in the brains of people with Alzheimer’s.

“What we want to do is measure not just two analytes [components], we want to measure multiple analytes in one pathway – multiple molecules that are related by metabolism or structure,” Garrett said. “We want to understand tryptophan metabolism better and that’s where metabolomics comes in.” This also has value for measuring drugs that may be used in these conditions as well as in examining them to determine the pathways they follow in the body to see how they are working.

Mass spectrometry is a complex technique that measures ions, which are positively or negatively charged particles. Only a very small sample of blood or fluid is needed, yet the technique can provide very specific information about

a host of small molecules and their components. After the proteins have been precipitated out of a sample (proteins are not small molecules and so are analyzed in a different lab), Superman or another mass spectrometer utilizes the liquid portion to generate charged molecules or molecule fragments and then measures the mass of this charged species (mass-to-charge ratio). These measurements can be used to determine the composition or structures of a sample or molecule and quantify the precise amount present.

At any given time, the Mass Spectrometry lab is assisting with seven to 10 studies, but Dr. Garrett hopes to make the lab a resource for more researchers. He welcomes those involved in studies that may benefit from molecular analysis to talk with him or the Mass Spectrometry lab’s other chemists. They will not only help identify the best

technique for analyzing the molecular substances of specific interest, but also can provide insight on other related substances that may be valuable in a study. In addition, the staff can suggest ways to properly prepare samples to ensure they are usable, including when it should be drawn, and whether it must be frozen or contain preservatives in order to ensure the samples are usable.

“We want investigators to know that we’re here to help them,” Garrett said, by providing support and advice that can assist them in making their next conclusion or perhaps in getting their next grant.



Dr. Tim Garrett, director of UF’s Biomedical Mass Spectrometry Laboratory, stands next to “Superman,” the lab’s newest instrument for analyzing blood and other biological fluids. Superman is a mass spectrometer that has enhanced sensitivity, and can identify and measure compounds in samples in about half the time and more cheaply than some older models.

## NIH ANNOUNCES FIRST NATIONAL RESEARCH STUDY RECRUITMENT REGISTRY

### *Nationwide Registry to “Match” Volunteers with Researchers*

**I**ndividuals who want to participate in research studies now can connect online with researchers nationwide through the first disease-neutral, volunteer recruitment registry.

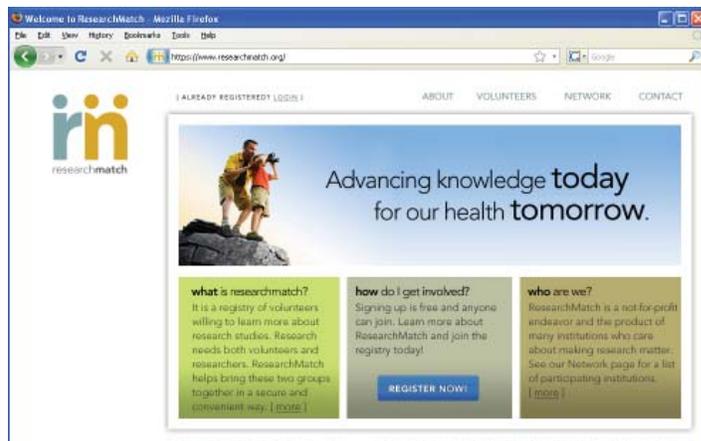
Researchmatch.org is a not-for-profit secure Web site, designed to provide people who are interested in participating in research the opportunity to be matched with studies that may be the right fit for them.

Researchmatch offers an easy-to-use, free and safe way for volunteers to connect with thousands of researchers who are conducting research on a wide range of diseases.

The site is a collaborative effort of the national network of medical research institutions affiliated with the Clinical and Translational Science Awards (CTSAs). The CTSA program, which is led by the , a part of the National Institutes of Health, is focused on enhancing local and national efforts to enhance the translation of laboratory discoveries into treatments for patients.

