North American Vascular Biology Organization - eNews
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MEETINGS

Kari Alitalo accepts the 2011 Earl P. Benditt Award

Tim Hla, NAVBO President, presents the 2011 Benditt Award to Dr. Kari Alitalo at the NAVBO Workshops in Vascular Biology this past October

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Dr. Kari Alitalo, 2011 recipient of NAVBO's Earl P. Benditt Award, presented the Benditt Award lecture, entitled "Lymphangiogenesis in Development and Human Disease," at the October 2011 Workshops in Vascular Biology at Hyannis, Massachusetts. This award is named in honor of pioneering vascular pathologist Earl Benditt who died in 1996. The Benditt Award is among the highest honors bestowed on vascular biologists, with the roster of previous recipients (www.navbo.org/awards/benditt) reading like a "who's who" of the most prominent researchers in the field. Each year, NAVBO's Meritorious Awards Committee selects an individual who has made outstanding discoveries or developed concepts seminal to our understanding of vascular biology or vascular pathology.

Dr. Alitalo, a well-known and highly-regarded figure in the vascular biology community, is Academy Professor in the Molecular Cancer Biology Program at the Haartman Institute, University of Helsinki, Finland. Kari was selected in recognition of his groundbreaking studies on angiogenesis and lymph-angiogenesis, in particular his work on the discovery and characterization of novel receptor tyrosine kinases and associated ligands that play critical roles in normal and pathological blood and lymphatic vessel growth. His previous accomplishments include the cloning and characterization of fibroblast growth factor receptor-4 and the first endothelial-specific receptor tyrosine kinase, Tie1. Together with Ulf Eriksson, he identified VEGF-B as an endothelial cell growth factor and determined that VEGFR-1

Congratulations! A toast to Kari and Holger

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New Location!! Vasculata 2012

The 2012 Vasculata will be held in Vanderbilt University and will be organized by Drs. Susan Smyth, University of Kentucky and David G. Harrison of Vanderbilt University. It will also be co-sponsored by Meharry Medical School. Save the dates of July 25-28. Details will be on the web in mid-January. Go to: www.navbo.org/events/vasculata

NAVBO 2011 Workshops in Vascular Biology

You can see photos from the meeting at: *www.navbo.org/events/vb2011*

NAVBO 2012 Workshops in Vascular Biology

Save the dates - October 14-18, 2012. The Developmental Vascular Biology and the Genetics and Genomics of Vascular Disease Workshops will be held in Monterey at the Asilomar Conference Grounds.
Visit the web sites: www.navbo.org/dvb2012 and www.navbo.org/ggvd2012

and NP-1 are its receptors. His lab cloned other VEGF genes and receptors and has gained many new insights into the molecular mechanisms regulating the growth and function of blood vessels, particularly and most recently lymphatic vessels. Much of Kari's recent research effort has focused on the molecular regulation of lymphangiogenesis by the VEGF-C and VEGF-D ligands and receptor VEGFR-3. The lymphatic vasculature has become the subject of greatly increased interest and scientific effort in recent years, thanks partly to evidence for the important role of lymphatics in tumor metastasis and rapid advances in our understanding of the molecular regulation of their growth, and Kari's lab has consistently been at the forefront of this rapidly evolving field.

Kari's exciting lecture at the NAVBO Workshops talk began with new data suggesting that VEGF-B over-production can protect hearts from ischemic damage. The theme of therapeutic use of VEGF family ligand expression was continued with discussion of pre-clinical data on use of VEGF-C/D over-expression to treat post-surgical lymphedema, an idea soon to be tested in clinical trials. Kari moved on to discuss targeting VEGF-C/VEGFR-3 for inhibition of angiogenesis, lymphangiogenesis, and tumor metastasis. He showed that photo-dynamic ablation of "transit" lymphatics downstream from primary tumor-associated lymph nodes can dramatically reduce satellite metastasis in mice. He also showed that blocking VEGFR-3 in combination with anti-VEGFR-2 antibodies can dramatically enhance inhibition of angiogenesis. These data, combined with other emerging evidence that VEGFR-3 plays an important role supporting angiogenesis as well as lymphangiogenesis, highlight the clinical potential of anti-angiogenic therapies that target VEGFR-3.

Brant Weinstein, Ph.D.

