

WORD ON THE STREET

THE NEWSLETTER OF THE DEPARTMENT OF MEDICINE

JANUARY/FEBRUARY 2008



THE FIRST WORD

ROBERT M. STRIETER, MD
CHAIRMAN

2008 has been off to an excellent start for the Department of Medicine. I am pleased to announce that our search for a new division chief for Cardiovascular Medicine has been successful. Dr. Brian Annex, currently a Professor of Medicine at

Duke University, has accepted our offer, and he will be joining our team this summer. I would like to thank Dr. Gary Owens and Heather Weller for their efforts on behalf of the search committee. I would also like to take a moment to acknowledge the excellent leadership of Dr. George Beller, who has served as interim



Chief of Cardiovascular Medicine since last April. Dr. Beller's able leadership made it possible for the committee to take the time needed for a thorough search that resulted in such an excellent conclusion. My thanks to everyone involved. National searches for the division chief positions in Endo-

crinology and Gastroenterology will begin shortly. The Department leadership will see another change this summer, with the retirement of Michael Rein after more than three decades at UVa. Dr. Amy Tucker will assume Dr. Rein's duties as Associate Chair for Undergraduate Medical Education. Dr. Tucker is an Associate Professor in the division of Cardiovascular Medicine, and Co-Director of the Congenital Heart Program. She has a long history at UVa, having completed both her residency and fellowship training here. Dr. Tucker will officially assume her duties this summer, but has already begun learning the intricacies of undergraduate medical education from Dr. Rein.

Finally, I would like to take this opportunity to introduce everyone to the UVa Department of Medicine Research Fund. This fund is intended to raise money for seed grants in biomedical research within the Department. As we all know, research dollars must be stretched further each year, and this research fund is a way for the Department to support its own faculty. Many of our faculty have already started donating to the Fund, and I would like to encourage everyone to give if possible. The DoM Research Fund will also be an available charity option for the CVC "red envelope" payroll deduction donations. If you have questions about the Fund, please contact Sue Moenter.

CONGRATULATIONS

Terri Washington was named School of Medicine Employee of the Month in February. Terri has worked for UVa for eight years, and has been with the Department of Medicine for the last two, where she is a key member of the administrative staff.

DATES AND DEADLINES

MARCH 7-8, 2008

ACP Virginia Chapter Scientific Meeting

APRIL 28, 2008

Carey, Marshall, Thomer Scholars' Day

MAY 30, 2008

DoM Research Day

MEDICAL GRAND ROUNDS

UPCOMING SPEAKERS:

MARCH 11

AVAL GREEN—GENERAL MEDICINE,
GERIATRICS, AND PALLIATIVE CARE

MARCH 18

ELIZABETH HENSKER—VISITING

MARCH 25

GERALD DONOWITZ—INFECTIOUS DISEASES
AND INTERNATIONAL HEALTH

APRIL 1

JOHN BELPERIO—VISITING

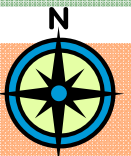
[Click to view the full schedule](#)

NAVIGATION

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- EDUCATION 5
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BESS WILDMAN

BILL INCLUDES FEE CUT REPRIEVE TO JULY

President Bush signed the Medicare, Medicaid and SCHIP Extension Act of 2007 into law Christmas week, and it includes a gift for providers worried about an expected 10.1 percent cut to payments.

The Medicare, Medicaid and SCHIP Extension Act of 2007 provides for a 0.5 percent increase to the physician fee schedule conversion factor for dates of service beginning January 1 through June 30, 2008, *instead* of the -10.1 percent that was scheduled to take place. Effective for dates of service on and after July 1, 2008, the -10.1 percent update to the physician fee schedule will go into effect. The new fees will be posted on your local contractor's website as soon as possible.

Since there is a change to the 2008 Medicare Physician Fee Schedule rates, CMS is extending the Participation Decision Period an additional 45 days. The participation decision period now runs through February 15, 2008, instead of ending on December 31, 2007. All participating status changes will be effective January 1, 2008.

ASSIGNMENT OF PALLIATIVE CARE CODE TO PATIENT MEDICAL RECORD

Definition: Palliative care is comfort care provided to patients in the final stages of an illness who are no longer receiving curative and/or aggressive treatment.

Purpose: UVA Health System defines guidelines for coding and documentation for patients that are provided palliative care within the inpatient setting.

Background for Palliative Care: The code for palliative care, V66.7, became effective October 1, 1996. Code V66.7 can be used for any terminally ill patient receiving end-of-life palliative care. Code V66.7 may be assigned as an additional code to identify patients who receive palliative in any health care setting, including a hospital. The code is never assigned as the principal diagnosis.

Physician Documentation: The physician documentation in the medical record must substantiate that palliative care is the primary goal of treatment rather than cure in a person with advanced disease that is life limiting and refractory to disease modifying treatment. Terms such as comfort care, end-of-life care, and hospice care, are synonymous with palliative care and

are phrases that facilitate assignment of the V66.7 palliative care code. Palliative care provided within the inpatient setting must be documented clearly within the:

Admission note
Consult Note (consult Palliative Care "only" is insufficient by itself)
Discharge Summary
Physician orders
Progress note

Coding for Palliative Care: Specific ICD-9-CM guidelines must be followed, and the palliative care code will be assigned with the secondary ICD-9-CM code V66.7. A separate primary diagnosis must be documented.

For example, if a patient has been receiving curative care and is transferred to another service for "Hospice" or "Palliative Care", the admission order or note by the receiving service should document that the patient is transferred for palliative care. Medical record documentation requirements must be followed to substantiate that palliative care was provided, and to justify the assignment of an ICD-9-CM code V66.7 as a secondary diagnosis for the inpatient encounter.

REFERENCES

American Hospital Association Coding Clinic. First Quarter 1998, PAGES 11-12

DROP YOUR CONSULT CARDS

It was recommended by the Billing Quality Council, that the DOM billing office provide a box on each of the inpatient floors for the attending to place their completed consult cards. The inpatient coders will check these boxes regularly and bring the cards back to the office for processing. Each box is labeled DOM Consult Cards and has been placed at/or near the HUCS desk on each of the following floors:

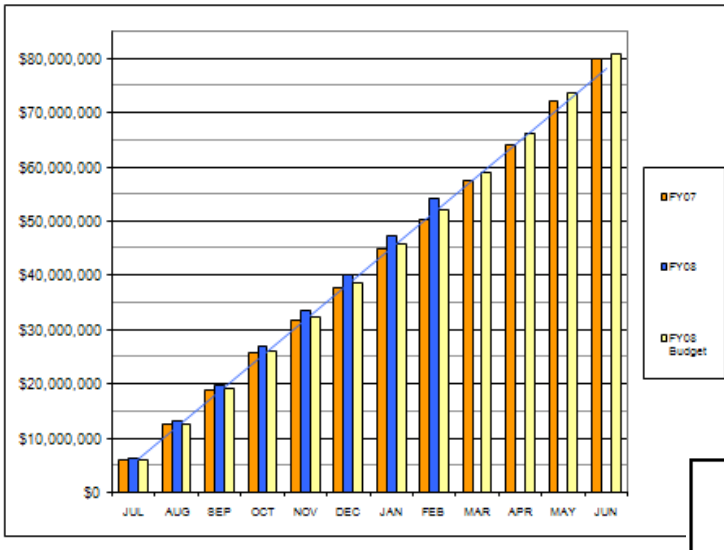
- 3 East, Central, West & MICU
- 4 East, Central, West & CCU
- 5 Central & West
- 6 East, Central & West

Please ask the HUC if you cannot locate a box in their area.

