

The New NCVC Research Institute Memorial Symposium at KENTO

Venue: Main Hall (Entrance Building 3F) at New NCVC
connecting to the JR Kishibe station (KENTO)

Date and TIME: July 26 (Fri), 2019

Registration starts from 9:00

Program starts at 10:00 and ends at 16:30



Guest Speakers: Ralf Adams (Germany)
Kari Alitalo (Finland)
Hellmut Augustin (Germany)
Christer Betsholtz (Sweden)
Didier Stainier (Germany)

PROGRAM

10:00 **Opening Remarks**
Dr. Hisao Ogawa (President of NCVC)

10:10 Announcement from the organizers

10:15 **Lecture 1** (chaired by Dr. Osamu Nakagawa)
Dr. Christer Betsholtz
“Vascular biology from the perspective of single cells”

11:00 **Lecture 2** (chaired by Dr. Yoshikazu Nakaoka)
Dr. Hellmut Augustin
“Building and maintaining organotypic vasculatures: The liver vasculature in health and disease”

11:45 **Group Photo** (in the hall and outside of the building)

12:00 **LUNCH** at the Science Café (Research Institute Building)
Round table discussion

13:30 **Mini-tour** in the Research Institute

14:00 **Lecture 3** (chaired by Dr. Yasunori Shintani)
Dr. Ralf Adams
“Organ-specific and functional specialization of vascular cells”

14:45 **Lecture 4** (Chaired by Dr. Kazu Kikuchi)
Dr. Didier Stainier
“Biological Robustness: genetic compensation and transcriptional adaptation”

15:30 **INTERMISSION**

15:45 **Lecture 5** (Chaired by Dr. Naoki Mochizuki)
Dr. Kari Alitalo
“A new pathway for coronary revascularization”

16:30 Closing Remarks
Dr. Naoki Mochizuki

CHRISTER BETSHOLTZ, born 11 July 1959 in Stockholm Sweden, Swedish citizen.

Affiliation: 1) Department of Immunology, Genetics and Pathology, Uppsala University. 2) Integrated Cardio Metabolic Centre (ICMC), Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden

Education and degrees: 1979-81: Uppsala University Medical School (Bachelor of Medicine). 1982-86: PhD studies at Uppsala University, Department of Pathology. PhD degree April 1986, Thesis title: "Role of platelet-derived growth factor in neoplastic transformation". 1987: Docent in Experimental Pathology, Uppsala University.



Active positions: Since 2016: Director of the Integrated Cardio-Metabolic Center (ICMC), Karolinska Institutet, Huddinge, Sweden. Since 2013: Professor of Tumor and Vascular Biology (endowed chair) at Uppsala University, Uppsala, Sweden. Since 2004: Professor of Vascular Biology (endowed chair) at Karolinska Institutet, Stockholm, Sweden.

Previous positions: 1994-2004: Professor of Medical Biochemistry (endowed chair) at Gothenburg University, Gothenburg, Sweden. 1991-1993: Associate professor, Department of Pathology, Uppsala University, Uppsala, Sweden. 1986-1990: Assistant professor, Department of Pathology, Uppsala University, Uppsala, Sweden

Commissions of trust (selected): Member of the Nobel Assembly for Physiology or Medicine since 2006; the Nobel Committee for Physiology or Medicine 2007-2010; European Molecular Biology Organization (EMBO) since 2004; Academia Europaea since 2004; Royal Swedish Academy of Sciences, Class VII, since 2007; the Royal Society of Sciences since 2014; Member of the following scientific advisory boards: Max Planck Heart and Lung institute, Bad Nauheim since 2012; Verselius Research Center, VIB-KU-Leuven since 2013 (Chairman); IFOM/EIO, Milan 2003-2010; the Structural Genomics Consortium, Stockholm Branch 2005-2010; Center of Excellence in Developmental Biology, University of Helsinki, 2002-2006; Foundation for Strategic Research, Life Sciences, 1999-2002 (chairman); Served on the following panels and study sections: LS(1)3 Panel of ERC Starting Grants 2008-2013, Chair 2010-13; EMBO Young Investigator Program 2013-2016; Scientific Board of the Swedish Cancer Foundation 2010-2012; the Swedish Cancer Foundation grant evaluation panel PkB 2000-2009 (Chairman 2006-9); Served as external PhD examiner ("opponent") at >25 occasions in Sweden, Finland, Norway, and Italy since 1987.

Awards, honors and major grants:

Oscar Prize for Young Scientists, Uppsala University 1989; Eric K. Fernström's Award for Young Investigators, Gothenburg University, 1995; Göran Gustafsson's Prize in Molecular Biology, Sweden, 1997; Alkis Seraphim Lecture, Cambridge University, UK, 2002; Lundberg Medal, Lundberg Foundation, Sweden, 2004; Russel Ross Endowed Lecture, Washington University, US, 2008; Söderberg Professor of Medicine, Royal Swedish Academy of Sciences 2009-2013; Distinguished Professor Award, Karolinska institutet 2009-2013; Axel Hirsch's Prize, Karolinska institutet, 2010; The Del Monte Medal in Neuromedicine, Rochester University, NY, US, 2010; Ranked outstanding in international evaluation of Karolinska institutet 2010; ERC Advanced Grant 2012-2017; Rockefeller University Nicholson Lecture, New York, US, 2012; Wallenberg Scholar Award, The Wallenberg Foundation, Sweden 2013-2017; Robert M Berne Memorial Lecture, University of Virginia, US, 2014; Distinguished Professor's Award, Swedish Science Council 2015-24; Journal of Vascular Research and European Society for Microcirculation (JVR/ESM) Award, 2017; Anders Jahre's Senior Medical Prize, University of Oslo, Norway, 2017; Biozentrum Basel Lecturer, University of Basel Oct 2017; Louis-Jeantet Medical Prize 2018.

