Volume 24
Summer 2018

NAVBO Newsletter

At the Heart of the Vascular Biology Community

Special Points of Interest

- Photos from IVBM 2018
- 2018 Meritorious Award Recipients
- Vascular Biology 2018

It is truly a great honor to start my term as your NAVBO president. As a longtime NAVBO member, I have enjoyed watching our little society grow and expand in membership and areas of interest. With increasing participation from international scientists, and an active role in supporting the International Vascular Biology Meetings, we are participating in a global endeavor to push the frontiers of vascular biology forward.

I would like to thank our president Ceci Giachelli for her energy in leading NAVBO for the last year. She has provided leadership for our ongoing meetings, the launch of a successful new series of webinars, and most recently through participation in the very successful IVBM 2018 in Helsinki. Thanks are also due to our past-president Jan Kitajewski, who provided sage advice through the last year, and considerable enthusiasm towards efforts to lobby for science and research, and to continue to organize the Lymphatic Forum meetings. And finally of course we owe many thanks to Bernadette Englert. She is the glue that holds us together, keeps us on time and on target, and knows more science than any other non-scientist that I have encountered.

We have another exciting year ahead. Vasculata will be in St. Louis MO, starting July 23 and including 13 different hands-on workshops, all organized by Dr. Gwen Randolph. Vascular Biology 2018 in October will be at a new site in scenic Newport Rhode Island. This year the meeting will include two concurrent workshops covering Biology of Signaling in the Cardiovascular System, and Vascular Inflammation. An outstanding program has been organized by Drs. Cleaver, Sessa, Aikawa and Muller, thank you to them for the hard work. Our meetings are the strong roots of our society, providing a forum for lively discussions and interactions among members. Trainee and junior members in particular enjoy the poster sessions, where we guarantee your work will be seen by an enthusiastic audience.

The strength of NAVBO lies with its committed volunteers. I would like to put out a call to members to get involved. Anyone who wants to participate to organize a future session, workshop or Vasculata, please contact me or Bernadette Englert, and we can discuss future ideas. In addition, there are many opportunities to get involved by serving on a committee: Development, Education, Membership, Meritorious Awards, and Communications.

Michelle Bendeck

Inside this issue:

NAVBO gratefully acknowledges unrestricted educational grants from the following organizations for Vascular Biology 2017:

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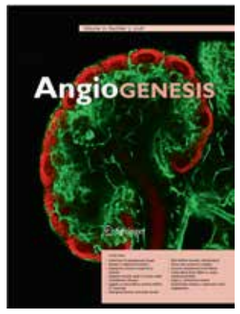
Springer Junior Investigator Award



Additional Travel Awards

UNIVERSITY OF TORONTO

TED ROGERS CENTRE FOR HEART RESEARCH

Rakesh Jain Named the 2018 Recipient of the Earl P. Benditt Award

William R. Huckle, Editor

The NAVBO Meritorious Awards Committee and Council is pleased to announce the selection of Rakesh K. Jain, Ph.D., as the 2018 recipient of the Earl P. Benditt Award, in recognition of his numerous contributions to our understanding of the unique characteristics of tumor vasculature. Dr. Jain is currently the Andrew Werk Cook Professor of Tumor Biology (Radiation Oncology) at Harvard Medical School and Director of the Edwin L. Steele Laboratory for Tumor Biology at Massachusetts General Hospital. He will present the Benditt Lecture and receive the award, one of NAVBO's highest honors, at Vascular Biology 2018 in Newport, Rhode Island (October 17, 2018).