FEBRUARY MONTH-END FINANCIALS

YEAR-TO-DATE COMPARISON

	FY07	FY08	%Δ	FY08 Budget	Variance to Budget	%Δ
JUL	\$5,851,458	\$6,335,053	8%	\$5,949,448	\$385,605	6.5%
AUG	12,500,428	13,110,407	5%	12,683,906	\$426,501	3.4%
SEP	18,830,763	19,708,190	5%	19,096,673	\$611,517	3.2%
OCT	25,644,357	26,931,842	5%	26,116,774	\$815,067	3.1%
NOV	31,670,233	33,496,706	6%	32,360,148	\$1,136,559	3.5%
DEC	37,716,603	40,023,760	6%	38,579,322	\$1,444,439	3.7%
JAN	44,845,409	47,415,170	6%	45,707,730	\$1,707,440	3.7%
FEB	50,211,444	54,165,899	8%	51,973,047	\$2,192,852	4.2%
MAR	57,407,325			58,983,413		
APR	64,138,887			66,063,570		
MAY	72,258,101			73,682,594		
JUN	79,838,936			80,830,486		



Charges

Collections

In other billing and coding related news, we have started an initiative with the division administrators to identify and remove barriers to efficient care in the clinic setting. Our first review will send many of the administrators into the clinics to observe scheduling, registration, patients flow and check out first hand. We encourage you to share your thoughts and comments with your division administrator so we can work together to improve the clinic experience for you and your patients.

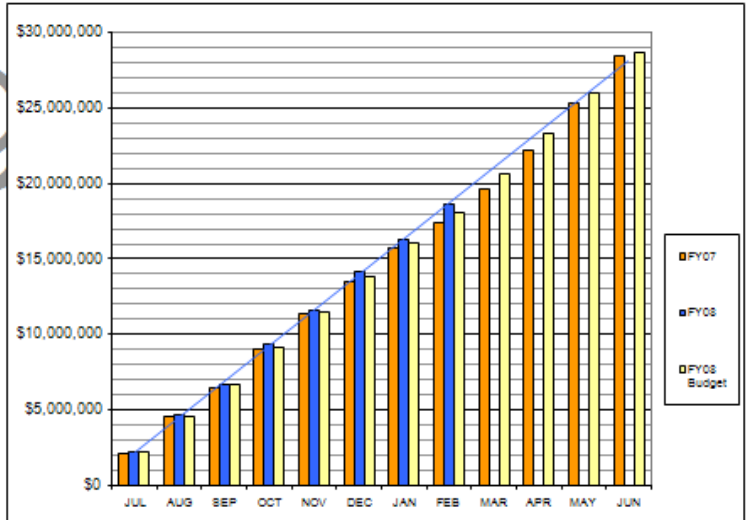
Clinical Revenue for the Department of Medicine for Fiscal year 2009 is off to a strong start. To date we have made both charge and collection budget every month. Collectively we are \$482,651 above budget in collections and \$661,302 above last year's collections at this time. Collections are up in every division but one and the areas that have seen the largest increases are:

- General Medicine, Geriatrics and Palliative Care (\$503,916),
- Pulmonary and Critical Care (\$256,987) and
- Gastroenterology (\$138,764).

Currently our Accounts Receivable (AR) are at an all time low of 31.2 days. Denials continue to trend downward.

YEAR-TO-DATE COMPARISON

	FY07	FY08	%Δ	FY08 Budget	Variance to Budget	%Δ
JUL	\$2,161,252	\$2,231,277	3%	\$2,226,213	\$5,064	0.2%
AUG	4,532,282	4,656,635	3%	4,533,120	\$123,515	2.7%
SEP	6,422,360	6,708,707	4%	6,648,679	\$60,028	0.9%
OCT	8,979,646	9,391,451	5%	9,137,857	\$253,594	2.7%
NOV	11,419,295	11,654,077	2%	11,517,720	\$136,357	1.2%
DEC	13,511,736	14,176,037	5%	13,852,958	\$323,079	2.3%
JAN	15,681,638	16,299,526	4%	16,013,580	\$285,946	1.8%
FEB	17,441,539	18,585,492	7%	18,102,841	\$482,651	2.6%
MAR	19,635,845			20,678,798		
APR	22,148,876			23,282,667		
MAY	25,280,640			26,031,253		
JUN	28,443,639			28,709,530		



DEPARTMENT OF MEDICINE
INPATIENT CONSULTATION POLICY

A. SUBJECT: Consultations

B. EFFECTIVE: March 1, 2008

C. POLICY:

The Clinical Staff, Housestaff, nurse practitioners, or physician assistants shall request consultation (including referrals and requests for minor procedures) based upon patients' assessed needs and shall respond to such requests in accordance with the procedures set forth in this policy

D. DEFINITIONS

1. Consultation only-consultant reviews and advises on diagnosis and potential treatment.
2. Consultation and treatment-consultant reviews and provides indicated treatment for one episode.
3. Referral request for ongoing care-consultant reviews and provides care for a specified period of time.
4. Request for minor procedure-A request for a service to perform a minor procedure when the primary service does not provide the indicated minor procedure. What is considered minor is defined by each consulting service.

E. DOCUMENTATION REQUIREMENTS:

1. The requesting Clinical Staff may delegate initiation of the request for consultation, to Housestaff or to nurse practitioners or physician's assistants who have been granted clinical privileges.

2. All consultation requests *require* a written order and should be confirmed prior to the evaluation.

Consult Request Form

MIS

Requesting MD's Documentation

3. Requests for consultation shall include the patient's name and history number, the name of the requesting physician or designee, the time and date of the request, the patient's pertinent medical history, reason for consultation and the type of consultation requested.

4. The types of consultation include "consultation only", "consultation and treatment" (one episode) "consultation and referral for ongoing care" (within the consultant's area of expertise), and "minor procedure".

5. Inpatient consultations shall be completed within twenty-four (24) hours of receipt (provided the patient is still an inpatient at the Medical Center) unless the consultation is designated an "emergent consultation". Consultation shall be complete after personal patient evaluation by the consulting clinician has been documented in the medical record.

6. The consultant must dictate a written report which includes the reason for the consultation: example: "Mr. Smith was seen in consultation today per the request of,for....., including an opinion and recommendations that reflect, when appropriate, an actual examination of the patient and the patient's medical record. While the consultant may acknowledge data gathered by a member of the Housestaff, a limited statement, such as "I concur" alone does not constitute an acceptable consultation report.