Main scientific achievements: Christer Betsholtz was the first to clone the platelet-derived growth factor (PDGF)-A gene (Betsholtz et al, **Nature** 1986) and to generate knockout mice for PDGF-A (Boström et al, **Cell** 1996) and PDGF-B (Leveen et al, **Genes Dev** 1994). Analysis of PdgfbKO mice led to the discovery of the critical role for PDGF-B signaling through PDGF receptor-beta for recruitment of pericytes during angiogenesis (Lindhögl et al, **Science** 1997, Hellström et al, **Development** 1999, Hellström et al, **J Cell Biol** 2001). His lab discovered endothelial tip cells (Gerhardt et al, **J Cell Biol** 1993) and elucidated the role of Notch signaling in tip/stalk cell selection (Hellström et al, **Nature** 2007). By mutagenesis of the Pdgfb gene in mice, they elucidated a critical role of pericytes in the blood-brain barrier (Armulik et al. **Nature**, 2010), and of the PDGFB or PDGFRB genes in human brain disease (Keller et al, **Nat Genet**, 2013). Using single cell RNA sequencing, his team has recently provided genome-wide insight into endothelial and mural cell gene expression patterns in the brain, providing a molecular definition to pericytes, as well as to new perivascular cell types (Vanlandewijck et al, **Nature**, 2018).

Scientific publication: Author of 228 original papers, 42 review articles and 34 book chapters. Web of Science lists 338 publications, 34,971 citations, h-index 90. PubMed lists 273 publications [Betsholtz C]. Google Scholar [Christer Betsholtz] lists 446 publications, 50,775 citations, h-index 103.

Ten selected publications:

Vanlandewijck M, He L, Mäe MA, Andrae J, Ando K, Del Gaudio F, Nahar K, Lebouvier T, Laviña B, Gouveia L, Sun Y, Raschperger E, Räsänen M, Zarb Y, Mochizuki N, Keller A, Lindahl U, **Betsholtz C**. A molecular atlas of cell types and zonation in the brain vasculature. **Nature**. 2018 Feb 14. doi: 10.1038/nature25739.

Keller A, Westenberger A, Sobrido MJ, García-Murias M, Domingo A, Sears RL, Lemos RR, Ordoñez-Ugalde A, Nicolas G, da Cunha JE, Rushing EJ, Hugelshofer M, Wurnig MC, Kaech A, Reimann R, Lohmann K, Dobričić V, Carracedo A, Petrović I, Miyasaki JM, Abakumova I, Mäe MA, Raschperger E, Zatz M, Zschiedrich K, Klepper J, Spiteri E, Prieto JM, Navas I, Preuss M, Dering C, Janković M, Paucar M, Svenningsson P, Saliminejad K, Khorshid HR, Novaković I, Aguzzi A, Boss A, Le Ber I, Defer G, Hannequin D, Kostić VS, Champion D, Geschwind DH, Coppola G, **Betsholtz C***, Klein C*, Oliveira JR*. Mutations in the gene encoding PDGF-B cause brain calcifications in humans and mice. **Nat Genet** 28,1077 (2013) *shared last authors

Gaengel, K., Niaudet, C., Hagikura, K., Siemsen, B.L., Muhl, L., Hofmann, J.J., Ebarasi, L., Nyström, S., Rymo, S., Chen, L.L., Pang, M.F., Jin, Y., Raschperger, E., Roswall, P., Schulte, D., Benedito, R., Larsson, J., Hellström, M., Fuxe, J., Uhlén, P., Adams, R., Jakobsson, L., Majumdar, A., Vestweber, D., Uv, A., **Betsholtz, C**. The Sphingosine-1-Phosphate Receptor S1PR1 Restricts Sprouting Angiogenesis by Regulating the Interplay between VE-Cadherin and VEGFR2. **Dev Cell** 23,587-99 (2012)

Armulik, A., Genové, G., Mäe, M., Nisancioglu, M.H., Wallgard, E., Niaudet, C., He, L., Norlin, J., Lindblom, P., Strittmatter, K., Johansson, B.R., **Betsholtz, C**. Pericytes regulate the blood-brain barrier. **Nature** 468,557-561 (2010)

Hellström, M., Phng, L.-K., Hofmann, J., Wallgard, E., Coultas, L., Lindblom, P., Alva, J., Nilsson, A.-K., Karlsson, L., Gaiano, N., Yoon, K., Rossant, J., Iruela-Arispe, M.L., Kalén, M., Gerhardt, H., **Betsholtz, C**. Dll4 signalling through Notch1 regulates formation of tip cells during

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angiogenesis. **Nature** 445,776-780, (2007)

Gerhardt, H., Golding, M., Fruttiger, M., Ruhrberg, C., Lundkvist, A., Abramsson, A., Jeltsch, M., Mitchell, C., Alitalo, K., Shima, D. and **Betsholtz, C.** VEGF guides angiogenic sprouting utilizing endothelial tip-cell filopodia. **J Cell Biol** 161:1163-1177 (2003)

Hellström, M., Kalén, M., Lindahl, P., Abramsson, A. and **Betsholtz, C.** Role of PDGF-B and PDGFR- β in recruitment of vascular smooth muscle cells and pericytes during embryonic blood vessel formation in the mouse. **Development** 126:3047-3055 (1999)

Lindahl, P., Johansson, B., Levéen, P., and **Betsholtz, C.** Pericyte loss and microaneurysm formation in PDGF-B deficient mice. **Science**, 277, 242-245 (1997)

Boström, H., Willetts, K., Pekny, M., Levéen, P., Hedstrand, H., Pekna, M., Schalling, M., Nilsson, M., Gebre-Medhin, S., Kurland, S., Törnell, J., Heath, J.K and **Betsholtz, C.** PDGF-A signaling is a critical event in lung alveolar myofibroblast ontogeny and alveogenesis. **Cell** 85, 863-873 (1996)

Betsholtz, C., Johnsson, A., Heldin, C.-H., Westermark, B., Lind, P., Urdea, M.S., Shows, T.B., Philpott, K., Mellor, A., Knott, T.J. and Scott, J. Complementary DNA sequence and chromosomal localisation of human platelet-derived growth factor A-chain and its expression in tumour cell lines. **Nature** 320,695-699 (1986)

HELLMUT G. AUGUSTIN, PROF. DR.MED.VET. PH.D.