Following undergraduate studies in Chemical Engineering at the Indian Institute of Technology in Kanpur, Dr. Jain received his M.S. and Ph.D. in Chemical Engineering from the University of Delaware. He held faculty positions in Chemical and Biomedical Engineering at Columbia University and Carnegie Mellon University prior to joining the Harvard faculty in 1991. He has served on a multitude of editorial boards, review panels, and advisory groups. Dr. Jain's research has been supported steadily for decades by the NIH and other agencies, including the Gates Foundation and Department of Defense. His scholarly contributions, reported in well over 650 publications, book chapters, and reviews, have earned Dr. Jain scores of awards and honors in the U.S. and internationally, including election to the United States National Academies of Medicine (2003), Engineering (2004), and Sciences (2009). He holds seven U.S. patents and received the United States National Medal of Science for 2013.

Dr. Jain is regarded as a trailblazer in the study of tumor microenvironment, examining in detail the notion that the relationships between tumors and their surrounding non-tumor tissue—including blood vessels—are essential determinants of disease progression, therapeutic efficacy, and patient prognosis. Dr. Jain's nominators note that, in sum, his work has provided "…unprecedented molecular, cellular, anatomical and functional insights into the vascular pathophysiology of tumors, for proposing the seminal hypothesis that anti-angiogenic therapy can 'normalize' the aberrant vasculature and microenvironment of tumors and thereby improve both delivery and efficacy of treatment of solid tumors." His studies revealed that the blood and lymphatic vasculature, fibroblasts, immune cells and the extracellular matrix associated with tumors are abnormal, collectively creating a hostile tumor microenvironment characterized by hypoxia, low pH and high interstitial fluid pressure. He and his collaborators subsequently hypothesized that normalizing the microenvironment may improve treatment outcome and subsequently have demonstrated that judicious use of antiangiogenic agents—originally designed to starve tumors—could transiently "normalize" tumor vasculature, alleviate hypoxia, increase delivery of drugs and anti-tumor immune cells, and improve the outcome of various therapies, including immunotherapy. Dr. Jain's more recent work includes efforts to improve the vascular competence of engineered tissue in the context of regenerative medicine. By generating endothelial and smooth muscle cells from human embryonic stem cells and induced pluripotent stem cells, his lab is bringing functional and durable engineered vessels closer to translation into the clinic.

Dr. Jain will give his talk, "Reengineering the tumor microenvironment to improve cancer treatment: Bench to bedside" on October 17, 2018 at Vascular Biology in Newport, RI.

Please join us for VB2018 in Newport this October to honor Dr. Jain as he receives this well-deserved award.

Christiana Ruhrberg is the Judah M. Folkman Award in Vascular Biology Recipient

William R. Huckle, Editor

Dr. Ruhrberg will give her talk, "Molecular and Cellular Mechanisms of Blood Vessel Growth," on October 17 at Vascular Biology in Newport, RI.

The NAVBO Meritorious Awards Committee, the Scientific Advisory Board, and the NAVBO Council announce with pleasure the selection of Christiana Ruhrberg, Ph.D., as the recipient of the 2018 Judah Folkman Award in Vascular Biology. This award recognizes outstanding contributions from vascular biologists who are at mid-career (within fifteen years of their first faculty appointment). Dr. Ruhrberg will present the Folkman Award Lecture and receive the award at Vascular Biology 2018 in Newport, Rhode Island (October 17, 2018).

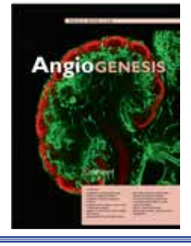
Dr. Ruhrberg completed BSc/MSc studies in Cell Biology at Justus Liebig University in Germany and received her Ph.D. in Biochemistry from Imperial College London in 1997 under the direction of Fiona Watt at the Imperial Cancer Research Fund. She was named Young Cell Biologist of the Year 1996 by the British Society for Cell Biology for her work on proteins that promote epidermal barrier function. She pursued post-doctoral studies in the laboratories of Robb Krumlauf at the National Institute of Medical Research studying cranial motor neuron development, and then with David Shima at the ICRF to elucidate molecular mechanisms of blood vessel growth, with support from the Medical Research Council and Imperial Cancer Research Fund. She joined the staff of the Institute of Ophthalmology at University College London as Principal Research Fellow in 2003, rising to the faculty ranks of Lecturer (2007), Reader (2008), and Professor (2011) of Neuronal and Vascular Development at UCL, where she is a Wellcome Trust Investigator.