7. The consultation report shall contain the date and time of the consultation, as well as the signature of the consultant (attending physician).

TOP 100 CARDIOVASCULAR HOSPITALS

Congratulations! For the fourth year in a row, UVa is among the Top 100 Cardiovascular Hospitals as awarded by Thomson Healthcare. UVa is the only hospital in Virginia this year to receive this distinction and the award reflects our expertise, focus and the care provided by our entire team surrounding the cardiovascular patient.

The study singles out hospitals that are the best examples at managing cardiac disease. The study found that if all hospitals (the 900 non-winners) had performed at the level of the Top 100 Cardiovascular Hospitals, survival rates would increase by more than 7,000 patients each year and more that 750 additional patients could be complication free. The Top 100 Heart Hospitals also demonstrated significantly lower costs and shorter lengths of stay for cardiac patients. Thomson hopes that other hospitals model their care after these selected hospitals.

In this study, Thomson focused on hospitals that treat a broad spectrum of cardiology patients, including those undergoing: acute myocardial infarction (AMI), congestive heart failure (CHF), percutaneous coronary intervention (PCI), and coronary artery bypass graft (CABG). The data used is from public sources-the Medicare Provider Analysis and Review (MedPAR) data set, the Medicare Cost Report, and the CMS Hospital Compare data set.

Please visit <http://www.100tophospitals.com> to view a complete listing of the noted hospitals. You may see Drs. Larry Gimple and John Kern on WCAV who made time on New Year's Day to tape a brief interview about this award.

JERRY DONOWITZ & MICHAEL REIN

Dear Colleagues:

Please plan to join me and your colleagues at the excellent ACP Virginia Chapter Scientific Meeting, which takes place at the Williamsburg Lodge in Williamsburg, VA, March 7 and 8, 2008. The meeting provides 15.5 category 1 CME credits and includes such useful topics as:

- The tough hypertensive patient
- Baby boomer dementia and mild cognitive impairment
- Diabetes management
- New antibiotics
- Management of *C. difficile* colitis
- Hospital medicine
- Cancer screening
- Management of hepatitis B and C
- Management of acute stroke and CVA
- Bones and bisphosphonates
- Cardiology 2008
- Genital infections in women
- CHF and atrial fibrillation
- Update on interventional radiology

Many of these lectures are being delivered by such local notables as: Dalkin, Gibson, Hillman, Koenig, Rein, and Wispelwey

In addition, there will be award-winning presentations by residents, the opportunity to hear what the ACP is doing for you, and a chance to tell our College leadership about the issues important to us in Virginia. And, if further inducement were necessary, there will be seminars on advancement to fellowship and the nuts and bolts of recertification. Meeting practitioners from throughout the state is a fine way to increase referrals.

You can register by going to www.acponline.org/chapters/va and clicking on "News and Meetings. If you have questions, please contact our Chapter Coordinator, Ann Tennett, at 802/525-3828 or by email at annethsd@earthlink.net.

Michael F. Rein, M.D., F.A.C.P.
Governor, Virginia Chapter,
American College of Physicians

U.V.A. DEVICE OFFERS PHARMACEUTICAL MAKERS A FAST, CHEAP AND SAFE WAY TO SCREEN POTENTIAL DRUG COMPOUNDS

A new device invented by researchers at the University of Virginia could save pharmaceutical companies significant time and money in screening potential new drug compounds.

"We want to help the pharmaceutical industry identify effective therapeutic compounds by allowing them to fail early, fail fast, and fail cheap before going to very expensive animal studies," said Brett Blackman, an assistant professor in biomedical engineering.

Blackman and Brian Wamhoff, assistant professor in the department of medicine (cardiovascular division), have teamed up to create the novel system, HemoShear 2.0, which offers researchers for the first time the ability to observe the behavior patterns of human vascular cells under a variety of blood flow conditions that occur inside the body's cardiovascular system.

HemoShear 2.0 models the early indicators of atherosclerosis — hardening or narrowing of the arteries — by placing actual human vascular cells (i.e., endothelial and smooth muscle cells) in an environment that mimics an artery with blood flowing through it. Data from the exposure can be measured and recorded.

HemoShear 2.0 can help test the efficacy of therapeutic compounds and aid in early stage toxicity studies. Instead of testing drug compounds on isolated cells, which can produce false negatives, drug companies can use the device to test compounds in a more realistic environment.

"What the pharmaceutical industry lacks is the ability to mimic an organ *ex vivo*," Wamhoff said. "We know that as soon as we take an organ and disperse the cells, those cells are no longer like they were in the body. If you apply a novel compound to that cell, the response you get might be real but it's not meaningful in the context of the disease. When you go to animal studies, that response may not carry over in the blood vessel. It is clear that human-based biomimetic models are needed to fill this gap"

Atherosclerosis is considered the most important underlying cause of heart attack or stroke. The disease tends to occur at locations in the arteries where blood flow is compromised, causing detrimental changes in both the cells lining the interior of blood vessels (endothelial cells) and the cells found in the wall of blood vessels (smooth muscle cells).

Using an MRI, the researchers determined the rhythmic pattern at which blood flows through different arteries in human subjects. "We are then able to simulate the same flow patterns in those areas that are more or less susceptible to atherosclerosis and observe how the cells respond to these flow patterns in HemoShear," Blackman said.

According to Wamhoff, this kind of modeling offers unique opportunities to observe the cells and their interaction. "Research has been conducted wherein human cells are isolated to observe behavior patterns, but there are no available models that allow one to accurately study the intricate communication between endothelial cells and smooth muscle cells in a setting that mimics actual blood flow in the body."

This communication is important, the researchers say, because the cells lining the interior of the blood vessels, the endothelial cells, recognize different blood flow patterns imposed upon them and respond by expressing or repressing genes. This, in turn, influences their interactions with the cells found in the walls of blood vessels, the smooth muscle cells — interactions that, the researchers found, may lead to the onset of early-inflammation-associated atherosclerosis in certain arteries.

Using HemoShear 2.0, the researchers have been able to recreate blood flow patterns in bifurcating and bulbous areas like the internal carotid that are more susceptible to the disease (atheroprone areas) and the pipe-like arteries like the common carotid that are less susceptible to the disease (atheroprotective areas).

Using a synthetic elastic layer that is similar to a real blood vessel wall, endothelial cells are plated on the top surface and smooth muscle cells on the bottom surface. Then, the different blood flow patterns modeled from human circulation are applied to the endothelial cells through rotation of a motor-driven cone system. The findings: the blood flow can influence both endothelial and smooth muscle cell behaviors.

When subjected to atheroprotective blood flow patterns, the endothelial cells aligned with the direction of the blood flow, and the smooth muscle cells aligned perpendicularly to the flow as is true in a healthy blood vessel. In stark contrast, the atheroprone type of flow caused the endothelial cells to move away from their parallel structure while smooth muscle cells moved away from their perpendicular structure. This remodeling mimics the early phases of the diseased state of the artery; the blood flow pattern associated with atheroprone areas resulted in inflammation in both cells reminiscent of early hallmarks of atherosclerosis. This was confirmed through evaluating gene and protein expression profiles in both cell types.