Professor and Director

PROFESSIONAL AFFILIATION

Joint Research Division Vascular Biology, European Center for Angioscience (ECAS) Medical Faculty Mannheim, Heidelberg University, and

German Cancer Research Center Heidelberg (DKFZ-ZMBH-Alliance)

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Web: www.angiolab.de; www.augustinlab.de;

www.twitter.com/HellmutAugustin

www.youtube.com/channel/UCvsiTZuzdjIhf0K1XRk71qg

EDUCATION

1984 DVM, School of Veterinary Medicine Hannover, Germany

1984-1987 Residency and graduate training in Veterinary Pathology,

School of Vet. Medicine Hannover, Germany 1987 Doctoral degree Dr. med. vet.,

School of Veterinary Medicine Hannover, Germany

1992 PhD, Cornell University, Ithaca, NY, USA

PROFESSIONAL EXPERIENCE AND APPOINTMENTS

1997 Venia legendi (Habilitation) in Molecular Cell Biology, University of

Göttingen, Germany 1992-2001 Research Assistant Professor (C1, C2), University of Göttingen, Germany

2001-2006 Head, Dept. of Vascular Biology & Angiogenesis Research, Tumor Biology Center, Freiburg, Germany

2002-2006 Adjunct Professor, Medical Faculty of the Albert-Ludwigs-University Freiburg, Germany

2006-2016 Aventis Foundation-endowed Chair for Vascular Biology and Angiogenesis Research, Medical Faculty Mannheim (CBTM), Heidelberg University, and German Cancer Research Center Heidelberg, Germany

2011-2016 Speaker, Cell and Tumor Biology Research Program, German Cancer Research Center, Heidelberg 2011-2016 Director, Center for Molecular Biology and German Cancer Research Center Alliance, Heidelberg

2011-2017 Deputy Director, Center for Biomedicine and Medical Technology Mannheim (CBTM), Medical Faculty Mannheim, Heidelberg University

5/2016- Chair for Vascular Biology and Angiogenesis Research, Medical Faculty Mannheim (CBTM), Heidelberg University, and German Cancer Research Center Heidelberg, Germany

1/2018- Founding Director, European Center for Angioscience, Medical Faculty Mannheim, Heidelberg University, and German Cancer Research Center Heidelberg, Germany (www.angioscience.de)

RESEARCH INTERESTS

The laboratory studies 1.) the molecular mechanisms of physiological blood vessel formation, assembly, and maturation focusing on angiogenesis regulating receptor tyrosine kinases, most notably on the Angiopoietin-Tie ligand-receptor system as well as on other selected novel candidate molecules, 2.) the mechanisms of organotypic vascular differentiation and angiocrine signaling studying the lung and liver vasculature as prototypic vascular beds, 3.) the molecular mechanisms of tumor progression focusing on tumor-vessel interactions during metastasis, and 4.) translational tumor angiogenesis experiments aimed at defining the therapeutic window of stromal targeted therapies. Conceptually, the lab's work is considered as basic vascular and



tumor biology research with the aim of identifying and validating novel therapeutic targets.

SCIENTIFIC COMMUNITY SERVICES

2/1997: Founder of the German vascular biology network (bi-annual meeting series [1997-2013]); 9/1998-5/2006: Coordinator of nationwide German angiogenesis Priority Research Grant (SPP1069; www.angiogenese.de); 5/2005- 12/2012: Coordinator of the nationwide German tumor-vessel interaction Priority Research Grant (SPP1190; www.tumorstvessel.de); 5/2005-pres.: Founding member and elected Chairman of VWFB e.V. (www.vwfb.de); 7/2005- 6/2009: Vice Speaker of the SFB-TR23 “Vascular Differentiation and Remodeling” of the Universities Frankfurt, Heidelberg, and Freiburg; 7/2009-6/2017: Speaker of the SFB-TR23 “Vascular Differentiation and Remodeling” of the Universities Heidelberg and Frankfurt (www.transregio23.de); 3/2012-pres.: Senior Editor, Cancer Research; 2013-2016: Director of the Helmholtz Alliance “Preclinical Comprehensive Cancer Center” (PCCC; www.helmholtz-pccc.de).

SELECTED RECENT PUBLICATIONS (OF >180)

