Volume 11, Issue 2
Fall/Winter 2004-05

NAVBO Newsletter

Special points of interest:

- **MEETING INFORMATION—Center Pull-out**
  - **Program**
  - **Call for Abstracts**
  - **Registration**
- **2005 Benditt Award**

CALL FOR ABSTRACTS INSIDE THIS ISSUE

MESSAGE FROM THE PRESIDENT: THE NEXT DECADE

William A. Muller

William A. Muller, M.D., Ph.D., NAVBO President, 2004-2005

Happy New Year! At this writing we are halfway through the academic year and into NAVBO's second decade. It has been a true honor to serve as President this year, and I look forward to many more years of serving the vascular biology community in other capacities. NAVBO is continuing its tradition as the collective voice of the vascular biologists. We can be proud of our role in sponsoring the XIIIth International Vascular Biology Meeting in Toronto last June; it was a great success, thanks to Avrum Gotlieb, Lowell Langille and their colleagues at the University of Toronto, Department of Laboratory Medicine and Pathology. The past decade has witnessed an explosion of both interest and achievement in vascular biology. Progress in our field is reported on the front pages of the New York Times; our relatives call us with questions about angiogenesis, atherosclerosis, and stem cell therapies. The consciousness of both the lay public and the scientific community has been raised. Scientific meetings on topics of vascular biology are proliferating.

However, this is the time to look forward, not backward. NAVBO has achieved its initial twin aims of bringing together vascular specialists who were all subsumed in different scientific societies and sponsoring the International Vascular Biology Meeting when it was held in North America. To keep NAVBO a vibrant, vital society, it will have to serve the needs of its members. How can we do that?

- For one thing, we need to get our general membership more involved. Come to the meetings. Send e-mails to the Councilors. Let us hear from you. As a small society we can change and adapt quickly to have meetings and forums where controversies in vascular biology can be discussed.
- We can facilitate the exchange of special reagents and the teaching of techniques among our members.
- We can (and should) go back to our roots and interact with other pathologists, physiologists, pharmacologists, and cardiologists to teach them what we've learned—and learn what they can

(Continued on page 2)

Inside this issue:

teach us about diseases and systems where the insights of a vascular biologist could be useful.

This year NAVBO has been working hard to implement some of these goals. Our annual meeting this year, "Vascular Biology and Medicine 2005: From Molecules to Man" will be an experiment in the promotion of translational research. While this is as close as we've ever come to a free-standing NAVBO meeting, we will meet with the Society for Vascular Medicine and Biology (SVMB). This is a group of clinicians who are eager to learn the basic science behind the therapies they are using to combat vascular disease. The NAVBO Program Committee, chaired by Martha Cathcart, has been working very hard to put together an outstanding program. They have consulted extensively with SVMB Program Chair John Cooke (also a NAVBO member) to design scientific sessions that are of interest to both societies. However, the main focus of the program is to highlight the most important advances in basic science. This will be a strong meeting, emphasizing such timely topics as vascular development, vascular stem cells, vascular signaling, imaging of vascular disease, leukocyte-endothelial cell interactions, adipocytes, and "vasculomics."

The officers of NAVBO have been working diligently to improve the society's financial position. We are optimistic that our annual meeting and future workshops such as the successful Vascular Development workshop held last year (and planned again for 2006) will bring money back into our treasury. Mary Gerritsen, former President and current chair of our Development Committee, is spearheading a campaign to solicit corporate memberships. Any NAVBO members who have personal contacts in pharmaceutical or biotech companies dealing in vascular biology-related products should e-mail her at mgerritsen@navbo.org.

Great meetings and a fuller treasury will help make NAVBO a stronger society. However, the most important thing we can do to strengthen NAVBO in the future is to interact with each other scientifically and socially. NAVBO is a vascular plexus—a plexus of vascular biologists. It is a plexus that matures not by apoptosis, but by trophic interactions. These trophic interactions are between scientists studying endothelial cells and those studying extracellular matrix and pericytes, and by investment with scientists studying smooth muscle cells, never forgetting the critical interactions we need with people studying the cellular and soluble elements of the blood. NAVBO calls us back from our specialty meetings and our artificial "Departments" and encourages us to come together as a community that is interactive, compliant, and vital—just like the vasculature we study. The future of NAVBO is as bright as we members want to make it.

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Newsletter Editor—William R. Huckle

Contact Information for the above members
is listed on our web site at:
www.navbo.org/governance.htm

2004 BENDITT AWARD PRESENTED AT THE IVBM

William R. Huckle, Editor

Linda L. Demer, NAVBO President 2003-04, presented the Earl P. Benditt Award to Dr. Peter Carmeliet at the IVBM in Toronto

A highlight of the XIIIth IVBM meeting in Toronto was the Benditt Award Lecture delivered by the 2004 awardee, Dr. Peter Carmeliet of the University of Leuven in Belgium. Dr. Carmeliet's talk, entitled "Functional Angiogenomics in Mice, Zebrafish and Humans," provided an overview of research in angiogenesis, as well as glimpses of exciting new findings in this field. Dr. Carmeliet's research over the past 10 years has laid the foundation for our understanding of the roles played by angiogenic growth factors in vascular development and maintenance. This work has taken excellent advantage of transgenic mouse technology and often has revealed surprising subtleties of function, indicated by the lethality of heterozygous VEGF knockout (1) and VEGF splice form-specific activities (2).

More recently, members of Dr. Carmeliet's laboratory and their international collaborators have employed novel gene-discovery and screening approaches to uncover new relationships between angiogenic mediators and humans diseases. The Benditt Award lecture described, for example, their investigations of the potential involvement of VEGF in DiGeorge Syndrome, a condition associated with cardiovascular birth defects in humans and caused by deletion of chromosome 22q11. Knockout of $VEGF_{164}$ expression in mice produced cardiovascular structural defects that resemble those in del22q11; the coupling between activities of VEGF and TBX1 (the gene deleted in DiGeorge Syndrome) found support in zebrafish studies, where defects in the pharyngeal arch provoked by TBX1 knockdown were exacerbated by concurrent VEGF knockdown (3). Further, sequence polymorphisms in the VEGF promoter associated with reduced VEGF expression were correlated with cardiovascular defect risk in del22q11 births.