"The results of this study validate the use of this novel co-culture system as a relevant biomimetic vascular model for studying early atherosclerotic events," said Tom Skalak, professor and chair of the U.Va. Department of Biomedical Engineering. "The cells' responses to these carefully controlled models of blood flow can now be used to develop therapeutic interventions for detection and treatment of vascular diseases — it has the potential to be revolutionary."

According to Dr. Sharon Hostler, interim dean and vice president at the University of Virginia School of Medicine called the research "a testament to the collaborative spirit found at the University of Virginia. The work by Drs. Blackman and Wam-

hoff could hold the key in the area of translational research; shortening the time it takes for a new therapy or procedure to go from the laboratory bench to helping patients."

Blackman, Wamhoff, and Dr. Norbert Leitinger (department of pharmacology) have formed a collaborative entity — the Laboratory of Atherogenesis — to begin using the HemoShear system to make these translatable discoveries in atherosclerosis.

Funding was also a collaborative effort. The research and product development was made possible by a U.Va. Fund for Excellence in Science and Technology (FEST) Award, provided by the Office of the Vice President for Research and Graduate Studies, and a U.Va. Heart Board Partner's Fund Award administered through the Robert M. Berne Cardiovascular Research Center. Additional funding came from the Department of Biomedical Engineering's Wallace H. Coulter Translational Partnership Award.

"There is a real need for biomimetic models like the one Professors Blackman and Wamhoff have developed," says U.Va. Engineering School Dean James H. Aylor. "When collaborations among the intersecting fields of engineering, medicine and biotechnology occur, the potential innovations are limitless."

A provisional patent has been filed for HemoShear 2.0. The research that HemoShear 2.0 made possible was spearheaded by a biomedical engineering graduate student, Nicole Hastings ('08), and is published in the American Journal of Physiology — Cell Physiology.

For more information, please visit the Laboratory of Atherogenesis at

<http://www.faculty.virginia.edu/labofatherogenesis>

Video link:

<http://www.virginia.edu/flashvideo/uvatoday/player.html?2007/nov/hemoshear.flv>

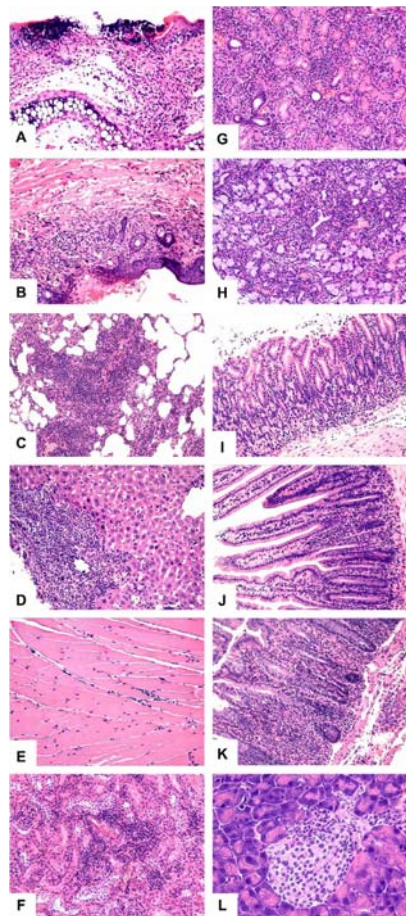
19TH ANNUAL VIRGINIA GERIATRICS CONFERENCE

The 19th Annual Virginia Geriatrics Conference will be at the Williamsburg Lodge April 11-13, 2008 offering 19 hours of CME credit. With expert faculty from UVA, EVMS and VCU the conference has a great reputation of clinical focus and value for primary care physicians. This year's theme is use of advanced technology in the care of elders. 50 Virginia physicians, including IM residents, may qualify for free registration (\$475 value) by early registration (March 1, 2008) for this special, first come, first served offer for Virginia physicians. Preference will go to first or second time VGC attendees who are not geriatricians. FAX requests to Beth Meyers at 804-827-1460. General internet registration is open at VaGeriatrics.org where the conference schedule is also posted. Register right away: we will sell out.

Research Highlight

Dr. Shyr-Te Ju was one of the five winners of the Departmental Awards for Excellence in Research, and has been invited to write a short description of his work and opportunities for collaboration to share with the rest of the DoM. Dr. Ju is a Professor in the division of Rheumatology, with a strong interest in transmembrane proteins.

Research Description:



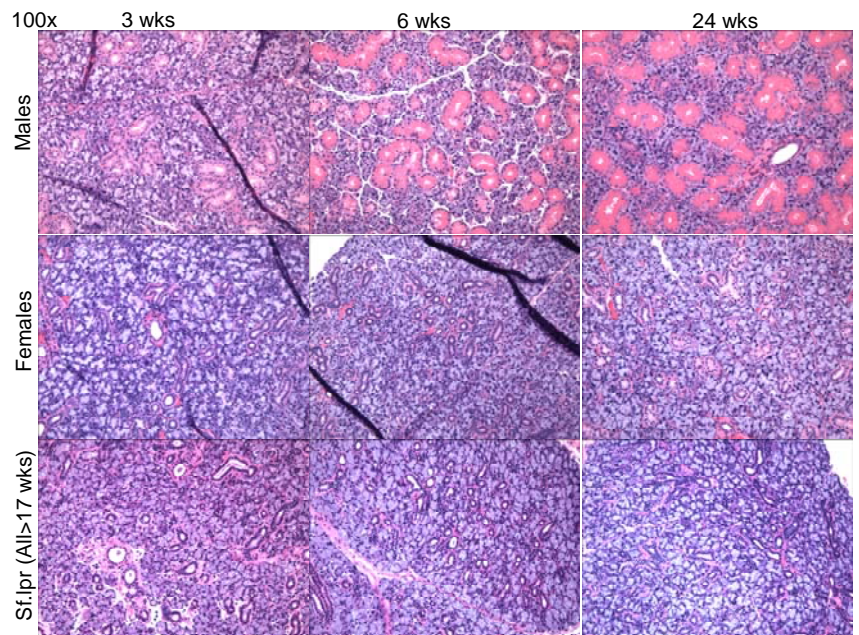
We are studying autoimmune inflammation controlled by the CD4⁺CD25⁺Foxp3⁺ regulatory T cells (Treg). Mice genetically deficient in Treg including *Il2*^{-/-}, *Il2ra*^{-/-} and *Foxp3*^{sf/Y} (Sf) are used. The Sf mice in particular are totally devoid of Treg and display the X-linked IPEX (Immune dysregulation, Poly-Endocrinopathy X-linked) syndrome characteristics of patients bearing mutations in the *Foxp3* gene. Sf mice die at 4 weeks after birth with severe multi-organ autoimmune inflammation. Inflamed organs include skin, ear, tail, lung, liver, and kidney. However, many organs/tissues are spared from autoimmune attack. Interestingly, Sf mice contain dormant autoimmune T cells capable of transferring

new diseases such as sialoadenitis, dacryoadenitis, pancreatitis, gastritis, intestinal inflammation, colitis, and myositis in *Rag1*^{-/-} recipients. [Figure in the left shows H&E stained slides for ear (A), skin (B), lung (C), liver (D), muscle (E), kidney (F), salivary gland (G), lacrimal gland (H), stomach (I), small intestine (J), colon (K), and pancreas (L).] Moreover, transfer of the multiple organ autoimmune diseases could be suppressed by Treg, mediated by inhibiting autoimmune T-cell expansion. Our study shows a large repertoire of autoimmune lymphocytes against various organs/tissues in Sf mice as well as Treg in B6 mice capable of suppressing the expansion of these autoimmune lymphocytes. My goal for the next few years is to characterize the autoimmune and Treg repertoires with respect to their organ/antigen specificity.