“Participant recruitment continues to be a significant barrier to the completion of research studies nationwide - recent NIH data indicates that just 4 percent of the U.S. population has participated in clinical trials,” said NCRR Director Barbara Alving, M.D. “Researchmatch is a tool that can improve the connection and communication between potential participants and researchers providing opportunities for the public to contribute to advancing new treatments.”

The convenient and user-friendly registry employs a familiar research matching model that is complementary to Clinicaltrials.gov. One key difference is that Researchmatch places the burden of connecting the right volunteers with the right study on the researchers, whereas Clinicaltrials.gov asks volunteers to identify the trials that could work for



them.

“Researchmatch offers a convenient solution to the complex, competitive and often costly participant recruitment system,” said Gordon Bernard, M.D., principal investigator of the Vanderbilt CTSA, which hosts the national registry. “NIH data indicates that 85 percent of trials don’t finish on time due to low patient participation, and 30 percent of trial sites fail to enroll even a single patient. We aim to help combat these challenges with Researchmatch.”

### *How Researchmatch Works*

Researchmatch will match any interested individual residing in the United States with researchers who are approved to recruit potential research volunteers through the system. After an individual has self-registered to become a volunteer, Researchmatch’s security features ensure that personal information is protected until volunteers authorize the release of their contact information to a specific study that may be of interest to them. Volunteers are notified electronically when they are a possible match and then make the decision regarding the release of their contact information. It also will promote choice as there are no obligations on the volunteer to participate in studies.

## NIH ANNOUNCES FIRST NATIONAL RESEARCH STUDY RECRUITMENT REGISTRY cont.

For the first year of the project, only researchers affiliated with participating CTSA institutions are eligible to use ResearchMatch. However, plans are in place to make ResearchMatch available beyond the CTSA consortium by 2011. Currently 52 individual institutions associated with 40 CTSA sites are part of the ResearchMatch network. A list of these institutions may be viewed here ([http://ncrr.nih.gov/clinical\\_research\\_resources/clinical\\_and\\_translational\\_science\\_awards/researchmatch](http://ncrr.nih.gov/clinical_research_resources/clinical_and_translational_science_awards/researchmatch)).

To learn more about ResearchMatch and to register as a volunteer, visit: [www.researchmatch.org](http://www.researchmatch.org).

## THE CTSI WEB PORTAL: THE RIGHT TECHNOLOGY AT THE RIGHT TIME

**T**he nascent Web portal is the virtual home for the CTSI, providing quick and easy access to a variety of resources beneficial to translational scientists. The portal was developed by the Clinical and Translational Research Informatics Program (CTRIP) and is administratively housed within the Regulatory Knowledge and Research Support (RKRS) core of the institute. As envisioned in the CTSA grant, the portal is eventually intended to provide access to many CTSI activities and services, and currently contains the following:

- The latest News & Events in translational research;
- CTSI Lecture Series announcements and archived seminar videos;
- Repository of CTSI Newsletters;
- Online course registration and document repository for GMS 7093: Intro to Clinical/Translational Research;
- Up-to-date information about each CTSI program, its goals and contact information for program leads;
- Quick Links to local and national resources on interest;
- Shands Clinical Research Unit electronic protocol applications and consultation request forms;
- Details about current funding opportunities as well as prior awardees;
- Connection to ResearchMatch research volunteer network;
- CTSI Annual Report upload mechanism.

In all, it has been a successful four months since the portal 'went live', but much more is planned in the near future. As we move into year two of the CTSA, additional features will be rolled-out, including document sharing & collaboration tools, distributed content management and the implementation of workflows to facilitate processes that currently take place via less efficient methods.

We look forward with excitement to building new portal tools that will benefit translational research here at UF. Got an idea? We'd love to hear it. Provide your feedback here.

## PILOT PROJECT GRANTS AWARDED

In September we announced an RFA for seed money support through our Pilot and Collaborative Projects Program. We received 38 proposals by the September 16 deadline for receipt of applications. The Programs' Executive Committee made the following awards on December 1, 2009 with funding available by December 1, 2009.