Dr. Ruhrberg research team at UCL seeks to determine how cells of the nervous and vascular systems interact in "co-patterning" during mammalian development and in disease, with the goal of identifying molecular targets for therapeutic intervention in vascular disease. Their experimental approaches combine reverse genetics with tissue culture models to examine how the vascular endothelial growth factor A and class 3 semaphorin proteins convey signals between cells in the brain, retina, heart and lung. Her research, performed in collaboration with NAVBO stalwarts Holger Gerhardt, Kari Alitalo, David Shima, Christer Betsholtz and others, has demonstrated that VEGF forms gradients that guide blood vessel growth in developing organs and that Neuropilin 1 has a dual role in VEGF and matrix signalling in the vascularization of the retina. She was the first to demonstrate that VEGF isoforms cooperate during vessel sprouting in the first stage of angiogenesis, and that macrophages act as bridge cells for vessel fusion in the subsequent stage of vessel networking. Further, Dr. Ruhrberg pioneered the mouse hindbrain as a powerful new model for angiogenesis research. To date, she and her associates has published more than 80 papers in the scientific literature, many of which are highly cited, and she has trained >15 doctoral students and postdocs since becoming an independent investigator.

Please join us for VB2018 in Newport this October to honor Dr. Ruhrberg as she receives this award in recognition of her accomplishments and bright future as a vascular biologist.

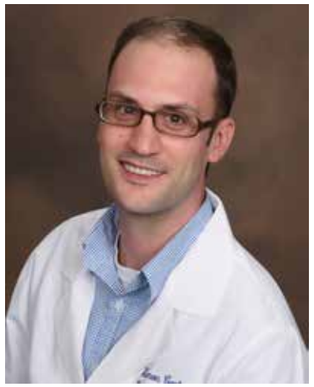
Apply for the Springer Junior Investigator Award

This is a junior faculty (or equivalent) award and is based on the abstract submitted to VB2018.
See full criteria at: *www.navbo.org/Springer2018*



***Supported by* Angiogenesis**

New for 2018 - NAVBO Webinar Series



August 2, 2018 - 1pm ET
Lymphatic Vessels & Vanishing Bones: Animal Models of Lymphatic Anomalies with Bone Involvement
Michael Dellinger, Ph.D.
UT Southwestern Medical Center

September 13, 2018 - 1pmET
Fast interactive genomics data visualization in AltAnalyze
Nathan Salomonis, Ph.D.
Cincinnati Children's Hospital Medical Center

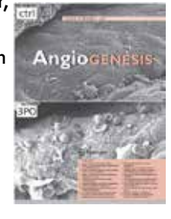
Available on-demand
Engraftment of bioengineered vascular networks
Juan Melero-Martin, Ph.D.
Boston Children's Hospital

LGDA Lymphangiomatosis & Gorham's Disease Alliance
LMI Lymphatic Malformation Institute

Availalbe on-demand
A Perfused Blood-Brain Barrier on a Chip
Christopher Hughes, Ph.D.
University of California, Irvine

Availalbe on-demand
Elastic fibers and the mechanics of maturing arteries
Jessica Wagenseil, D.Sc.
Washington University

Availalbe on-demand
GTPase regulation of actomyosin during blood vessel tubulogenesis
Ondine Cleaver, Ph.D.
UT Southwestern Medical Center



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DMT

A Pore Poem – A Rich Life: Morris Karnovsky, M.B.B.Ch, D.Sc.

Elazer R. Edelman and John Castellott

The amazing John Pappenheimer,
(Whose name defies any rhymer!)
And many others, postulated small and large pores to be
The basis of capillary permeability
I, perhaps foolishly, ascribed small pore function
To the endothelial junction
Which I opined is incompletely tight
But I was told this is not right!
Suppose there are also rare gaps, sufficiently large
Thru which big macromolecules can barge
Others fervidly disagree, And localize to Palade's caveolae
Not only large, but small pores as well!
What is correct? Will time tell?
Will this 35 year old dispute
Be one day rendered mute?