A massive systemic expansion of CD8⁺ memory T (T_M) cells and a remarkable increase in circulating IL-2 were observed only in *Il2ra*^{-/-} mice but not in *Il2*^{-/-} and Sf mice, although all three mutants are deficient in Treg. However, both phenotypes in *Il2ra*^{-/-} mice were suppressed by the transfer of Treg. Treg-deficiency drives naive T cells to T_M cells. In addition, high serum IL-2 was present in *Il2ra*^{-/-} mice and was preferentially used by CD8⁺ T_M cells through its abundant low-affinity IL-2R, resulting in systemic CD8⁺ T_M cell dominance. We are studying the mechanism(s) accounting for high serum IL-2 in *Il2ra*^{-/-} mice. One involves consumption due to lack of high affinity IL-2R and the other involves BLIMP-1 transcription factor which is a feedback control for IL-2 production and may be dysregulated in the absence of high affinity IL-2/IL-2 interaction.

Mutation of the *Foxp3* in Sf mice results in severe multi-organ autoimmune syndrome, and early death at 4 weeks old. However, Sf mice simultaneously bearing the *Il2*^{-/-} (*Sf.IL2*^{-/-}) or *Fas*^{lpr/lpr} gene (*Sf.Fas*^{lpr/lpr}) have extended lifespan despite totally lacking Treg, indicating a role of IL-2 and CD95 (*Fas*) signaling pathways in the multi-organ autoimmune syndrome beyond the Treg checkpoint. Importantly, the pattern of organ-specific autoimmune response of *Sf.IL2*^{-/-} mice resembled *Il2*^{-/-} mice whereas that of *Sf.Fas*^{lpr/lpr} was similar to Sf mice, indicating that the distinct and weakened autoimmune manifestation in *Il2*^{-/-} mice was not caused by the residual Treg and that *Il2*^{-/-} and *Fas*^{lpr/lpr} genes prolong the lifespan of Sf mice but by different mechanisms. One of our goals is to understand how IL-2 regulates autoimmune inflammation in an organ-specific manner.

Il2^{-/-} or *Il2ra*^{-/-} mice invariably develop inflammation in the submandibular gland (SMG) and salivation dysfunction. In contrast, the SMG of Sf mice were not inflamed. Moreover, Sf



mice co-expressing *Fas*^{lpr/lpr}, *Il2*^{-/-} or *Il2ra*^{-/-} gene remained free of inflammation in their SMG even though they lived significantly longer and contained autoimmune T cells capable of inducing inflammation in the SMG of *Rag1*^{-/-} recipients. The SMG of *Foxp3*^{sf/Y} mice was growth arrested before the stage when dominant sexual-dimorphic display of granular convoluted tubules (GCT, red color in the left figure) normally occurred (The lower 3 panels showed SMG growth arrest in 3 *Sf.Fas*^{lpr/lpr} mice), yet testosterone treatment restored GCT development but not inflammation. These observations indicate that *Foxp3*^{sf/Y} inhibits SMG development and define a critical development stage that renders SMG resistance to inflammation induced by competent autoimmune T cells. We hypothesize that the expression of a critical antigen(s) (not associated with GCT development) is inhibited in Sf mice. One of the goals in this project is to identify the antigen(s) and define the specific autoimmune T cells.

Relevant publications

- Sharma R, Bagavant H, Jarjour WN, Sung S-s, and Ju S-T. The Role of Fas in the immune system biology of IL-2Ra knockout mice: Interplay among regulatory T cells, inflammation, hemopoiesis and apoptosis. *J. Immunol.* 2005. 175: 1965-1973.
- Sharma R, Zheng L, Guo X, Fu SM, Ju S-T*, and Jarjour WN. Novel animal models for Sjögren's syndrome: transfer of salivary gland dysfunction from regulatory T cell-deficient mice. *J. Autoimmunity.* 2006; 27: 289-296. (*co-senior author)
- Sharma R, Zheng L, Deshmukh US, Jarjour WN, Sung S-s, Fu SM, and Ju S-T. Cutting Edge: A regulatory T cell-dependent novel function of CD25 (IL-2Ra) controlling memory CD8⁺ T cell homeostasis. *J. Immunol.* 2007. 178: 1251-1255.
- Sharma R, Jarjour WN, Zheng L, Gaskin F, Fu SM, and Ju S-T. Large functional repertoire of regulatory T-cell suppressible autoimmune T cells in scurfy mice. *J. Autoimmunity.* 2007. 29: 10-19.
- Zheng L, Sharma R, Gaskin F, Fu SM, and Ju S-T. A novel role of IL-2 in organ-specific autoimmune inflammation beyond regulatory T-cell checkpoint: Both IL-2 knockout and Fas mutation prolong lifespan of scurfy mice but by different mechanisms. *J. Immunol.* 2007. 179: 8035-8041.
- 129. Zheng L, Sharma R, Kung JT, Deshmukh US, Jarjour WN, Fu SM, and Ju S-T. Pervasive and stochastic changes in the TCR repertoire of regulatory T cell-deficient mice. *Int. Immunol.* 2008. (in press).

Important New NIH Public Access Requirements

New NIH rules have been adopted to ensure that the public has access to published results of NIH funded research: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html> These rules require all peer-reviewed journal articles resulting from NIH funds to be deposited into the open-access digital archive, PubMed Central (PMC) within twelve months of publication. The NIH has released comprehensive guidance on these new rules at <http://publicaccess.nih.gov/> including an extensive FAQ <http://publicaccess.nih.gov/FAQ.htm>.