1. Helfrich I, Scheffrahn I, Bartling S, Weis J, von Felbert V, Middleton M, Kato M, Ergün S, Augustin HG*, Schadendorf D*: Resistance to antiangiogenic therapy is directed by vascular phenotype, vessel stabilization, and maturation in malignant melanoma. **J Exp Med**, 207:491-503, 2010 (*equal contribution).
2. Thomas M, Felcht M, Kruse K, Kretschmer S, Deppermann C, Biesdorf A, Rohr K, Benest AV, Fiedler U, Augustin HG: Angiopoietin-2 stimulation of endothelial cells induces α v β 3 integrin internalization and degradation. **J Biol Chem**, 285: 23842-9, 2010.
3. Héroult M, Schaffner F, Pfaff D, Prahst C, Kirmse R, Kutschera S, Riedel M, Ludwig T, Vajkoczy P, Graeser R, Augustin HG: EphB4 promotes site-specific metastatic tumor cell dissemination by interacting with endothelial cell expressed ephrinB2. **Mol Cancer Res**, 8: 1297-3, 2010.
4. Kutschera S, Weber H, Weick A, De Smet F, Genove G, Takemoto M, Prahst C, Riedel M, Mikelis C, Baulande S, Champseix C, Kummerer P, Conseiller E, Multon MC, Heroult M, Bicknell R, Carmeliet P, Betsholtz C, Augustin HG: Differential endothelial transcriptomics identifies Semaphorin 3G as a vascular class 3 semaphorin. **Arterioscler Thromb Vasc Biol**, 31: 151-9, 2011.
5. Felcht M, Luck R, Schering A, Seidel P, Srivastava K, Hu J, Bartol A, Kienast Y, Vettel C, Loos EK, Kutschera S, Bartels S, Appak S, Besemfelder E, Terhardt D, Chavakis E, Wieland T, Klein C, Thomas M, Uemura A, Goerdt S, Augustin HG: Angiopoietin-2 differentially regulates angiogenesis through TIE2 and integrin signaling. **J Clin Invest**, 122:1991-2005, 2012.
6. Benest AV, Kruse K, Savant S, Thomas M, Laib AM, Loos EK, Fiedler U, Augustin HG: Angiopoietin-2 is critical for cytokine-induced vascular leakage. **PLoS One**, 8:e70459, 2013.
7. Hu J, Srivastava K, Wieland M, Runge A, Mogler C, Besemfelder E, Terhardt D, Vogel MJ, Cao L, Korn C, Bartels S, Thomas M, Augustin HG: Endothelial cell-derived Angiopoietin-2 controls liver regeneration as a spatiotemporal rheostat. **Science** 343:416-9, 2014.
8. Runge A, Hu J, Wieland M, Bergeest JP, Mogler C, Neumann A, Géraud C, Arnold B, Rohr K, Komljenovic D, Schirmacher P, Goerdt S, Augustin HG: An inducible hepatocellular carcinoma model for preclinical evaluation of antiangiogenic therapy in adult mice. **Cancer Res**, 74: 4157-69, 2014
9. Korn C, Scholz B, Hu J, Srivastava K, Wojtarowicz J, Arnsperger T, Adams RH, Boutros M*, Augustin HG*, Augustin I*: Endothelial cell-derived non-canonical Wnt ligands control vascular pruning in angiogenesis. **Development**, 141(8):1757-66, 2014 (*equal contribution).
10. Srivastava K*, Hu J*, Korn C, Savant S, Teichert M, Kapel S, Jugold M, Besemfelder E,

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- Thomas M, Pasparakis M, Augustin HG: Postsurgical adjuvant tumor therapy by combining anti-Angiopoietin-2 and metronomic chemotherapy limits metastatic growth. **Cancer Cell**, 26:880-95, 2014.
11. Mogler C, Wieland M, König C, Hu J, Runge A, Korn C, Besemfelder E, Breitkopf-Heinlein K, Komljenovic D, Dooley S, Schirmacher P, Longerich T, Augustin HG: Hepatic stellate cell expressed Endosialin balances fibrogenesis and hepatocyte proliferation during liver damage. **EMBO Mol Med**, 7:332-6, 2015
 12. Savant S, La Porta S, Budnik A, Busch K, Hu J, Tisch N, Korn C, Valls AF, Benest AV, Terhardt D, Qu X, Adams RH, Baldwin HS, Ruiz de Almodóvar C, Rodewald HR, Augustin HG: The orphan receptor Tie1 controls angiogenesis and vascular remodeling by differentially regulating Tie2 in tip and stalk cells. **Cell Rep**, 12: 1761-73, 2015.
 13. Scholz B, Korn C, Wojtarowicz J, Mogler C, Augustin I, Boutros M, Niehrs C, Augustin HG: Endothelial RSPO3 controls vascular stability and pruning through non-canonical WNT/Ca(2+)/NFAT signaling. **Dev Cell**, 36: 79-93, 2016.
 14. Roth L, Prahst C, Ruckdeschel T, Savant S, Weström S, Fantin A, Riedel M, Héroult M, Ruhrberg C, Augustin HG: Neuropilin-1 mediates vascular permeability independently of vascular endothelial growth factor receptor-2 activation. **Science Signal**, 9(425):ra42, 2016.
 15. Viski C, König C, Kijewska M, Mogler C, Isacke C*, Augustin HG*: Endosialin-expressing pericytes promote metastatic dissemination. **Cancer Res**, 76: 5313-25, 2016 (*equally contributing senior authors).
 16. Augustin HG*, Koh GY*: Organotypic vasculature: From descriptive heterogeneity to functional pathophysiology. **Science**, pii: eaal2379, 2017 (*equal contribution).
 17. Hasanov Z, Ruckdeschel T, König C, Mogler C, Kapel SS, Korn C, Spegg C, Eichwald V, Wieland M, Appak S, Augustin HG: Endosialin promotes atherosclerosis through phenotypic remodeling of vascular smooth muscle cells. **Arterioscler Thromb Vasc Biol**, 37: 495-505, 2017.
 18. Gengenbacher N, Singhal, M, Augustin HG: Preclinical mouse solid tumor models: Status quo, challenges, perspectives. **Nat Rev Cancer**, 17:751-765, 2017.
 19. Mogler C, König C, Wieland M, Runge A, Besemfelder E, Komljenovic D, Longerich T, Schirmacher P, Augustin HG: Hepatic stellate cells limit hepatocellular carcinoma progression through the orphan receptor endosialin. **EMBO Mol Med**, 9: 741-749, 2017.
 20. Teichert M, Milde L, Holm A, Stanicek L, Gengenbacher N, Savant S, Ruckdeschel T, Hasanov Z, Srivastava K, Hu J, Hertel S, Bartol A, Schlereth K, Augustin HG: Pericyte-expressed Tie2 controls vessel maturation. **Nat Commun**. 8:16106, 2017.
 21. Holm A, Heumann T, Augustin HG: Microvascular mural cell heterogeneity and functional plasticity. **Trends Cell Biol**, pii: S0962-8924(17)30235-0, 2018.
 22. La Porta S, Roth L, Singhal M, Mogler C, Spegg C, Schieb B, Qu X, Adams RH, Baldwin HS, Savant S, Augustin HG: Endothelial Tie1-mediated angiogenesis and vascular abnormalization promote tumor progression and metastasis. **J Clin Invest**, 8: 834-845, 2018
 23. Schlereth K, Weichenhan D, Bauer T, Heumann T, Giannakouri E, Lipka D, Jaeger S, Schlesner M, Aloy P, Eils R, Plass C*, Augustin HG*: The transcriptomic and epigenetic map of vascular quiescence in the continuous lung endothelium. **Elife**, pii:e34423, 2018 (*equally contributing senior authors).
 24. Singhal S[#], Liu X[#], Inverso D, Jiang K, Dai J, He H, Bartels S, Li W, Abdul Pari, AA, Gengenbacher N, Besemfelder E, Hui L, Augustin HG*, Hu J*: Endothelial cell fitness dictates the source of regenerating liver vasculature. **J Exp Med**, 215: 2497-2058, 2018 ([#]equally contributing first authors; *equally contributing senior authors).