The studies related to DiGeorge Syndrome reflect Dr. Carmeliet's goal of increasing our grasp of the complex morphogenic activities of VEGF and related factors. He noted that improved prospects for successful pro-angiogenic therapies will require greater appreciation of regulators of vessel maturation and smooth muscle recruitment, such that the neovasculature forming after short-term, high-dose VEGF exposure may be appropriately remodeled and stabilized. Of particular interest is PlGF, which, via interaction with Flt-1, may enlist monocytes to promote vessel branching by releasing proteases (4). Ongoing studies, using morpholino screens in zebrafish, seek to discover still other modifiers of angiogenesis and vessel remodeling.

Perhaps the most exciting and unexpected findings reviewed by Dr. Carmeliet concerned the potential role of VEGF as a neuroprotective agent. Previous work from the Carmeliet lab demonstrated that disruption of the hypoxia-responsive element in the VEGF gene could reduce VEGF expression in the central nervous system and produce a neuromotor phenotype strongly reminiscent of amyotrophic lateral sclerosis (ALS). Within the past year, Azzouz *et al.* (5) have reported that retrovirus-encoded VEGF expressed spinal motor neurons can enhance survival in a mouse model of ALS ($SOD1^{G93A}$). Most recently, direct intracerebroventricular injection of VEGF protein was shown to postpone the onset of paralysis and improve motor function in an analogous rat ALS model (6). Moreover, available evidence suggests that VEGF may act directly on neurons in these situations. These observations naturally provided strong rationale for more thorough examination of the role of VEGF in the maintenance of the nervous system, and offer hope for new and more effective ALS treatments.

(Continued on page 11)

THOMAS MACIAG – 2005 BENDITT AWARDEE

Joseph Miano

Only six days prior to his untimely passing, I telephoned Dr. Thomas Maciag with news of NAVBO's naming him as the recipient of the 2005 Earl P. Benditt Research Career Award. He was humbly thrilled with this news, and we spoke for some time about the latest research developments in his lab (and some playful banter about Bob Dylan's versus John Lennon's contribution to Western culture). Dr. Maciag was selected as this year's Benditt Award recipient for his seminal work relating to endothelial cell growth factors and angiogenesis.

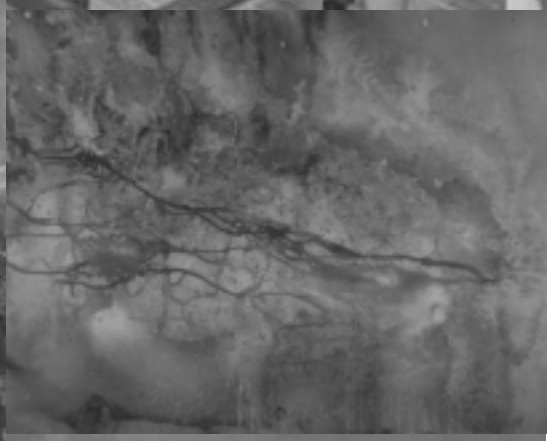
Thomas Maciag, Ph.D.
1946-2004

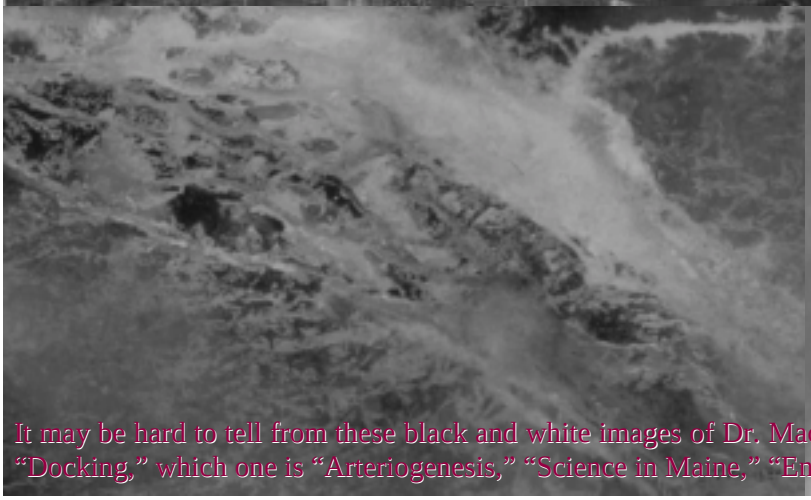
Dr. Maciag received his Ph.D. in Molecular Biology and Biochemistry at the University of Pennsylvania in 1975. Following some post-doctoral training at U Penn and biotech work at Collaborative Research, Dr. Maciag went to Harvard where, in 1979, he quickly established himself as a major force in the nascent field of growth factor biology. He was essentially the first to purify endothelial cell growth factor, aka FGF1 (1), which he and others subsequently cloned (2). During this explosive time in growth factor biology, Dr. Maciag paved the way for the continuous culture of such cells as keratinocytes (3), smooth muscle cells (4), and endothelial cells (5,6). In another landmark study, Dr, Maciag showed how heparin binds FGF1 (7), which we all appreciate now to be essential for FGF ligand-receptor interaction and activity. Then in 1985, Dr. Maciag's team showed that FGF1-heparin was potently chemotactic for endothelial cells (8). The latter finding was an important advance for the newly emerging field of angiogenesis, as it rapidly accelerated interest in this critical biologic process. Subsequent work from Dr. Maciag and his colleagues showed site-directed neovessel formation in vivo (9) and the involvement of FGF1 in this process (10). Dr. Maciag's early work in angiogenesis inspired an entire generation of scientists who continue to make important contributions in this field of science.