Key Elements of the New Rules:

- The Policy applies to any peer-reviewed article based on work in one or more of the following categories:
 - Directly funded by an NIH grant or cooperative agreement active in federal fiscal year 2008 (October 1, 2007- September 30, 2008) or beyond;
 - Directly funded by a contract signed on or after April 7, 2008;
 - Directly funded by the NIH Intramural Program;
 - If NIH pays the investigator's salary.
- For more details see FAQ B.1. <http://publicaccess.nih.gov/FAQ.htm#b7>
- The policy imposes new responsibilities on NIH Principal Investigators and their home institutions. See FAQ B.7. <http://publicaccess.nih.gov/FAQ.htm#b7>
- "Principal Investigators and their Institutions are responsible for ensuring all terms and conditions of awards are met. This includes the submission of articles that arise directly from their awards, even if they are not an author or co-author of the publication. Principal Investigators and their Institutions should ensure that the authors are aware of and comply with the NIH Public Access Policy."
- Authors must address copyright before signing agreements with publishers. See FAQ C.3. <http://publicaccess.nih.gov/FAQ.htm#b7>
- Most journal agreements offered today do not allow authors to retain rights sufficient to comply with the new NIH rules. While it can be hoped that increasing numbers of publishers will include appropriate language as the new rules are implemented, for the time being authors must be careful to ensure that some reservation of rights is made.
- The NIH has provided sample language that can be used in agreements to address the new submittal requirements: "Journal acknowledges that Author retains the right to provide a copy of the final manuscript to the NIH upon acceptance for Journal publication, for public archiving in PubMed Central as soon as possible but no later than 12 months after publication by Journal."
- The NIH suggested language is not required; other formulations can address the PMC requirements. Additional resources for UVa faculty on author's rights and copyright will be posted by the University of Virginia Library and the

Claude Moore Health Sciences Library by the end of February, 2008.

- The Policy requires submittal of the author's final peer-reviewed manuscript including all modifications from the peer-reviewed process, but not the journal's final, published version of the work. See FAQ C.5. <http://publicaccess.nih.gov/FAQ.htm#general>
- Some journals have already agreed to submit articles directly to PMC on behalf of their authors. Investigators publishing in one of these journals need take no further action to comply with the submission requirement of the NIH Public Access Policy. A complete list of participating journals is located at: http://publicaccess.nih.gov/submit_process_journals.htm
- Any NIH applications submitted after May, 25, 2008 must include the PMC reference number for any articles covered by the new policy. FAQ C.3. <http://publicaccess.nih.gov/FAQ.htm#general>

Questions:

- Madelyn Wessel, University Library: mfw2y@virginia.edu
- Gretchen Arnold, Claude Moore Health Sciences Library: GVN8R@hscmail.mcc.virginia.edu

Legal Advice:

- Office of General Counsel: 924-3586

DIVISION

NEWS, PUBLICATIONS, AND GRANTS

ALLERGY AND CLINICAL IMMUNOLOGY NEWS

- Judith Woodfolk has been named the recipient of the 2008 John E. Salvaggio Memorial Lectureship by the American Academy of Allergy, Asthma & Immunology. This Honorary lectureship is presented in recognition of outstanding service to the specialty and science of allergy and immunology.

PUBLICATIONS

- Borish, L., Woodard, C.R., and Steinke, J.W. Role of hypoxia in inflammatory upper airway disease. *Current Opinion in Allergy & Clinical Immunology* 1:16-20 (2008)

CARDIOVASCULAR MEDICINE

PUBLICATIONS

- West JJ, Norton PT, Kramer CM, Moorman JR, Mahapatra S, Dimarco JP, Mangrum JM, Mounsey JP, Ferguson JD. Characterization of the mitral isthmus for atrial fibrillation ablation using intracardiac ultrasound from within the coronary sinus. *Heart Rhythm*. 2008 Jan;5(1):19-27. Epub 2007 Sep 1.
- Rembold CM. Age predicts cancer incidence better than statin-induced low-density lipoprotein level. *J Am Coll Cardiol*. 2008 Jan 1;51(1):90-1; author reply 92. No abstract available.
- Marine JE, Nazarian S, Bilchick KC, Dong J. Computed tomography image-guided catheter ablation of a focal atrial tachycardia from the noncoronary sinus of Valsalva. *Heart Rhythm*. 2007 Dec;4(12):1582. Epub 2007 Sep 19. No abstract available.
- Bell JR, Kennington E, Fuller W, Dighe K, Donoghue P, Clark JE, Jia LG, Tucker AL, Moorman JR, Marber MS, Eaton P, Dunn MJ, Shattock MJ. Characterization of the phospholemman knockout mouse heart: depressed left ventricular function with increased Na/K ATPase activity. *Am J Physiol Heart Circ Physiol*. 2007 Dec 7; [Epub ahead of print]
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- Ragosta M. Determination of the source and severity of a transvalvular left ventricular outflow tract gradient in patients with a prosthetic aortic valve. *Catheter Cardiovasc Interv*. 2007 Nov 15;70(6):809-14. No abstract available.
- Klibanov AL. Ultrasound molecular imaging with targeted microbubble contrast agents. *J Nucl Cardiol*. 2007 Nov-Dec;14(6):876-84. No abstract available.
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- Srinivasan S, Bolick DT, Lukashev D, Lappas C, Sitkovsky M, Lynch KR, Hedrick CC. Sphingosine-1-Phosphate Reduces

CD4+ T Lymphocyte Activation in Type 1 Diabetes Through Regulation of Hypoxia-inducible Factor Short Isoform I.1 and CD69. *Diabetes*. 2007 Nov 14; [Epub ahead of print]

- Yadava RS, Frenzel-McCardell CD, Yu Q, Srinivasan V, Tucker AL, Puymirat J, Thornton CA, Prall OW, Harvey RP, Mahadevan MS. RNA toxicity in myotonic muscular dystrophy induces NKX2-5 expression. *Nat Genet*. 2008 Jan;40(1):61-8. Epub 2007 Dec 16.
- Isbell DC, Voros S, Yang Z, DiMaria JM, Berr SS, French BA, Epstein FH, Bishop SP, Wang H, Roy RJ, Kemp BA, Matsu- bara H, Carey RM, Kramer CM. Interaction between bradykinin subtype 2 and angiotensin II type 2 receptors during post-MI left ventricular remodeling. *Am J Physiol Heart Circ Physiol*. 2007 Dec;293(6):H3372-8. Epub 2007 Oct 12.
- Hastings NE, Simmers MB, McDonald OG, Wamhoff BR, Blackman BR. Atherosclerosis-prone hemodynamics differentially regulates endothelial and smooth muscle cell phenotypes and promotes pro-inflammatory priming. *Am J Physiol Cell Physiol*. 2007 Dec;293(6):C1824-33. Epub 2007 Oct 3.
- Clark AN, Youkey R, Liu X, Jia L, Blatt R, Day YJ, Sullivan GW, Linden J, Tucker AL. A1 adenosine receptor activation promotes angiogenesis and release of VEGF from monocytes. *Circ Res*. 2007 Nov 26;101(11):1130-8. Epub 2007 Sep 27.
- Dong J, Dalal D, Scherr D, Cheema A, Nazarian S, Bilchick K, Almasry I, Cheng A, Henrikson CA, Spragg D, Marine JE, Berger RD, Calkins H. Impact of heart rhythm status on registration accuracy of the left atrium for catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol*. 2007 Dec;18(12):1269-76. Epub 2007 Sep 11.
- Vandsburger MH, French BA, Helm PA, Roy RJ, Kramer CM, Young AA, Epstein FH. Multi-parameter in vivo cardiac mag- netic resonance imaging demonstrates normal perfusion reserve despite severely attenuated {beta}-adrenergic functional re- sponse in neuronal nitric oxide synthase knockout mice. *Eur Heart J*. 2007 Nov;28(22):2792-8. Epub 2007 Jun 30.