NAME: **Ralf H. Adams, Ph.D.**
 TITLES: Department Head and Managing Director
 Max Planck Institute for Molecular Biomedicine,
 GERMANY
 Professor at the University of Münster
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 Biomedicine
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 EDUCATION:
 1996 Ph.D., Johann Wolfgang Goethe
 University,
 Frankfurt
 1996-2000 Postdoctoral Fellow at EMBL, Heidelberg



ACADEMIC APPOINTMENTS:

2000-2005 Head (tenure track) of the Vascular Development Laboratory at the Cancer Research UK London Research Institute, UK
 2005-2008 Tenured Group Leader, Cancer Research UK London Research Institute, UK
 2007-2018 Professor for ‘Vascular Biology’ at the University of Münster
 2007- Director at the Max Planck Institute for Molecular Biomedicine
 2019- Associated Professor at the University of Münster

MAJOR RESEARCH INTERESTS:

Molecular and functional heterogeneity and specialization of vascular cells:
 1. Role of vascular cells in bone formation and the regulation of hematopoiesis
 2. Heterogeneity of endothelial cells and its role in artery formation
 3. Functional roles of pericytes in vessel growth and tissue morphogenesis

Recent PUBLICATIONS: (2014-2019 selected)

- Kato K, Diéguez-Hurtado R, Park DY, Hong SP, Kato-Azuma S, Adams S, Stehling M, Trappmann B, Wrana JL, Koh GY, Adams RH (2018). Pulmonary pericytes regulate lung morphogenesis. **Nat Commun.** 9:2448.
- Pitulescu ME, Schmidt I, Giaimo BD, Antoine T, Berkenfeld F, Ferrante F, Park H, Ehling M, Biljes D, Rocha SF, Langen UH, Stehling M, Nagasawa T, Ferrara N, Borggreffe T, Adams RH (2017). Dll4 and Notch signalling couples sprouting angiogenesis and artery formation. **Nat. Cell Biol.** 19:915-927.
- Langen UH, Pitulescu ME, Kim JM, Enriquez-Gasca R, Sivaraj KK, Kusumbe AP, Singh A, Di Russo J, Bixel MG, Zhou B, Sorokin L, Vaquerizas JM, Adams RH (2017). Cell-matrix signals specify bone endothelial cells during developmental osteogenesis. **Nat. Cell Biol.** 19:189-201.
- Ramasamy SK, Kusumbe AP, Wang L, Adams RH (2014). Endothelial Notch activity promotes angiogenesis and osteogenesis in bone. **Nature** 507:376-80.
- Kusumbe AP, Ramasamy SK, Adams RH (2014). Coupling of angiogenesis and osteogenesis by a specific vessel subtype in bone. **Nature** 507:323-8.

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NAME: **Didier Stainier, Ph.D.**
TITLES: Director
Max Planck Institute for Heart and Lung Research
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EDUCATION:

1979-1981 International Baccalaureate, UWC Atlantic College, Wales, U.K.
1981-1982 Certificate in Biology, Université de Liège, Liège, Belgium
1982-1984 B.A. in Biology (*summa cum laude*), Brandeis University, Waltham, MA
1984-1990 Ph.D. Harvard University (Walter Gilbert's Lab), Cambridge, MA, USA
1990-1994 Postdoctoral Fellow, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

ACADEMIC APPOINTMENTS:

1994-2012 Assistant (1994), Associate (2000), Full (2003) Professor, Department of Biochemistry & Biophysics, University of California, San Francisco
2012-present Director, Department of Developmental Genetics, Max Planck Institute for Heart and Lung Research

MAJOR RESEARCH INTERESTS:

Vertebrate organ formation/cardiovascular development/endoderm, liver, pancreas, gut and lung development/regeneration/stem cell differentiation/gluconeogenesis/metabolism/genetic compensation/biological robustness

Recent PUBLICATIONS: (2014-2019, selected)