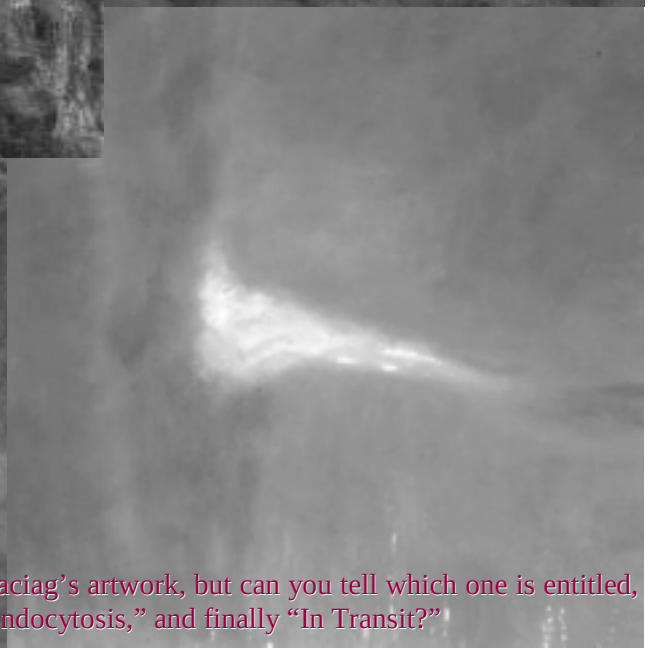
Dr. Maciag was an accomplished artist. His scientific interests reflected his creativity in art. So it was no surprise when Dr. Maciag created the Center for Molecular Medicine at Maine Medical Research Institute to attract a number of talented scientists, many of whom are NAVBO members. The work initiated by Dr. Maciag and his team span the spectrum of developmental vascular biology to the biochemistry of protein processing to the role of copper metabolism in vascular pathology. Thus, beyond the greater than 150 publications, 12 patents, and over 13,000 citations, Dr. Maciag was still advancing new frontiers in biology. His legacy is rich and will endure for generations.

Dr. Robert Friesel, a longtime collaborator of Dr. Maciag's, will deliver the Benditt Award Lecture entitled, "
" on Friday, June 17, 2005 at the Vascular Biology and Medicine Meeting in Chicago.

1. *Proc Natl Acad Sci USA* **76**:5674-5678, 1979
2. *Science* **233**:541-645, 1986
3. *Science* **211**:1452-1454, 1981
4. *Science* **212**:818-820, 1981
5. *Blood* **58**:788-796, 1981
6. *J Cell Biology* **91**:420-426, 1981
7. *Science* **225**:932-935, 1984
8. *J Cell Biology* **101**:2330-2334, 1985
9. *Science* **241**:1349-1352, 1988
10. *Proc Natl Acad Sci USA* **86**:7928-7932, 1989







It may be hard to tell from these black and white images of Dr. Maciag's artwork, but can you tell which one is entitled, "Docking," which one is "Arteriogenesis," "Science in Maine," "Endocytosis," and finally "In Transit?"

TAKING CARE OF BUSINESS

Bernadette M. Englert

Well, 2004 certainly was a busy year – the Developmental Biology Workshop in Monterey, the Atherosclerosis Symposium at Stanford University, the Blood Vessel Club at Experimental Biology, Vasculata, a summer course for trainees at the University of Washington organized by Dr. Stephen Schwartz and of course the IVBM, hosted by the University of Toronto. I hope you were able to attend at least one of these events. These meetings were a huge success. Plans are underway for a second Workshop on Developmental Vascular Biology (in February 2006, also at the Asilomar Conference Grounds near Monterey); we will continue to host the Blood Vessel Club at Experimental Biology – this year's topic is the "Aging of Blood Vessels is Coming of Age" and is being organized by Zorina Galis of Eli Lilly and Company. This summer NAVBO hopes to co-sponsor a second presentation of Vasculata at an east coast university. Check the web site for more details as they become available.

2005 Annual Meeting This year's annual meeting is entitled "**Vascular Biology and Medicine 2005: From Molecules to Man**." I am personally very excited about this year's meeting. For the first time, we are meeting with the Society for Vascular Medicine and Biology.. The program is on page 9 of this newsletter and all meeting information is available on the web site – *www.navbo.org/vbm2005/*. I hope you plan to attend the meeting and look forward to seeing you in Chicago.

Membership As usual, I make my appeal to all NAVBO members to encourage colleagues, especially junior colleagues, to join NAVBO.

Workshops As stated above, we will be offering another workshop on Developmental Vascular Biology, February 1-5, 2006, so mark your calendar. This meeting is once again being organized by Brant Weinstein of the NIH and working with him is Dr. Gary Owens, University of Virginia. Look for updates on the web site.

In 2007 we will be offering a workshop on Vascular matrix biology and bioengineering and will be organized by Cecelia Giachelli, University of Washington. No date has been set, but Dr. Giachelli would like skiing to be part of the curriculum!

See you in Chicago in June!

HIGHLIGHTS OF THE 2005 MEETING

Martha K. Cathcart

This year's annual meeting features an exciting program created by a dedicated Program Committee consisting of Myron Cybulsky, University of Toronto, Zorina Galis, Eli Lilly and Company, Mary Gerritsen, Exelixis, Joseph Miano, University of Rochester, Michael Riedy, University of Washington, and Michael Simons of Dartmouth Medical School. Sessions include presentations of research at the forefront of vascular biology.

On **Friday** June 17th, we begin with *Imaging* ***Atherosclerosis in vivo***. This symposium will include talks on the use of various imaging techniques to monitor blood cell interaction with diseased arteries, locate vulnerable plaques and monitor disease progression. The next symposium, ***Leukocyte interaction with endothelial cells*** features recent studies of hematopoietic progenitor cell tracking and the contributions of selectin and mechanotransduction to leukocyte extravasation.