Morris J. Karnovsky, Shattuck Professor of Pathological Anatomy at Harvard Medical School, passed away in January 2018 at the age of 91. Aside from his many accomplishments and contributions to science he was, in 1999, the first recipient of the NAVBO Earl P. Benditt Award. On that occasion he composed and NAVBO published the poem printed above. He was recognized then as we remember him now as one the elite scientists whose work changed our understanding of the world around us. Karnovsky was a towering intellect of prodigious productivity – the most quoted author in pathology, the sixth most widely quoted author in all of medicine. He authored six "Citation Classics"—six of his papers have been cited more than 1,000 times. His discoveries span the breadth of medical science and his inventions have changed medical research and diagnostics. The chemical reactions he intuited and then reduced to practice forever changed science.

Karnovsky was born in Johannesburg, South Africa. His father became one of the first pharmacists in South Africa. His mother was an opera singer and their family hosted world leaders in arts and music. Indeed, Karnovsky learned to play the piano on the lap of Sergei Rachmaninoff. Trained in the public schools, he became simultaneously a life-long devotee of art, music and especially poetry and a dedicated proponent and activist for educational equality and universal access to healthcare.

Two common threads link Morris' research through the years -- the study of the structural components of cells and their function, and the analysis of how disease states change structure and function. His research pioneered the invention and development of different technologies and are often an elegant weave of innovative methods, creative experimental techniques and sophisticated models. His work defined the gap junction, revealed the endothelial nature of the blood-brain barrier and vascular permeability, the essence of glomerular permeability, the biochemistry of the reactive oxygen species, immunoglobulin and lymphocyte biology, and how lipid domains arise to generate the phenotypic dynamism of endothelial cells.

One of Morris' most widely recognized contributions was the extension of the horseradish peroxidase (HRP) tracer method of Werner Straus to both the light and electron microscopic level, by introducing diaminobenzidine (DAB) as an electron donor. The first paper to introduce this technique authored by Morris Karnovsky and Richard Graham traced the endocytotic uptake of HRP from the glomerular filtrate into cells of the proximal tubules. This study is not only a citation classic, it is one of the most highly quoted studies in the biomedical literature having now been cited more than 8000 times.

With Thomas Reese, Morris used the HRP method to establish that the endothelial cells in the brain vasculature form the cellular correlate of the so-called blood brain barrier. This endothelial barrier prevents macromolecules in the blood from reaching neurons. Likewise, with Elio Raviola, Morris established the blood-thymus barrier, and with Eveline Schneeberger, the blood-air barrier of the lungs. The small pore system of Pappenheimer was identified in muscle capillaries at the level of permeable intercellular junction, an observation that is still controversial today (see poem above).

Another innovation developed by Morris was the introduction of colloidal lanthanum as an electron opaque tracer. Using this tracer, Morris and Jean-Paul Revel succeeded in revealing the fine structure of gap junctions, the structural correlate of electrophysiologically defined electrical synapses that were known to occur in cells of excitable tissues.