## CTSI Pilot and Collaborative Project Program Awards (December, 2009).

Category Awardee	Academic Affiliation	Title of Project	Award
<b>Graduate Student</b>			
Emily Plowman Prine	College of Medicine	Neural Mechanisms of Oral Motor Dysfunction in an Animal Model of Parkinson's Disease.	\$ 7,500
Catherine Marcinkiewicz	College of Medicine	Elucidating the role of the organic cation transporter 3 (OCT3) in the pharmacological response to antidepressant treatment.	\$ 7,500
<b>Junior Faculty</b>			
Azra Bihorac, M.D.	College of Medicine	Hypoxia-induced angiogenic factors, progenitor endothelial cells and urinary markers of hypoxic injury as an early tool for the assessment of endothelial injury and repair in severe trauma and hemorrhagic shock.	\$ 15,000
Ginger Clark, M.D. M.S.	College of Medicine	Assessment of Liver Test Abnormalities in Adults with Alpha-1 Antitrypsin Deficiency.	\$ 20,000
<b>Major Initiatives Program</b>			
Michael Haller, M.D.	College of Medicine	Reversing Type 1 Diabetes After it is Established: A Pilot Safety and Feasibility Study of Anti-Thymocyte Globulin (Thymoglobulin®) and Pegylated GCSF (Neulasta®) in Established Type 1 Diabetes.	\$ 49,668
Hartmut Derendorf, Ph.D.	College of Pharmacy	Pharmacokinetic / Pharmacodynamic Modeling of the Psychomotor Vigilance, Simulated Driving, Go/No-Go Performance, and Electroencephalogram Effects of Armodafinil in Sleep Deprived Healthy Adults.	\$ 62,250
John F. Valentine, M.D.	College of Medicine	Genetic and Microbial Interactions in Crohn's Disease.	\$ 48,921
Roger B. Fillingim, Ph.D.	College of Dentistry	Effects of OA-Related Pain on Telomere Length and Telomerase Activity.	\$ 38,938
C. Leeuwenburgh, Ph.D.	College of Medicine	Diaphragm Mitochondrial Dysfunction During Prolonged Mechanical Ventilation.	\$ 45,869
Erin M. Dunbar, M.D.	College of Medicine	Phase I, Open-Label, Single-Arm, Clinical and Metabolic Study of Dichloroacetate DCA in Adults With Recurrent Malignant Brain Tumors.	\$ 54,861

## PILOT PROJECT GRANTS AWARDED

CTSI Pilot and Collaborative Project Program Awards (December, 2009) (Continued).

Category	Academic Affiliation	Title of Project	Award
Major Initiatives Program			
Awardee			
Connie J. Mulligan, Ph.D.	College of Liberal Arts and Sciences	Pilot investigation of the role of epigenetic methylation in mediating risk of hypertension in a study population of African Americans in Tallahassee.	\$ 47,655
Novel Methods* and Technology			
Peter P. Sayeski, Ph.D.	College of Medicine	In vivo characterization of a novel Jak2 tyrosine kinase inhibitor for the treatment of Jak2 mediated human pathologies.	\$ 25,000
Mark D. Tillman, Ph.D.	College of Health and Human Performance	Wheelchair Ergonomic Hand Drive.	\$ 24,756
			Total \$ 447,917

\*Multiple co-investigators and/or colleges were represented by these proposals, but only the PIs and their colleges are listed.

Congratulations to the awardees! Competition was stiff and many meritorious proposals could not be funded. For those who did not apply or who were unsuccessful this round, we plan to announce the next RFA in the Spring of 2010.