Saturday's symposia include sessions on ***Arteriogenesis***, ***Signaling Pathways as Therapeutic Targets*** and *Adipocytes*. *Arteriogenesis* will include presentations on angiogenic cell therapy and the contribution of local and circulating cells to arterial growth and remodeling. Results of recent studies on the role of oxidant stress and lipid signaling in vascular pathogenesis will be presented in the signaling session. Then we will focus on adipocytes, cells whose functionality is only beginning to be appreciated. The importance of adipokines in inflammation and atherogenesis will be addressed.

Sessions on ***Stem Cells and Tissue Repair*** and ***"Vasculomics"*** are featured on the final morning, **Sunday**, June 19th. The stem cell session will emphasize talks on the role of stem cell progenitors in atherosclerosis and vascular calcification. The *Vasculomics* session highlights the results of recent studies using comparative genomics, SNPs and arrays to identify genes that are related to inflammation and cardiovascular disease.

This meeting, held jointly with the Society of Vascular Medicine and Biology, will foster interactions that bridge basic and clinical science. Young investigator competitions, mini-symposia (selected abstracts for oral presentation) and poster sessions will enhance the program and allow presentations by scientists at all phases of their careers. We look forward to a stimulating meeting in a vibrant city with our colleagues.

Vascular Biology and Medicine 2005: From Molecules to Man

June 16-19, 2005
Hyat Regency Chicago

Call for Abstracts and Meeting Program

A Joint Meeting of the

NAVBO
North American Vascular Biology Organization

and

S V M B

Annual Scientific Sessions of the

Society for Vascular Medicine and Biology

and the

North American Vascular Biology Organization

Symposia: June 17-19

Poster Sessions: June 17-18

Satellite Session:
Clinical Research in Peripheral Arterial Disease
Sponsored by NHLBI
June 16

Abstract Submission (Online only)
Deadline: March 1, 2005

Early Registration
Deadline: March 1, 2005

Applications for Junior Investigator Awards
Deadline: March 1, 2005

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(301) 581-3464
Fax: (301) 897-9745
Email: LBELL@svmb.org

Meeting information and Online Registration are available at:
www.navbo.org/vbm2005/

Vascular Biology and Medicine 2005:

Meeting Registration
Online meeting registration is available at www.navbo.org/register.html. If you prefer to register by mail or fax, you can download a registration form from the meeting web site – www.navbo.org/vbm2005/RegForm.pdf. Registration fees are as follows (early/regular): Society members - $200/$300; trainee members - $100/$150 and non-members - $400/$500. Early registration deadline is March 1, 2005.

Continuing Medical Education
Category 1 Continuing Medical Education (CME) credits will be offered at this meeting. CME application forms will be available at the registration desk. For the purpose of granting Continuing Medical Education credits toward the American Medical Association Physician's Recognition Award, this meeting is jointly sponsored by the American Society for Investigative Pathology and the Federation of American Societies for Experimental Biology (FASEB).

Meeting Objectives
Vascular Biology and Medicine 2005: From Molecules to Man will provide a forum for basic and clinical researchers in vascular biology and vascular medicine to share their most recent and novel science. It will be the ideal forum for graduate students and other trainees to present their work. This meeting is jointly sponsored by the North American Vascular Biology Organization and the Society for Vascular Medicine and Biology and will foster interactions between basic and clinical scientists and promote translational research.

Clinical practitioners, research scientists, graduate students, fellows, or medical education professionals involved in any aspect of vascular biology, vascular medicine and/or translational research will greatly benefit from this meeting. Participants will have a clearer understanding of current research in the area of vascular biology and its application to vascular medicine. Participants will attain new information concerning methodology, such as imaging and will cover new concepts in this area, such as adipocytes and vasculomics.

The program is characterized by the presentation of cutting edge research in areas pertaining to vascular function, signal transduction, arteriogenesis, vasculogenesis, vasculomics, molecular imaging, inflammation and vascular repair mechanisms.

Disclosure Policy
The Federation requires that audiences at FASEB-sponsored educational programs be informed of a presenter's (speaker, faculty, author, or contributor) academic and professional affiliation, and the existence of any significant financial interest or other relationship a presenter has with the manufacturer(s) of any commercial product(s) discussed in an educational presentation. When an unlabeled use of a commercial product, or an investigational use not yet approved for any purpose is discussed during the presentation, it is required that presenters disclose that the product is not labeled for the use under discussion or that the product is still investigational.

This policy allows the listener/attendee to be fully knowledgeable in evaluating the information being presented. The Program will note those speakers who have disclosed relationships, including the nature of the relationship and the associated commercial entity.

Disclosure includes any relationship that may bias one's presentation or which, if known, could give the perception of bias. These situations may include, but are not limited to: 1) stock options or bond holdings in a for-profit corporation or self-directed pension plan; 2) research grants; 3) employment (full or part-time); 4) ownership or partnership; 5) consulting fees or other remuneration; 6) non-remunerative positions of influence such as officer, board member, trustee, or public spokesperson; 7) receipt of royalties; 8) speaker's bureau; 9) other. For full-time employees of industry or government, the affiliation listed in the Program will constitute full disclosure.

Abstract authors are required to complete the disclosure form online in conjunction with their abstract submission. Invited speakers will be asked to complete a form and return it to the meeting office via mail or fax. The list of speakers and authors who have disclosed relationships will be included in the program. This list will include the nature of the relationship and the associated commercial entity.

Hotel Information
This meeting is being held at the Hyatt Regency Chicago. Reservation line will be opened on March 1, 2005. Check the meeting web site for updated information – www.navbo.org/vbm2005/hotelinfo.htm

Abstract Topic Categories
- Angiogenesis/vasculogenesis
- Arterial and aortic disease
- Cerebrovascular disease and stroke
- Development
- Exercise physiology
- Free radicals, ischemia and hypoxia
- Gene regulation, Genetics and Genomics and Proteomics
- Hypertension and vasoactive molecules
- Imaging
- Inflammation and connective tissue disorders
- Lymphology and lymphatic disease
- Metabolism and Endocrine
- Stem Cells/tissue engineering/regenerative medicine
- Thrombosis and Hemostasis
- Vascular cell biology and signaling
- Venous disease
- Vascular surgery
- Other

Abstracts must be submitted online by 12:00 pm EST, March 1, 2005.