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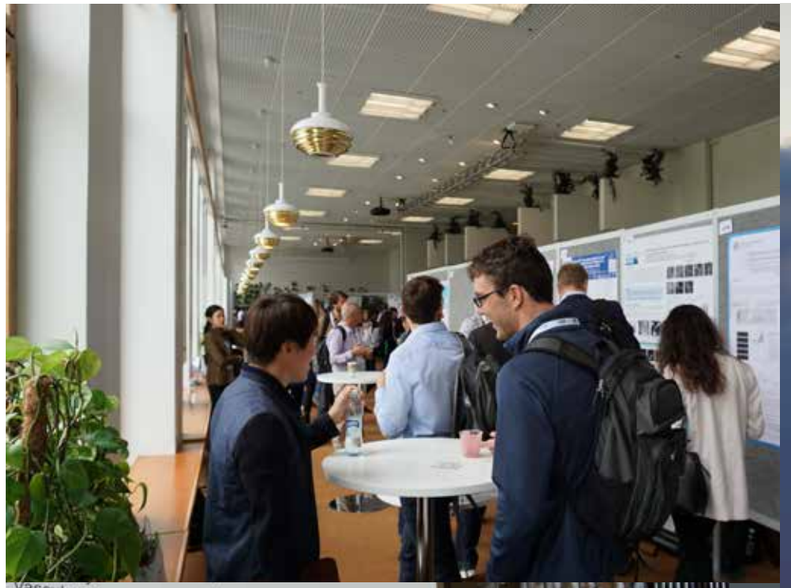
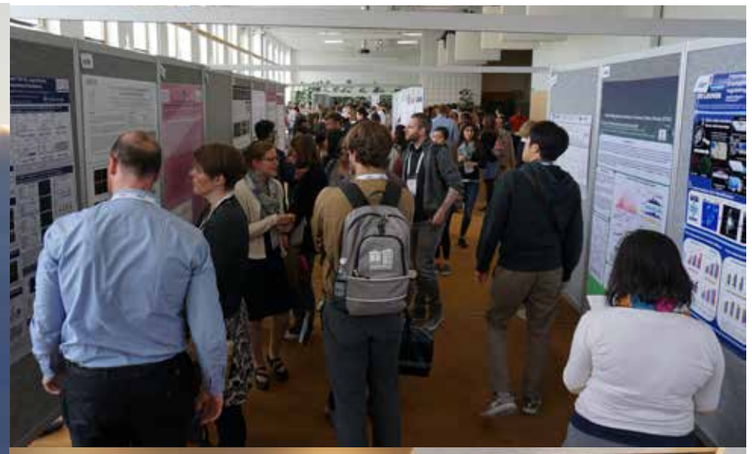
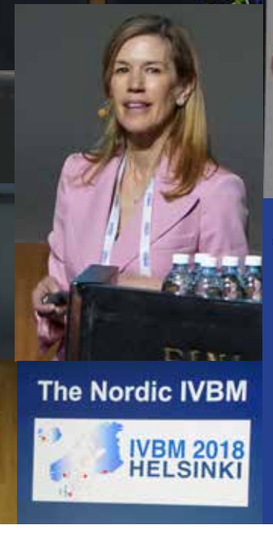
Highlights from the 20th International Vascular BiologyMeeting - June 3-7, Helsinki, Finland







Congratulations to the 20th IVBM Organizers:

- Kari Alitalo
- Christer Betsholtz
- Lena Claesson-Welsh
- Jozef Dulak
- Pipsa Saharinen

Past President's Message

Cecilia M. Giachelli

Dr. Giachelli was on hand out the IVBM 2018 in Helsinki to present eight NAVBO Travel Awards.

It's been truly a pleasure to serve as NAVBO president over the past year. We've been able to put together a full slate of successful scientific conferences, starting with the Lymphatics Forum at Northwestern University, followed by Vasculata at the University of Illinois at Chicago, the NAVBO annual meeting at Asilomar, and culminating with last month's IVBM meeting in Helsinki. I was delighted to see so many NAVBO members there! I hope you enjoyed the meeting as much as I did.

At each of these venues, NAVBO has been providing training, leadership and research communication opportunities for members at all training and career stages, and providing networking and collaborative opportunities for all. Beyond our meetings, NAVBO launched it's first ever webinars series this past year, which has been a great success. In addition, NAVBO has been developing educational materials to help us reach out to budding vascular biologists. A big thanks to the members of the Education Committee for spearheading these new activities! Finally, NAVBO continues to be a tireless advocate for vascular biology and scientific research to the public and our national leaders.