Holger Gerhardt - Third Recipient of the Judah Folkman Award

President's Message

Our first joint meeting was a success! Over 350 members participated in the meeting and many of them congratulated us on an excellent meeting. So, I want to thank and congratulate my fellow organizers - Elaine Davis, McGill University, and Themis Kyriakides, Yale University (Vascular Matrix Biology and Bioengineering) and of course Michael Simons, Yale University, who co-organized the Biology of Signaling in the Cardiovascular System Workshop with me. I would also like to thank Naren Vyavahare, Clemson University and Pierre Moreau, University of Montreal, who worked with Elaine and Themis. Dr. Vyavahare will be organizing the 2013 matrix/bioengineering workshop; Mark Kahn, University of Pennsylvania and Martin Schwartz, Yale University will be organizing the signaling workshop in 2013. We received such favorable reviews about the location that we have decided to return to the Resort and Conference Center at Hyannis.

A rich assortment of presentations in the different scientific sessions in both workshops showed how various matrix, cell surface, and intracellular factors influence vascular growth and homeostasis. One "take-home message" clearly evident in many of the speakers' presentations was that there are extensive inter-relationships and cross-signaling between all of these cellular and extracellular compartments, underscoring the value of a

William R. Huckle, Ph.D.
NAVBO Newsletter Editor

Dr. Gerhardt receives the Folkman Award from Dr. Klaus Ley, Meritorious Awards Committee Chair.

Holger Gerhardt, recipient of the 2011 NAVBO Judah Folkman Award in Vascular Biology, presented his award lecture at the October 2011 NAVBO workshops in Hyannis, Massachusetts. The Folkman award recognizes outstanding contri-butions from vascular biologists who are at a mid-career level (within fifteen years of their first faculty appointment). Dr. Gerhardt is Group Leader in the Vascular Biology Laboratory/Cancer Research UK at the London Research Institute.

When Holger was a postdoctoral fellow in Christer Betsholtz's lab, he discovered TIP cells, the pioneering endothelial cells that drive the tip of a newly forming sprout into the tissue. The TIP cell phenotype is induced by VEGF-A acting through its receptor VEGFR2, which is mainly expressed on filopodia, whereas the "stalk" cells that follow the TIP cells and form the body of the sprout, preferentially express Jagged1 and Robo. The TIP cells appear to follow a VEGF-A gradient, which seems to be modified by extracellular matrix proteins and heparan sulfate proteoglycans expressed by astrocytes. In his lecture, Holger presented data showing that the provisional matrix protein fibronectin is transiently produced ahead of growing sprouts. Next, he highlighted select aspects of signaling in TIP cells. The kinase AKT is activated at the base of TIP cell filopodia. Surprisingly, integrins do not contribute to speed of migration.

The identity of TIP and stalk cells is determined mainly by DLL4 notch signaling. Indeed, inhibiting Notch signaling by a gamma secretase inhibitor drives all endothelial cells in a sprout to become TIP cells, suggesting that the TIP cell is the default response to VEGF-A, whereas Notch signaling is needed for maintenance of stable "adult" vessels. Further, elements of the meeting where scientists from all of these disciplines can interact under one roof. The meeting included several lectures by award honorees. Kari Alitalo received the Earl Benditt award for his work on VEGF signal transduction, lymphangiogenesis, and angiogenesis, Holger Gerhardt was awarded the Judah Folkman Award in Vascular Biology for his work on endothelial tip cell biology, while Carlos Fernandez-Hernando was the recipient of the first Springer Junior Investigator Award. The conference also included keynote and "featured" presentations by Eugene Stanley and Joseph Loscalzo on systems approaches, which are playing an increasingly prominent role in biology research in general and vascular biology in particular. The use of systems and/or large-scale approaches was echoed in many of the other presentations in the two workshops. Many presentations also highlighted important new insights continuing to come from studies of developing vessels in model organisms such as mice, avians, and zebrafish, providing a small taste of the great science certain to be on display at the Developmental Vascular Biology Workshop in 2012. The 2011 workshops also featured a new focus area – a Special Symposium on Vascular Immunology. This important area is sure to receive additional attention in future workshops.

Right now we are looking forward to the International Vascular Biology Meeting in Germany this June. Go to www.ivbm2012.net for all meeting information. Not long after the IVBM we will hold the 8th presentation of Vasculata – at Vanderbilt University, July 25-28. Next year's organizers are Susan Smyth of the University of Kentucky and David Harrison of Vanderbilt. A feature of this popular summer course is the hands-on labs and trainees will be happy to see that feature included in 2012 program.