All meeting participants are invited to submit abstracts of work related to vascular biology, vascular medicine or translational research. Complete abstracts should be submitted online at www.navbo.org/vbm2005/. Full instructions concerning format, publication, and presentation are available at *www.navbo.org/vbm2005/rules.pdf.*

Junior Investigator Awards
NAVBO and SVMB will sponsor awards in both vascular biology and vascular medicine. In order to be eligible you must be either a trainee member of NAVBO or an associate member of SVMB. You must be a graduate student, postdoctoral fellow, research fellow or junior faculty (within three years of training). Complete information regarding the award criteria and application can be found at *www.navbo.org/vbm2005/jiaward.htm.*

From Molecules to Man

Abstract Submission Deadline: March 1, 2005
Early Registraion Deadline: March 1, 2005

Program

Program Committee Chair for NAVBO - Martha K. Cathcart, Ph.D., Cleveland Clinic Foundation
Program Committee Chair for SVMB - John P. Cooke, M.D., Ph.D. Stanford University

THURSDAY, JUNE 16

8:30 am - **Satellite Meeting**
Clinical Research in Peripheral Arterial Disease
Conference sponsored by the NHLBI

FRIDAY, JUNE 17

8:00 am - **Welcome Address from Society Presidents**
Michael Jaff, SVMB and William A. Muller, NAVBO

8:30 am - ***Imaging Atherosclerosis in vivo***
Chair: W.A. Muller, Cornell Univ. Weill Medical College and M.V. McConnell, Stanford University

Visualizing the interactions of blood cells with diseased arteries
Yuqing Huo, University of Minnesota

Targeted MRI approaches for atherosclerosis imaging
Michael V. McConnell, Stanford University

Nuclear imaging of experimental and clinical atherosclerosis
Jagat Narula, University of California, Irvine

10:00 am - Coffee Break

10:30 am - ***Leukocyte Interactions with Endothelial Cells***
Chairs: M.I. Cybulsky, University of Toronto and G.S. Kansas, Northwestern University

Molecular and cellular contributions to selectin-dependent leukocyte adhesion under flow
Rodger McEver, Oklahoma Medical Research Foundation

Mechanotransduction: a role in leukocyte recruitment under flow
Kamala D. Patel, University of Calgary

Parallels and contrasts between leukocyte and stem cell adhesion to venular endothelium
Paul Frenette, Mount Sinai School of Medicine

12:00 pm - **Poster Sessions/Lunch (2 hour session)**
SVMB Membership Business Meeting

2:00 pm - **Two concurrent Mini-symposia**
- abstract presentations

3:30 pm -Coffee Break

4:00 pm - **Two concurrent Mini-symposia**

5:15 pm - **Benditt Lecture/Award Presentation**
Award Recipient (posthumously):
Thomas Maciag, Maine Medical Research Center
Lecturer: Robert Friesel, Maine Medical Research Center

6:15 pm - **Member Reception**

SATURDAY, JUNE 18

8:30 am - ***Arteriogenesis: Recent Insights***
Chair: M. Simons, Dartmouth-Hitchcock Medical Center and J.P. Cooke, Stanford University

Angiogenic cell therapy
Stephen Epstein, Washington Hospital Center

Role of circulatory stem cells in cholinergic angiogenesis
John Cooke, Stanford University

Contribution of local and circulating cells to arterial growth and remodeling
Armin Helisch, Dartmouth University

10:00 am - Coffee Break

10:30 am - ***Signaling Pathways as Therapeutic Targets***
Chairs: Z.S. Galis, Eli Lilly & Co. and Indiana University and M. Reidy, Univ of Washington

Barking up the right vascular tree with sphingosine 1-phosphate (S1P) signaling
Tim Hla, University of Connecticut Health Center

Oxidant-mediated signaling
Richard A. Cohen, Boston University School of Medicine

Vascular remodeling: Insights from biochemical and genetic studies
Bradford C. Berk, University of Rochester

12:00 pm - **Poster Sessions/Lunch (2 hours session)**
Vascular Jeopardy (1 hour session)

2:00 pm - **Two concurrent Mini-symposia**

3:30 pm - Coffee Break

4:00 pm - ***Adipocytes: At the crossroads of energy homeostasis, inflammation and atherosclerosis***
Chairs: M.E. Gerritsen, Exelixis, Inc. and P. Scherer, Albert Einstein College of Medicine

Adipocyte-derived factors as modulators of the metabolic syndrome
Philipp Scherer, Albert Einstein College of Medicine

Leptin: An inflammatory and atherogenic adipokine
Stavros Konstantinides, Georg August University of Goettingen

Do adipokines talk to the endothelium?
Willa Hsueh, University of California at Los Angeles

5:30 pm -**Junior Investigator Award Ceremony**
NAVBO Membership Business Meeting

SUNDAY, JUNE 19

8:30 am - ***Stem Cells and Tissue Repair: Risk vs Benefit***
Chairs: C. E. Murry, University of Washington and M. Penn, Cleveland Clinic Foundation

Vascular progenitors and atherosclerosis
Noel M. Caplice, Mayo Clinic College of Medicine

Origin and Fate of Vascular Progenitors
Karen Hirschi, Baylor College of Medicine

Artery wall stem cells in vascular calcification
Linda L. Demer, University of California, Los Angeles

10:00 am - Coffee Break

10:30 am - ***Vasculomics***
Chairs: J.M. Miano, Univ of Rochester and L. Pennacchio, Lawrence Berkeley

Exploiting comparative genomics to identify functional sequences in the human genome
Len Pennacchio, Lawrence Berkeley

SNPs and haplotypes in genes related to inflammation and CVD
Mark Rieder, University of Washington

Arrays for EC and SMC-restricted genes
Tom Quertermous, Stanford University

Vascular Biology and Medicine 2005: From Molecules to Man

June 16-19, 2005
Hyatt Regency Chicao, Chicago, Illinois

This meeting is supported in part by educational grants from:

Eli Lilly and Co.