- Vanhollebeke B, Stone OA, Bostaille N, Cho C, Zhou Y, Maquet E, Gauquier A, Cabochette P, Fukuhara S, Mochizuki N, Nathans J and Stainier DYR (2015). Tip cell-specific requirement for an atypical Gpr124- and Reck-dependent Wnt/ β -catenin pathway during brain angiogenesis. *eLife* 06489.
- Rossi A, Kontarakis Z, Gerri C, Nolte H, Hölper S, Krüger M and Stainier DYR (2015). Genetic compensation induced by deleterious mutations but not gene knockdowns. *Nature* 524, 230-233.
- Reischauer S, Stone O, Villasenor A, Chi N, Jin SW, Martin M, Lee MT, Fukuda N, Marass M, Witty A, Fiddes I, Kuo T, Chung WS, Salek S, Lerrigo R, Alsiö J, Luo S, Tworus D, Augustine SM, Mucenieks S, Nystedt B, Giraldez AJ, Schroth GP, Andersson O and Stainier DYR (2016). Cloche is a bHLH-PAS transcription factor that drives haemato-vascular specification. *Nature* 535, 294-298.
- Lai SL, Marín-Juez R, Moura PL, Kuenne C, Lai JKH, Tsedeke AT, Guenther S, Looso M and Stainier DYR (2017). Reciprocal analyses in zebrafish and medaka reveal that harnessing the immune response promotes cardiac regeneration. *eLife* 25605.
- El-Brolosy MA, Kontarakis Z, Rossi A, Kuenne C, Günther S, Fukuda N, Kikhi K, Boezio GLM, Takacs CM, Lai SL, Fukuda R, Gerri C, Giraldez AJ, Stainier DYR (2019). Genetic compensation triggered by mutant mRNA degradation. *Nature* 568, 193-197.

KARI KUSTAA ALITALO

Born 21.05.1952

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Biomedicum Helsinki, University of Helsinki
Haartmaninkatu 8, P.O. Box 63
00014 Helsinki, Finland

Tel.: +358 9 1912 5511**E-mail:** Kari.Alitalo@helsinki.fi**ResearcherID:** J-5013-2014**EDUCATION**

1976 Educational Commission for Foreign Medical Graduates

(USA) - exam 1977 M.D., University of Helsinki

1981 Dr. Med.Sci. (basic sciences, corresponding to Ph.D.
degree), University of Helsinki**PRESENT POSITIONS**

1993- Academy Professor, Research Council for Health, Academy of Finland

2013-2022 Director, Wihuri Research Institute

2014-2019 Director, Academy of Finland Centre of Excellence in Translational
Cancer Biology, University of Helsinki and University of Turku

2019-2024 Director, Translational Cancer Medicine Research Program, University of Helsinki

2019-(2026) Scientific Director, Academy of Finland Flagship in the Digital Precision Cancer
Medicine platform iCAN**JOURNAL EDITORIAL BOARD MEMBERSHIPS**Cancer Cell, Cancer Discovery, Cancer Research, EMBO Molecular Medicine, Journal of Clinical Investigation,
Journal of Experimental Medicine, Molecular Oncology, Trends in Molecular Medicine.**MENTOR DOCTORAL STUDIES (49 completed so far)****HONORS/AWARDS****1981**

1. Primus Doctorum in the X Promotion of The Medical Faculty, University of Helsinki

1987

2. The Anders Jahre Prize for Young Investigator, Norway

3. Farnos Oy Science Prize, Turku, Finland

1990

4. The Medix Prize for the Best Finnish Paper in the Biosciences in 1989

5. Member, European Molecular Biology Organization (EMBO)

1998

6. The Äyräpää Prize, Finland

7. The Medix Prize for the Best Finnish Paper in the Biosciences in 1997

1999

8. Europe Medicine Senior Prize

2002

9. The Lundbeck Foundation Nordic Prize, Denmark

10. Stiftung für die Erforschung und Bekämpfung der Krebskrankheiten, Liechtenstein

2003

11. Leopold Griffuel Prize, France

2005

12. Pfizer Advances in Oncology Award

13. Eric K Fernström Foundation's Nordic Prize, Sweden

2006

14. Louis-Jeantet Prize For Medicine, Switzerland

2009

15. The InBev-Baillet Latour Health Prize, Belgium

16. Fellow of The European Academy of Cancer Sciences

2010

17. The Michael O'Connor Award, Mayo Clinic, USA

18. The Anders Jahre Senior Medical Prize, Norway

2011

19. Moosa Plenary Award and Lecture, South Korea

20. Earl P. Benditt Award and Lecture, USA

21. The Medix Prize for the Best Finnish Paper in the Biosciences in 2010

2012

22. Commander of the Order of the Lion of Finland

2013

23. A.I. Virtanen Prize, Finland

24. Finnish Science Prize, Finland

25. Niilo Voipio Award, Finland

2014

26. Dr A.H. Heineken Prize for Medicine, The Netherlands

2016

27. Jacob Henle Medal, Medical Faculty of Göttingen University, Germany

28. Joseph Austin McCartney and Ruth McCartney Hauck Visiting Professorship, Mayo Clinic, USA

2018

29. Honorary Doctorship, Uppsala University, Sweden

INVITED PRESENTATIONS

About 400 invited talks in international meetings since 1984.

PATENTS

Inventor in numerous patents filed to the United States Patent and Trademark Office since 1995.

PUBLICATIONS

536 original publications in peer-reviewed journals, 143 reviews and editorials. Publications cited 78 063 times according to the Institute of Scientific Information. H-index: 147.

RESEARCH INTERESTS AND MAJOR ACCOMPLISHMENTS

My laboratory is interested in vascular biology, pathophysiology of cancer, tumor angiogenesis and metastasis. We have unraveled the molecular basis of lymphangiogenesis, the formation of lymphatic vessels and their involvement in several human diseases. We identified by molecular cloning several receptors and growth factors that govern the development and maintenance of blood vessels and lymphatic vessels. In fact, three of the currently known five vascular endothelial growth factors (VEGF-B, VEGF-C and VEGF-D) and two of the five endothelial-specific growth factor receptors (VEGFR3, and Tie1, the founding member of the angiopoietin-Tie signaling system) were identified in studies of us and our collaborators.