ENDOCRINOLOGY AND METABOLISM NEWS

- Dr. Fournier was selected for a John Haddad Young Investigator Award, from the AIMM-ASBMR (Advances in Mineral Me- tabolism – American Society for Bone and Mineral Research).
- Beginning October 2008, Dr. Barrett will chair the NIH Clinical Integrative Diabetes and Obesity (CIDO) study section for 2 years

PUBLICATIONS/PRESENTATIONS

- Park J, Kemp BA, Howell NL, Gildea JJ, Keller SR, Carey RM. Intact Microtubules Are Required for Natriuretic Responses to Nitric Oxide and Increased Renal Perfusion Pressure. *Hypertension*. 2008 Jan 2; [Epub ahead of print] PMID: 18172053
- Padia SH, Kemp BA, Howell NL, Fournie-Zaluski MC, Roques BP, Carey RM. Conversion of Renal Angiotensin II to An- giotensin III Is Critical for AT2 Receptor Mediated Natriuresis In Rats. *Hypertension*. 2007 Dec 24; [Epub ahead of print] PMID: 18158338
- Hu C, Dandapat A, Chen J, Liu Y, Hermonat PL, Carey RM, Mehta JL. Over-expression of angiotensin II type 2 receptor (agtr2) reduces atherogenesis and modulates LOX-1, endothelial nitric oxide synthase and heme-oxygenase-1 expression. *Atherosclerosis*. 2007 Dec 18; [Epub ahead of print] PMID: 18096165
- Dandapat A, Hu CP, Chen J, Liu Y, Khan JA, Remeo F, Carey RM, Hermonat PL, Mehta JL. Over-expression of angiotensin II type 2 receptor (agtr2) decreases collagen accumulation in atherosclerotic plaque. *Biochem Biophys Res Commun*. 2007 Nov 26; [Epub ahead of print] PMID: 18037370
- Isbell DC, Voros S, Yang Z, Dimaria JM, Berr SS, French BA, Epstein FH, Bishop SP, Wang H, Roy RJ, Kemp BA, Matsu- bara H, Carey RM, Kramer CM Interaction between bradykinin subtype 2 and angiotensin II type 2 receptors during post-MI left ventricular remodeling. *Am J Physiol Heart Circ Physiol*. 2007;293(6):H3372-8. Epub 2007 Oct 12. PMID: 17933966
- Ahmed F, Kemp BA, Howell NL, Siragy HM, Carey RM. Extracellular renal guanosine cyclic 3'5'-monophosphate modu- lates nitric oxide and pressure-induced natriuresis. *Hypertension*. 2007;50(5):958-63. Epub 2007 Sep 10. PMID: 17846351

GASTROENTEROLOGY AND HEPATOLOGY NEWS

- Shiela Crowe has been recognized as as one of the 2008 "Outstanding AGA Women in Gastroenterology" by the AGA Foun- dation.
- Dr. Stephen Bickston gained approval (FDA IND #79,307) to study conjugated linoleic acid in patients with Crohn's disease.
- Dr. Bickston was named to the AMA Consortium: Endoscopy/Colonoscopy Work Group to develop measures for Medicare PQRI.

PUBLICATIONS

- Barnes, S.L., Vidrich, A., Wang, M.-L., Wu, G., Bamias, G, Cominelli, F., and Cohn, S.M. "Resistin-Like Molecule Beta

(RELM- β) Is Highly Expressed in the ileum of SAMP1/YitFc Mice and is Associated with the Initiation of Ilietis" (2007) *J. Immunol.* 179(10): 7012-7020

- Cohn, S.M. and Bickston, S.J. : Chapter 113. "Radiation Injury in the Gastrointestinal Tract" in Textbook of Gastroenterology., 5h Edition. (2008) Yamada, T., Alpers, D.H., Owyang, C., Powell, D.W., and Silverstein, F.E., Editors, J.B. Blackwell Publishing . In press

GRANTS

- Brooks Brodrick, a MSTP (MD, PhD) student in Dr. Steven Cohn's laboratory has received a PhRMA Foundation predoctoral fellowship award.
- Shiela Crowe has received the AGA Funderburg award for Gastric Cancer Research.

GENERAL MEDICINE, GERIATRICS, AND PALLIATIVE CARE

NEWS

- Eugene Corbett has been invited by the Robert Wood Johnson Foundation to participate in a workshop in February, 2008 on "Translating Research to Public Policy".
- Eugene Corbett has been invited by the Uniformed Services University for Health Sciences to give a faculty development session and student workshop on ophthalmoscopic skills. This is part of a research project to study the impact of these sessions upon student performance outcome of basic ophthalmoscopic skills.

PUBLICATIONS/PRESENTATIONS

- Corbett E, Elnicki M, Conaway M. When should students learn essential physical examination skills? Views of internal medicine clerkship directors in North America. *Academic Medicine*, January, 2008, 83;1:96-99.

INFECTIOUS DISEASES AND INTERNATIONAL HEALTH

NEWS

PUBLICATIONS/PRESENTATIONS

- Moore CC, Jacob ST, Pinkerton R, Meya DB, Mayanja-Kizza H, Reynolds SJ, Scheld WM. Point-of-care lactate testing predicts mortality of severe sepsis in a predominantly HIV type 1-infected patient population in Uganda. *Clin Infect Dis.* 2008 Jan 15;46(2):215-22
- Spellberg B, Guidos R, Gilbert D, Bradley J, Boucher HW, Scheld WM, Bartlett JG, Edwards J Jr; Infectious Diseases Society of America. The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society of America. *Clin Infect Dis.* 2008 Jan 15;46(2):155-64.
- Boettner DR, Huston CD, Linford AS, Buss SN, Sherman NE, Petri Jr WA. *Entamoeba histolytica* Phagocytosis of Human Erythrocytes Involves EEAK1, a Novel Protein Found in the Amebic Phagosome. *PloS Pathogens*, January 18, 2008.
- Petri WA Jr., Kirkpatrick BD, Haque R, Duggal P. Genes influencing susceptibility to infection. *J Infect Dis* 2008; 197:4-6.
- Snider C, Petri WA Jr. Travel Medicine. In *Conn's Current Therapy 61st Edition* (Rakel RE, ed.), W.B. Saunders Co., New York, NY, 2008, pp156-164.
- Haque R, Petri WA Jr. Amebiasis. In *Conn's Current Therapy 61st Edition* (Rakel RE, ed.), W.B. Saunders Co., New York, NY, 2008, pp61-63.
- Phillips EK, Owusu-Ofori A, Jagger J. Bloodborne pathogen exposure risk among surgeons in sub-Saharan Africa. *Infection Control & Hospital Epidemiology*. 2007;28(12):1334-1336.
- Warren, Cirle Alcantara, MD; Raul V Destura, MD; Jesus Emmanuel A D Sevilleja, MD; Luis F. Barroso, MD; Humberto Carvalho; Leah J Barrett; Alison D O'Brien, PhD and Richard L Guerrant, MD. *Detection of Epithelial Cell Injury and Quantification of Infection in the HCT8 Organoid Model of Cryptosporidiosis.* *Journal of Infectious Diseases*, Accepted for Publication.
- Jagger J. "Bloodborne Pathogen Risk to Healthcare Workers During Blood Drawing Procedures: Considerations for Developing Countries." Presented to the PEPFAR group at John Snow International, Arlington, VA, December 10, 2007

GRANTS

- The Kedes Laboratory was awarded additional funding from the Cancer Center Support Grant (CCSG) for their project entitled "Controlling a Tumorigenic Herpesvirus Infection: From Novel Mouse Models to Human Patients". This project focuses on understanding the immune response to the oncogenic herpesvirus that causes a number of human malignancies including Kaposi's sarcoma.