Vasogen

VEC Technologies, Inc.

ATVB Council of the American Heart Association

◇◇◇◇◇◇

Additional Opportunities for Meeting Support are available

Please contact the NAVBO Administrator if you are interested in providing support for this meeting. Thank you.

Registration Form

Name/Degree: _____

Position/Title: _____

Dept: _____

Institution: _____

Address: _____

_____

City/State/Postal Code: _____

Phone: _____

Fax: _____

Email: _____

Registration Fees – Regular Members		Early (March 1)	After March 1
❒	NAVBO Member	$200	$300
❒	SVMB Member	$200	$300
❒	Non-Member	$400	$500
Trainee Members/Students*			
❒	NAVBO Member	$100	$150
❒	SVMB Member	$100	$150

❒ I plan to attend the NHLBI Conference on June 16.

*Students, post-docs, research fellows, etc. must be a trainee member in NAVBO or an associate member in SVMB to qualify for this special rate.

❒ **Check Enclosed**

Credit Card Information –
Credit Card Number: _____

❒ VISA ❒ MC ❒ Amex Expiration Date:_____

Name on card: _____

Signature: _____

Cancellations –
Cancellations received by written notification through May 15, 2005 will receive a refund (less a $50 processing fee). No refunds will be given after May 15.

(Continued from page 3)

The progress made in clinical application of fundamental discoveries in angiogenesis, exemplified by the approval of AvastinÆ® in early 2004 to treat colorectal cancer, justifiably was celebrated at the IVBM meeting. Dr. Carmeliet emphasized the need to press ahead in our exploration of additional therapeutic strategies, noting that anti-Flt-1 antibodies have shown promise as inhibitors of tumor vascularization and in models of arthritis.

The qualities NAVBO honored with the Benditt Award were clear from Dr. Carmeliet's lecture: the vision to embrace and enhance new technologies, an admirable spirit of collaboration, and attention to the implication of his work beyond the traditional bounds of vascular biology.

1. Carmeliet *et al.*, Abnormal blood vessel development and lethality in embryos lacking a single VEGF allele. *Nature* 1996 **380**:435-439.
2. Carmeliet *et al.*, Impaired myocardial angiogenesis and ischemic cardiomyopathy in mice lacking the vascular endothelial growth factor isoforms VEGF164 and VEGF188. *Nat Med* 1999 **5**:495-502
3. Stalmans *et al.*, VEGF: a modifier of the del22q11 (DiGeorge) syndrome? *Nat Med* 2003 **9**:173-182.
4. Pipp *et al.*, VEGFR-1-selective VEGF homologue PlGF is arteriogenic: evidence for a monocyte-mediated mechanism. *Circ Res* 2003 **92**:378-385.
5. Azzouz *et al.*, VEGF delivery with retrogradely transported lentivector prolongs survival in a mouse ALS model. *Nature* 2004 **429**:413-417.
6. Storkebaum *et al.*, Treatment of motoneuron degeneration by intracerebroventricular delivery of VEGF in a rat model of ALS. *Nat Neurosci* 2005 **8**:85-92.

TECHNICIAN'S CORNER—THE FACTS ON MACS

Timothy Peterson

Protocol for Isolating Endothelial Progenitor Cells from Human Peripheral Blood

1. Withdraw 30-50 ml blood into a syringe containing heparin or EDTA.
2. Dilute whole blood (1:2 dilution) in Hanks Balanced Salt Solution (HBSS) containing 1 mM EDTA and 5% BSA (35 ml blood, 70 ml HBSS).
3. Add 15 ml HISTOPAQUE-1077 to a 50 ml conical tube and gently layer 21 ml of the diluted blood on top.
4. Centrifuge for 30 minutes at 1400 rpm (320 xg) at room temperature.
5. Remove mononuclear cell (cloudy band above RBC pellet) with a pipette and transfer to a new 50 ml conical tube.
6. Centrifuge at 1100 rpm (200 xg) for 10 minutes (4° C) and remove two-thirds of the supernatant.
7. Centrifuge again at 1100 rpm for 5 minutes (4°C) and remove the remaining supernatant.
8. Add 6 ml RBC lysing solution, pipette mix for 1-2 minutes (more than that may damage mononuclear cells), spin for 5 minutes at 1100 rpm (200 xg; 4°C) and remove supernatant. If the pellet is red at this point repeat Step 8.
9. Wash with 4 ml wash medium (EGM-2 media without serum) and centrifuge for 10 minutes at 1100 rpm (4°C). Remove supernatant and repeat wash (Step 9).
10. Resuspend in 1.5 ml of complete EGM-2 media (containing serum) and plate onto fibronectin-coated chamber slides and 10 cm^2 tissue culture plates at a density of at least $5x10^6$/well.
11. Change media daily for the first 7 days then change media every other day until colony formation.
12. Trypsinize and passage cells when they reach 80% confluence.

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Technical tips:

- The key to this assay is patience! Feed cells gently and methodically. Within the first 4-7 days there will be a mixed population of adherent cells that vary in size (5-50 μm) as well as morphological shape. From this population of cells, morphologically distinct endothelial colonies will form around day 14 to day 21. A working stock of "outgrowth-endothelial cells" usually takes around 30 days. It is worthy to note here that not all "day-7, EPCs" will form "outgrowth-endothelial colonies". Only about 1-5 outgrowth-endothelial colonies can be expected using this protocol.
- Culture the isolated MNCs (Step 10 above) in either 6-well culture dishes or 10 cm^2 tissue culture plates coated with fibronectin (50 μg/ml). If you want to analyze adherent day-7 cells by confocal microscopy, culture cells on fibronectin-coated, 2-well chamber slides as well.