15 RECENT PUBLICATIONS:

1. Holopainen T, Räsänen M, Anisimov A, Tuomainen T, Zheng W, Tvorogov D, Hulmi JJ, Andersson LC, Cenni B, Tavi P, Mervaala E, Kivelä R, Alitalo K. Endothelial Bmx tyrosine kinase activity is essential for myocardial hypertrophy and remodeling. *Proc Natl Acad Sci USA* 112: 13063-13068, 2015.
2. Nurmi H, Saharinen P, Zarkada G, Zheng W, Robciuc MR, Alitalo K. VEGF-C is required for intestinal lymphatic vessel maintenance and lipid absorption. *EMBO Mol Med* 7: 1418-1425, 2015.
3. Robciuc MR, Kivelä R, Williams IM, de Boer JF, van Dijk TH, Elamaa H, Tigistu-Sahle F, Molotkov D, Leppänen VM, Käkälä R, Eklund L, Wasserman DH, Groen AK, Alitalo K. VEGFB/VEGFR1-induced expansion of adipose vasculature counteracts obesity and related metabolic complications. *Cell Metab* 23: 712-724, 2016.
4. Fang S, Nurmi H, Heinolainen K, Chen S, Salminen E, Saharinen P, Mikkola HKA, Alitalo K. Critical requirement of VEGF-C in transition to fetal erythropoiesis. *Blood* 128: 710-720, 2016.
5. Korhonen EA, Lampinen A, Giri H, Anisimov A, Kim M, Allen B, Fang S, D'Amico G, Sipilä TJ, Lohela M, Strandin T, Vaheri A, Ylä-Herttuala S, Koh GY, McDonald DM, Alitalo K, Saharinen P. Tie1 controls angiopoietin function in vascular remodeling and inflammation. *J Clin Invest* 126: 3495- 3510, 2016.
6. Kivelä R, Salmela I, Nguyen YH, Petrova TV, Koistinen HA, Wiener Z, Alitalo K. The Transcription factor Prox1 is essential for satellite cell differentiation and muscle fibre-type regulation. *Nat Commun* 7: 13124, 2016.

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7. Räsänen M, Degerman J, Nissinen TA, Miinalainen I, Kerkelä R, Siltanen A, Backman JT, Mervaala E, Hulmi JJ, Kivelä R, Alitalo K. VEGF-B gene therapy inhibits doxorubicin-induced cardiotoxicity by endothelial protection. *Proc Natl Acad Sci USA* 113: 13144-13149, 2016.
8. Heinolainen K, Karaman S, D'Amico G, Tammela T, Sormunen R, Eklund L, Alitalo K, Zarkada G. VEGFR3 modulates vascular permeability by controlling VEGF/VEGFR2 signaling. *Circ Res* 120: 1414-1425, 2017.
9. Leppänen V-M, Saharinen P, Alitalo K. Structural basis of Tie2 activation and Tie2/Tie1 heterodimerization. *Proc Natl Acad Sci USA* 114: 4376-4381, 2017.
10. Antila S, Karaman S, Nurmi H, Airavaara M, Voutilainen MH, Mathivet T, Chilov D, Li Z, Koppinen T, Park J-H, Fang S, Aspelund A, Saarma M, Eichmann A, Thomas J-L, Alitalo K. Development and plasticity of meningeal lymphatic vessels. *J Exp Med* 214: 3645-3667, 2017.
11. Zhang Y, Ulvmar MH, Stanczuk L, Martinez-Corral I, Frye M, Alitalo K, Mäkinen T. Heterogeneity in VEGFR3 levels during lymphatic vessel hyperplasia through cell-autonomous and non-cell-autonomous mechanisms. *Nat Comm* 9: 1296, 2018.
12. Hominick D, Silva A, Khurana N, Liu Y, Dechow PC, Feng JQ, Pytowski B, Rutkowski JM, Alitalo K, Dellinger MT. VEGF-C promotes the development of lymphatics in bone and bone loss. *Elife* 7: e34323, 2018.
13. Högström J, Heino S, Kallio P, Lähde M, Leppänen VM, Balboa D, Wiener Z, Alitalo K. Transcription factor PROX1 suppresses Notch pathway activation via the nucleosome remodeling and deacetylase complex in colorectal cancer-like cells. *Cancer Res* 78: 5820-5832, 2018.
14. Crona D, Skol A, Veli-Matti Leppänen, Glubb D, Etheridge A, Hilliard E, Peña C, Peterson Y, Klauber- DeMore K, Alitalo K, and Innocenti, F. Genetic variants of VEGFA and FLT4 are determinants of survival in renal cell carcinoma patients treated with sorafenib. *Cancer Res* 79: 231-241, 2019.
15. Kivelä R, Hemanthakumar KA, Vaparanta K, Robciuc M, Izumiya Y, Kidoya H, Takakura N, Peng X, Sawyer DB, Elenius K, Walsh K, Alitalo K. Endothelial Cells Regulate Physiological Cardiomyocyte Growth via VEGFR2 -Mediated Paracrine Signaling. *Circulation*, 139: 2570-2584, 2019.