NEPHROLOGY AND THE CENTER FOR IMMUNITY, INFLAMMATION, AND REGENERATIVE MEDICINE

NEWS

- Dr. Shyr-teJu will serve as Chairperson, NIH ZRG1 HAI-G (09) F Special Emphasis Panel.

- Dr. Shu Man FU was recently honored by the American College of Rheumatology and received recognition as a Master of the American College of Rheumatology. This is one of the highest honors the College bestows. The designation of Master is conferred on ACR members who have made outstanding contributions to the field of rheumatology through scholarly achievement and/or service to their patients, students, and profession. This honor is usually bestowed upon no more than 15 members per year.
- New Initiatives in Immunology award to Rahul Sharma from Beirne B Carter Center for Immunology Research. June 2007.
- Dr. Mark Okusa was appointed: 1) Regular member, American Society of Nephrology Grant Review Committee, 2) Chairman, Acute Kidney Injury Advisory Committee to the American Society of Nephrology.
- Dr. Shyr-teJu was appointed chairperson, NIH ZRG1 HAI-G (09) F Special Emphasis Panel.

PUBLICATIONS/PRESENTATIONS

- Sharma R, Jarjour WN, Zheng L, Gaskin F, Fu SM, and Ju, S-T. Large functional repertoire of regulatory T-cell suppressible autoimmune T cells in scurfy mice. *J. Autoimmunity*. 2007. 29: 10-19. (#1 most downloaded research paper (excluding reviews) for the third quarter of 2007 of the Journal).
- Zheng L, Sharma R, Gaskin F, Fu SM, and Ju S-T. A novel role of IL-2 in organ-specific autoimmune inflammation beyond regulatory T-cell checkpoint: Both IL-2 knockout and Fas mutation prolong lifespan of scurfy mice but by different mechanisms. *J. Immunol*. 2007. 179: 8035-8041. (selected for "in this issue" for the journal)
- Zheng L, Sharma R, Kung JT, Deshmukh US, Jarjour WN, Fu SM, and Ju S-T. Pervasive and stochastic changes in the TCR repertoire of regulatory T cell-deficient mice. *Int. Immunol*. 2008. (in press).
- Lobo PI, Schlegel KH, Yuan W, Townsend GC, and White JA: Inhibition of HIV-1 Infectivity through an Innate Mechanism Involving Naturally Occurring IgM Anti-Leukocyte Autoantibodies *J. Immunol.*, Feb 2008; 180: 1769 - 1779.
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- Mangrum, A.J. and Mark D. Okusa. Invited review. Mechanisms of Vascular Access Dysfunction. *Drug Discovery Today: Disease Mechanism* in press 2008.
- Tholpady SS, Freyman TF, Chachra D, Ogle RC: Application of cyclic tensional force delays cranial suture fusion and activates TGF- β signaling in vitro. *Plast. & Recon. Sur*, 120 (3):601-11; discussion 612-3., 2007.
- Petrie, CE, Tholpady, SS, Ogle, RC and Botchwey, EA: Proliferative Capacity and Osteogenic Potential of Novel Dura Mater Stem Cells on Poly-lactic-co-glycolic acid. *Journal of Biomedical Materials Research: Part A*, on line and in press, 2007.
- Gagan, J.R., Tholpady, S.S., and Ogle, R.C.: Cellular Dynamics and Tissue Interactions of the Dura Mater during Head Development. *Birth Defects: Embryo Today*, in press, 2007.
- Petrie CE, Cooper, JA, Jr, Sefcik, L, Tholpady SS, Ogle, Botchwey EA: Osteogenic differentiation of dura mater stem cells cultured in vitro on 3D porous scaffolds of poly-caprolactide; Evaluation of a novel technique combining co-extrusion and gas foaming to yield optimal pore size distribution., *Acta Biomaterialia*, in press, 2008.
- Tholpady, S.S., Katz, A.J., and Ogle, R.C.: Adipocytes in Stem Cell Biology. In: *Essential Wound Healing in the Face and Neck*. (Gosain, A., Friedman, D., Horn, D., and Hebda, P., eds.) B.C. Decker Inc., pp.368-380, in press, 2008.
- Petrie CE, Sadik KW, Tholpady SS, Ogle, Botchwey EA: Comparative Effects of Scaffold Pore Size, Pore Volume, and Total Void Volume on Cranial Bone Healing Patterns Using Microsphere-Based Scaffolds. *Journal of Biomedical Materials Research*, in press, 2008.
- Sefcik, L, Parker, A, Neal, R, Kaszuba, S, Katz, A, Ogle RC, Botchwey EA: Collagen Nanofiber Scaffolds are a Biomimetic Substrate for the Osteogenic Differentiation of Human Adipose-derived Stem Cells, *J. Tis. Eng & Reg Med.*, in press, 2008.
- Alaa S. Awad, Michael Rouse, Lixia Liu, Amy L. Vergis, Diane L. Rosin, Joel Linden, John R. Sedor, and Mark D. Okusa: Activation of Adenosine 2A Receptors Preserves Structure and Function of Podocytes *J Am Soc Nephrol* 19: 59-68.
- Jo. S.-K, A. Bajwa, A. Awad, K. Lynch and M.D. Okusa. Invited review. Sphingosine 1-phosphate Receptors: Biology and Therapeutic Potential in Kidney Disease. *Kidney Int.* in press 2008.
- Rosner, M.D. and Okusa, M.D. Editors, in *Biomarkers in Renal Disease*. Nova Publications. In press 2008.
- Massive Changes in the TCR Repertoire of Regulatory T Cell-Deficient Mice: Multiple V β spectra type alterations indicate strong responses by a large repertoire of autoimmune T cells. Lingjie Zheng, Rahul Sharma, Umesh S Deshmukh, Wael N Jarjour, John Kung, Shu Man Fu and Shyr-Te Ju. *Immunology* 2007, Miami Beach, FL, (May 18-22, 2007).

GRANTS

- Dr. Shu Man Fu was the recipient of a 3 year grant (~\$430,000) from the Alliance for Lupus Research -Target Identification in Lupus- Grant Award # 68164 Entitled "Identification of Genes Conferring End-Organ Resistance in Lupus Nephritis" (02/01/2008-01/31/2010)