(Continued on page 14)

JOB OPPORTUNITIES

POSTDOCTORAL OPPORTUNITY-
DEPARTMENT OF SURGERY AT
WEILL MEDICAL COLLEGE
OF CORNELL UNIVERSITY

Position available immediately for a Ph.D. or equivalent to conduct research on signaling transduction and gene regulation in vascular smooth muscle cells in relationship with vascular disorders in the laboratory of Drs. K. C. Kent and B. Liu. Experience in biochemistry, cell biology and molecular biology are required. Qualified applicants should send their curriculum vitae and names of three references by e-mail to *bol2001@med.cornell.edu.* For further information, contact:

Dr. B. Liu
Department of Surgery
Weill Medical College of Cornell University
Pason 707, 1300 York Avenue
New York, NY 10021.

Weill Medical College of Cornell University is an Equal Opportunity Employer.

POSTDOCTORAL FELLOW
UNIVERSITY OF MICHIGAN

Postdoctoral fellow in NIH/VA-funded laboratory studying rheumatoid arthritis gene therapy, angiogenesis, cell adhesion, and cytokines (including IL-4, IL-13, IL-18) (*Nature* **376:**517, *Science* **258:**1798, *J. Clin. Invest.* **101:**746). Experience with adenovirus, adeno-associated virus, angiogenesis, immunoassays, cell adhesion assays, animal arthritis/angiogenesis models, cell signaling, and molecular biology desirable. US citizen/ permanent resident training grant eligible. Send c.v. and three reference letters to:

Dr. Alisa Koch
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University of Michigan Medical School
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Ann Arbor, MI 48109-0680
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FELLOWSHIPS IN
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The Division of Cardiothoracic Surgery at Beth Israel Deaconess Medical Center and Harvard Medical School offers four 2 years positions in the broad area of Cardiovascular Surgery Research for residents in surgery who have completed their second or third year of training. Positions are funded through a T-32 Training Grant from the National Heart Lung and Blood Institute. Areas of research include stem cell biology, therapeutic angiogenesis, gene and cell-based therapy for the treatment of heart failure, epidemiology, myocardial and vascular signal transduction, myocardial protection and other topics in cardiovascular research. All mentors (CV surgeons, anesthesiologists, cardiologists, and research scientists) are funded by the NIH. Research fellowships generally begin July 1, but other start dates may be possible. Interested residents should send their CV and letter of interest to:

Frank Sellke, MD
Chief, Division of Cardiothoracic Surgery
Beth Israel Deaconess Medical Center
110 Francis St, Suite 2A
Boston, MA 02215
Email: fsellke@bidmc.harvard.edu.

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which provides stipends, tuition, travel funds, and health insurance as well as tuition for special interest courses off campus. Pre-doctoral trainees can enroll in any of 7 different degree-granting programs and training usually requires 5-6 years. We also offer a unique opportunity for MD's who wish to obtain the PhD degree in an accelerated program. The breadth of interests of the faculty members as well as the local environment can be explored at our web site at *http://www.med.virginia.edu/medicine/inter-dis/cvrc/*. If you are interested in applying, please contact Dr. Brian R. Duling (*brd@virginia.edu*) . Please note that we are an Equal Opportunity Employer, and that these positions are restricted to US citizens or to permanent resident.

Dr. Brian R. Duling
Robert M. Berne Professor of Cardiovascular Research
Member, Cardiovascular Research Center
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RESEARCH INVESTIGATOR/
RESEARCH ASSISTANT PROFESSOR
UNIVERSITY OF MICHIGAN

Research Investigator/Research Assistant Professor in NIH/VA-funded laboratory studying rheumatoid arthritis gene therapy, angiogenesis, cell adhesion, and cytokines (including IL-4, IL-13, IL-18) (*Nature* **376:**517, *Science* **258:**1798, *J. Clin. Invest.* **101:**746). Experience with adenovirus, adeno-associated virus, angiogenesis, immunoassays, cell adhesion assays, animal arthritis/angiogenesis models, cell signaling, and molecular biology desirable. US citizen/permanent resident training grant eligible. Send c.v. and three reference letters to:

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CALENDAR OF SCIENTIFIC MEETINGS

February 6-11, 2005. Ventura Beach Marriott, Ventura, CA. **Gordon Research Conference on Vascular Cell Biology.** Go to *www.grc.uri.edu/*

April 2, 2005. Moscone Convention Center, San Francisco, CA. **Blood Vessel Club.** Go to *www.navbo.org*

April 2-6, 2005. Moscone Convention Center, San Francisco, CA. **Annual Meeting of the American Society for Investigative Pathology at Experimental Biology.** Go to *www.asip.org*

April 3-8, 2005. Steamboat Springs, CO. **Keystone Symposium on Molecular Biology of Cardiac Diseases and Regeneration**.
Go to w*ww.keystonesymposia.org/*.