Leading NAVBO has really been a team effort. I especially want to thank President-elect Michelle Bendeck and past-President Jan Kitajewski for their dedicated leadership and support throughout the past year. Kudos and thanks also go to NAVBO councilors for their hard work and integrity in all of our proceedings: Rosemary Akhurst, Kayla Bayless, Jason Fish, Courtney Griffin, Chris Hughes, Bill Muller, and Wayne Orr. Of course, huge thanks goes to Bernadette Englert who keeps us all on task and on track. And last but not least, thanks to all the NAVBO members. Without your impactful research, participation, leadership and vision, we wouldn't have such a fun and vital organization.

Thank you,

Ceci Giachelli

Member News

William R. Huckle, Editor

*Additional information related to these stories can be found on our web site, go to **www.navbo.org/2017NewsLinks***

Calendar of Events

13th User Training Workshop Developing Multi-Scale, Virtual Tissue Simulations with CompuCell3D
Bloomington, Indiana | 5 - 11 August, 2018
http://www.compucell3d.org/register2018

11th World Congress of Microcirculation (WCM2018)
Vancouver, Canada | 9 - 13 September, 2018
https://www.wcm2018.org

ISACB 2018 - 16th Biennial Meeting
Bordeaux, France | 16 - 19 September, 2018
https://isacb-bordeaux2018.com/

10th Kloster Seeon Meeting Angiogenesis
Germany | 22 - 25 September, 2018
http://www.vwfb.de/Seeon2018/Seeon2018.html

Vascular Biology 2018
Newport, RI | 14 - 18 October, 2018
http://www.navbo.org/vb2018

APVBO Conference 2019
Guangzhou, China | 10 - 13 May, 2019
http://www.vwfb.de/Seeon2018/Seeon2018.html

Morris advanced a number of other cytochemistry techniques including methods to detect mitochondrial cytochrome c oxidase, cholinesterases, and oxygen derived products of the oxygen burst. With Richard Rodewald, he described the slit diaphragm of the glomerulus, and with Graeme Ryan, he demonstrated that the glomerular basement membrane serves as the barrier to endogenous albumin.

Later, Morris brought all of these methods and perspectives to define the vibrancy of the endothelium, erasing by elegance of his work the conventional view of this structure a passive physical barrier to reveal the dynamic regulatory organ we recognize today. It was this work that served as the subject of his Benditt Award Lecture.

Though one of the most acknowledged scientists in history, Karnovsky did not seek fame or fortune – he refused to patent ideas that he felt should be in the public domain. The horseradish peroxidase (HRP)-diaminobenzidine (DAB) method and Karnovsky fixative are worth millions if not more, yet Morris felt they belonged to the public and went to great lengths to ensure unfettered access. He never wrote a paper on his fixative because he preferred to give away the recipe.

Karnovsky was unique in that he served as President of both a basic science organization (the American Society of Cell Biology) and a clinical organization (the American Association of Pathologists). He served on the editorial boards of The Journal of Cell Biology, and The American Journal of Pathology, among others. He had drawers full of awards, including the Benditt, Rous-Whipple, E.B. Wilson, and the Gold-Headed Cane. He was the Maude Abbott Lecturer of the US and Canadian Academy of Pathology, member of the National Academy of Medicine and American Academy of Arts and Sciences, Fellow of Royal Microscopy Society, and on and on–while he was grateful for what these awards represented, these accolades remained in his drawer.

Karnovsky was most proud of the dozens of students and trainees he mentored. They have gone on to have outstanding and productive careers as scientists and clinicians in their own right, and this gave Karnovsky more satisfaction than any of his own discoveries and achievements. During the last few months of his life, he cherished the many visits and calls from his students, asking about their latest research discoveries and catching up on their personal lives as well.

Karnovsky was a giant in the dual realms of experimental pathology and cell biology, a dedicated mentor, and a true renaissance man. He leaves a legacy of scholarship, mentoring, and service that is rarely achieved and may never be surpassed.

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