ResearchMatch.org

## NIH RESEARCH INTERNSHIP AT BOSTON CHILDREN'S HOSPITAL

*NIH Student Research and Education Awards  
Mental Health & Developmental Disabilities (MH/DD)  
Children's Hospital, Boston, Harvard Medical School*

The National Institute of Mental Health (NIMH) sponsored Mental Health & Developmental Disabilities (MHDD) Research and Education Program based in the University Center for Excellence in Developmental Disabilities (UCEDD) at the Children's Hospital Boston, in collaboration with Harvard Medical School and the Institute for Community Inclusion, invites applications for NIH Student Internship Awards. These internships aim to stimulate interdisciplinary research interests and early experiences in mental health aspects of developmental disorders affecting children, adolescents, and young adults. The program includes participation in a research education practicum with mentored-experience, participation in relevant lectures and coursework. The program activities are expected to lead to scholarly presentation and peer-review publication.

There are two levels of awards for medical students:

(1) NIH Summer Internships in MH/DD for end-of-first-year medical students with a seven-week full-time commitment in Boston usually from mid-June to end of July. Awardees receive a \$4,000 stipend plus support for well-justified travel to conduct scientific presentations. (2) NIH Scholars Program in MH/DD for more advanced year medical students (3rd year or above) interested in developing in-depth national or international research projects related to MH/DD. Awardees receive a flexible stipend that is pro-rated to the duration of their program commitment. Awardees may also receive support for additional research related coursework and well-justified travel for scientific presentations.

Eligibility: US citizenship or permanent resident status is required. Women, minorities and individuals with a special commitment to disabilities affecting developing children are particularly encouraged to apply. Eligible applicants should submit: (1) an up to date CV; (2) official copy of college and medical school transcripts; (3) two letters of reference (one from a current academic dean/faculty adviser); and (4) a personal statement (500 words) describing interest in MH/DD and related interests. Applications are rolling. Applications received by February 15 will be decided by March 1.

Areas of study include research projects on autism spectrum disorder, intellectual disabilities, or related mental health aspects of behavioral phenotypes of known genetic and metabolic developmental disorders. Clinical, epidemiological, operational, services, policy, and/or research ethics questions in MH/DD are particularly welcome.

For inquiries and applications please contact:

Dr. Kerim Munir, Program Director ; Beverley Gilligan, Program Coordinator

Division of Developmental Medicine & Department of Psychiatry

Children's Hospital Boston, 300 Longwood Avenue

Boston, Massachusetts 02115

Tel 617 818 1853; Fax 617-730-0049

E-mail: [kerim.munir@childrens.harvard.edu](mailto:kerim.munir@childrens.harvard.edu) ; [beverley.gilligan@childrens.harvard.edu](mailto:beverley.gilligan@childrens.harvard.edu)

## THE LAST PAGE . . . .

### *Employment*

Did you know that there are multiple venues through which both internal and external jobs are posted?

### *For Job Seekers*

<https://jobs.ufl.edu> - University of Florida jobs postings.

<http://www.union.ufl.edu/jobs/> - Reitz Union student job listings.

<http://www.sfa.ufl.edu/programs/workstudy> - Federal Work-Study Program.

<http://www.sfa.ufl.edu/programs/ops.html> - Other Personnel Services jobs.

<http://www.sfa.ufl.edu/programs/oce.html> - Off-Campus jobs.

<http://www.sfa.ufl.edu/programs/vaworkstudy.html> - Veteran's Affairs Work-Study.

### *Subscribe to the CTSI Listserv*

Ensure that you receive future editions of this Newsletter by subscribing to the CTSI-ANNOUNCE-L Listserv.

It's quick and easy to do and will allow you to also receive other CTSI announcements as they are distributed.

To subscribe, simply send an email to [listserv@lists.ufl.edu](mailto:listserv@lists.ufl.edu) with the message:

**SUBSCRIBE CTSI-ANNOUNCE-L your-first-name your-last-name**

### *Publication Acknowledgement*

For all publications, CTSI investigators and trainees should remember to acknowledge the CTSI thusly:

This work was supported in part by NIH grant 1UL1RR029890 (Clinical and Translational Science Award)