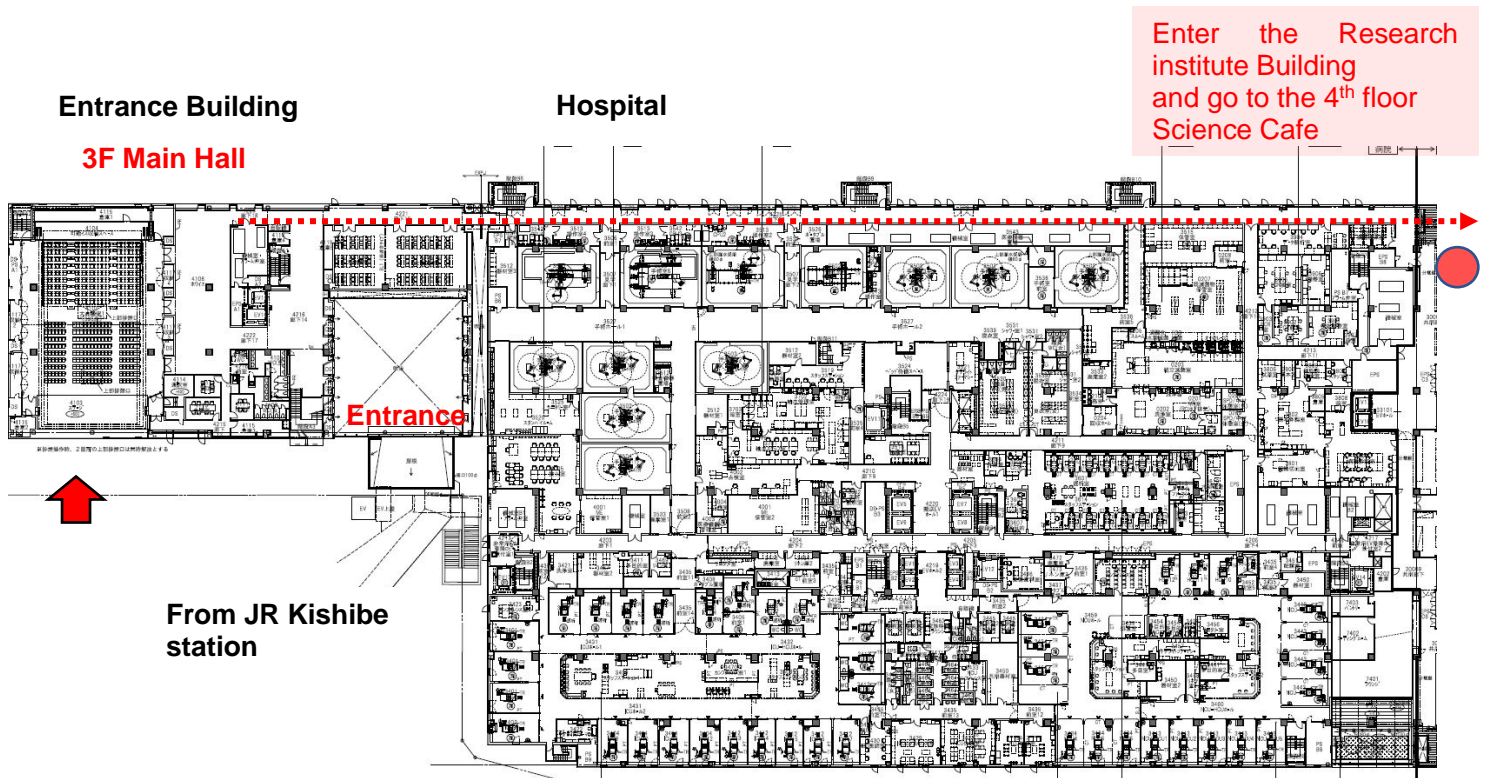
RECENT RVIIEWS:

16. Simons M, Alitalo K, Annex BH, Augustin HG, Beam C, Berk BC, Byzova T, Carmeliet P, Chilian W, Cooke JP, Davis GE, Eichmann A, Iruela-Arispe ML, Keshet E, Sinusas AJ, Ruhrberg C, Woo YJ, Dimmeler S, American Heart Association Council on Basic Cardiovascular Sciences and Council on Cardiovascular Surgery and Anesthesia. State-of-the-Art Methods for Evaluation of Angiogenesis and Tissue Vascularization: A Scientific Statement From the American Heart Assosiation. *Circ Res* 116: e99-e132, 2015.
17. Aspelund A, Robciuc MR, Karaman S, Mäkinen T, Alitalo K. Lymphatic system in cardiovascular medicine. *Circ Res* 118: 515-530, 2016.
18. Saharinen, P, Eklund L, Alitalo, K. Therapeutic targeting of the Angiopoietin-TIE pathway. *Nat Rev Drug Discov* 16: 635-661, 2017.
19. Karaman S, Alitalo K. Midkine and melanoma metastasis: a malevolent mix. *Dev Cell* 42: 205-207, 2017.
20. Louveau A, Plog BA, Antila S, Aliatlo K, Nedergaard M, Kipnis J. Understanding the functions and relationships of the glymphatic system and meningeal lymphatics. *J Clin Invest* 127: 3210-3219, 2017.
21. Vaahtomeri K, Karaman S, Mäkinen T, Alitalo K. Lymphangiogenesis guidance by paracrine and pericellular factors. *Gene Dev* 31:1615-1634, 2017.
22. Saharinen P, Leppänen V-M, Alitalo K. SnapShot: Angiopoietins and their functions. *Cell* 171: 724- 724.e1, 2017.

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23. Nowak-Sliwinska P, et al. Consensus guidelines for the use and interpretation of angiogenesis assays. *Angiogenesis* 21: 425-532, 2018.
24. Karaman S, Leppänen VM, Alitalo K. Vascular endothelial growth factor signaling in development and disease. *Development* 20;145, 2018.
25. Karaman S, Nurmi H, Antila S, Alitalo K. Stimulation and Inhibition of Lymphangiogenesis Via Adeno- Associated Viral Gene Delivery. *Methods Mol Biol* 1846: 291-300, 2018.
26. Brakenhielm E, Alitalo K. Cardiac lymphatics in health and disease. *Nat Rev Cardiol* 16: 56-68, 2019.

MAP of NCVC



4th floor of RI building Science Cafe