April 28-30, 2005. Grand Hyatt Hotel-Washington, DC. **6th Annual Conference on Arteriosclerosis, Thrombosis and Vascular Biology.** Go to *www.americanheart.org/*

June 4-7, 2005. San Diego Convention Center, San Diego, CA. **Annual Meeting of the Endocrine Society (ENDO 2005).** Go to *www.endo-society.org/*

June 16-19, 2005. Hyatt Regency Chicago, Chicago, IL. **Vascular Biology and Medicine 2005: From Molecules to Man** (NAVBO 2005 Annual Meeting). Go to *www.navbo.org/vbm2005/*

See Center Pull-Out for NAVBO Annual Meeting Program

June 19-24, 2005. Kimball Union Academy, Meriden, NH. **Gordon Research Conference on Atherosclerosis**. Go to *www.grc.uri.edu/*

July 24-27, 2005. Keystone Conference Center - Keystone, CO. **2nd Annual Symposium of the American Heart Association Council on Basic Cardiovascular Sciences-Targeting Heart Failure**. Go to *www.americanheart.org/*

July 18-21, 2005. Dartmouth Medical School, Hanover, NH. **Vasculata 2005.** Go to *www.navbo.org*

August 6-12, 2005. Sydney, Australia. **XXth Congress of the International Society on Thrombosis and Haemostatis.** Go to *www.isth2005.com/*

(Continued on page 16)

- While the literature still regards the uptake of acetylated LDL and isolectin as good markers for EPCs, almost every cell type at day-7 takes up acetylated-LDL/isolectin, but only a select few will form "outgrowth-endothelial colonies". To try this, purchase Alexa Fluor-488 conjugated acetylated LDL (10 μg/ml for 4 hours at 37°C.) and Alexa fluor-647 conjugated Isolectin GS-IB4 (5 μg/ml for 30 minutes at 37°C) from Molecular Probes and visualize with a fluorescent microscope.

Shopping list:

Item	Vendor
1) HBSS	Invotrogen
2) HISTOPAQUE-1077	Sigma
3) EGM-2 Media	Cambrex
4) Nunc 2-well chamber slides	Fisher Scientific
5) Fibronectin	BD Biosciences

Buffers/Media preparation:

- HBSS and HISTOPAQUE-1077 are ready to use as provided by the manufacturer.
- The growth media used for these cells is EGM-2 media. The purchased media contains: 500 ml of endothelial basal media (EBM), 10 ml FCS (2% final concentration), hEGF, VEGF, hFGF-B, IGF-1, Ascorbic Acid, Hydrocortisone, Gentamicin, Amphotericin-B and Heparin.
- The wash media used for this protocol is EGM-2 media (above) without the addition of FCS.
- The red blood cell (RBC) lysis solution can be purchased from Cambrex as "ACK Cell Lysing Buffer" or made in the lab using the following protocol:

  1X RBC lysing solution (for 1 liter):
  8.29 g NH_4Cl (Ammonium Chloride) [0.15M]
  1.0 g $KHCO_3$ (Potassium Bicarbonate) [10 mM]
  0.0367 g Na_2-EDTA [0.1 mM]
  Adjust pH to 7.4 with 1N HCl

General Protocol for FACS Analysis

1. Remove media from cells and wash twice with phosphate buffered saline (PBS).
2. Remove PBS and add 2 mL of 0.05% trypsin/EDTA. Incubate at 37°C for 5-10 minutes. Gently rock plate if necessary. Confirm under microscope that all cells have lifted.
3. Transfer cells to a 15 mL centrifuge tube and wash cells with PBS-A (PBS + 1% albumin) at 4°C and centrifuge for 5 minutes at 1000 rpm (160 xg).
4. Suction off supernatant and resuspend pellet in 1 ml of PBS-A, and transfer to 1.5 ml Eppendorf tubes. Divide the samples at this step for appropriate controls (see below).
5. Centrifuge for 5 minutes at 1000 rpm at 4°C. Resuspend pellet in 1 mL of PBS-A, and centrifuge again for 5 minutes at 4°C.
6. Resuspend pellet in primary antibody (usual dilution is 1:200 with PBS being diluent) at 4°C for 1 hour. Usually 0.3-0.5 mL total volume is used. For control, use the same concentration of isotype control antibody.
7. Centrifuge cells as above at 1000 rpm in 4°C centrifuge for 5 minutes.
8. Wash cells twice with PBS-A, and centrifuge again at 1000 rpm in 4°C.
9. Suspend cells in secondary antibody (1:1000 dilution) for 30 minutes at 4°C and cover with aluminum foil to protect from light.
10. Centrifuge for 5 minutes at 1000 rpm at 4°C. Resuspend pellet in 1 mL of PBS-A, and centrifuge again for 5 minutes at 4°C.
11. Resuspend in 0.5 mL of 2% paraformaldehyde and transfer to tube (5 ml polystyrene tube from Falcon #352058) for FACS Analysis.

Technical tips:

- About 50,000 to 100,000 cells are required for good FACS analysis.
- Several controls are required for optimal gating of the cells: a negative control containing primary antibody with no secondary antibody and a negative control containing IgG-isotype control antibody with secondary antibody. If labeling cells with more than one fluorochrome, for gating purposes, include a sample containing each fluorochrome separately.
- This assay is much easier if antibodies preconjugated to fluorchromes are used. This allows the user to skip Steps 8-10. A preconjugated control IgG can then be used as a control.
- The purpose of the albumin is to keep cells from sticking together. It is important that after each centrifugation to fully resuspend the pellets to avoid cell clumping.

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CALENDAR OF SCIENTIFIC MEETINGS continued

August 14-19, 2005. Salve Regina University, Newport, RI. **Gordon Research Conference on Angiogenesis and Microcirculation**. Go to *www.grc.uri.edu/*

September 10-13, 2005. Univ of New Hampshire Durham, NH. **Special Transatlantic Meeting of The Microcirculatory Society, Inc. and The British Microcirculatory Society.** Go to: *http://microcirc.org* (click on "Joint Meeting with British Society)

September 28-30, 2005. Hamburg, Germany. **3rd European Meeting on Vascular Biology and Medicine**. Go to *www.emvbm.org*

November 13-16, 2005. Dallas, TX. **American Heart Association Scientific Sessions 2005**. Go to *http://scientificsessions.americanheart.org/*

November 23-25 2005. Bournemouth International Centre, Bournemouth, UK **The Vascular Society Annual Meeting**.
Go to *www.vascularsociety.org.uk/*

February 1-5, 2006. Asilomar Conference Center, Monterey, CA. **Developmental Vascular Biology Workshop II.** Go to *www.navbo.org*

Vascular Biology and Medicine 2005: From Molecules to Man

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