Following Vasculata will of course be the next annual meeting, NAVBO Workshops in Vascular Biology 2012 (October 14-18) at the Asilomar Conference Grounds in Pacific Grove (Monterey), CA. It will feature the Developmental Vascular Biology Workshop (organized by Brant Weinstein, NICHD/NIH and Kari Alitalo, University of Helsinki) and the Genetics and Genomics of Vascular Disease Workshop (organized by Douglas Marchuk, Duke University and Miikka Vikkula, Université

extracellular matrix influence vessel stability. TIP cells produce laminin 4.1.1, and *Lama4*$^{-/-}$ mice lacking this laminin produce too many small vessels and sprouts. Holger concludes that laminin is a strong inhibitor of sprouting and suppresses DLL4 signaling. But Notch signaling not only induces the stalk cell phenotype, it also downregulates VEGFR2 and upregulates VEGFR1. VEGFR1 may serve as a decoy receptor to sequester VEGF. The functional consequences of this were illustrated by a remarkable, otherworldly movie produced using agent-based modeling software. The model predicts that cells compete for the tip and may fall back into the stalk.

How does this work? Are there oscillations in signaling pathways? Or is this the consequence of some sort of temporal regulation? What are the dynamics of Notch signaling? Or is this dance an emergent property, a collective mechanism only observed in the whole assembly of cells? These questions remain to be answered by future research. Amazingly, each TIP cell reaches a full capillary length into the plexus, connected by a thin dendrite or filopodium.

Holger's award presentation was data-rich, yet visually pleasing and very inspiring. It was a beautiful testament to the strength of angiogenesis research conducted by NAVBO members and the tremendous progress that was made over the last 20 years, a degree of progress that would be unthinkable without Holger's work. Congratulations, Holger, on an honor well deserved.

Klaus Ley, M.D.

2011 Springer Awardee Carlos Fernandez-Hernando

Carlos Fernandez-Hernando, New

catholique de Louvain). Asilomar is already a favorite of the Development Workshop attendees and I'm sure will prove to be a hit with everyone. Plan to attend!

Tim Hla, Ph.D.

Member News

The American Association for Cancer Research has published its "AACR Cancer Progress Report 2011: Transforming Patient Care Through Innovation," documenting the progress made in the prevention, diagnosis, and treatment of cancer accomplished in the forty years since the signing of the National Cancer Act of 1971. NAVBO Scientific Advisory Board member Napoleon Ferrara served on the AACR progress report writing committee, and NAVBO member Shawn Sweeney was the AACR's project leader for production of the progress report. The report highlights the development of anti-angiogenic agents, including vascular growth receptor kinase inhibitors and anti-VEGF antibodies, as providing valuable and selective new weapons in the treatment of cancers of the kidney, gastrointestinal tract, thyroid gland and lung. The full report may be found at: *http://www.aacr.org/home/public--media/science-policy--government-affairs/cancer-progress-report.aspx*

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Avrum I. Gotlieb, Senior Scientist in the Division of Cellular & Molecular Biology, Toronto General Research Institute, and Acting Vice Dean of Graduate Affairs for the University of Toronto Faculty of Medicine, is the recipient of the 2012 Distinguished Achievement Award from the Society for Cardiovascular Pathology. This international Society, established in 1985, is devoted to the advancement of the study of cardiovascular disorders, especially with respect to pathogenesis, diagnosis and treatment. Dr. Gotlieb also has been appointed as a Senior Fellow of the Association of Pathology Chairs. In January of 2012, Dr. Gotlieb will begin a five-year term as an associate editor of *Cardiovascular Pathology*, an Elsevier journal focused on the basic and clinical science of cardiovascular disease.

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NAVBO President Tim Hla reports the sad news that Dr. James F. O'Rourke, professor emeritus of immunology at the University of Connecticut and co-founder of the UCONN Health Center's vision research program and Center for Vascular Biology, has died at the

York University School of Medicine, is the first recipient of the ***Springer Junior Investigator Award***. Here he is accepting the award from former mentor and NAVBO Past President William Sessa. The award recognizes a junior faculty member within five years of his/her first appointment.

Dr. Hernando presented his talk, "miR-33a/b Contributes to the Regulation of Fatty Acid Metabolism and Insulin Signaling," on Thursday, October 20 at the NAVBO Workshops in Vascular Biology. This award will once again be sponsored by Springer, publisher of Angiogenesis, in 2012.

age of 86. Dr. O'Rourke's research focused on the dynamics of hemostasis in the retinal vasculature and the relationship between stress and secretion of endogenous thrombolytics. Tim notes that Dr. O'Rourke was "a steadfast champion of vascular biology at UCONN." Dr. O'Rourke will be remembered fondly by Bernadette, who had a many a pleasant conversation with him. One of our earliest members (joined March 1994) will be sorely missed. More information on Dr. O'Rourke's career may be found at: *http://today.uconn.edu/blog/2011/11/health-center-family-loses-a-founding-father/#.Tr56VgWS03w.email*