

CURRICULUM VITAE

Arie Horowitz, D.Sc.

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CITIZENSHIP

U.S.A.

ADDRESSES

Work: Department of Molecular Cardiology, NB-50
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EDUCATION

1980	B. Sc.	Technion - Israel Institute of Technology
1984	M.Sc.	Technion - Israel Institute of Technology (Bioengineering)
1988	D.Sc.	Technion - Israel Institute of Technology (Bioengineering)

POSTDOCTORAL TRAINING

1988-1990	Department of Bioengineering, University of Washington
1990-1993	Rosenstiel Research Center, Brandeis University

ACADEMIC APPOINTMENTS

1982-1987	Teaching Assistant, Department of Mechanical Engineering, Technion - Israel Institute of Technology
1988-1990	Senior Fellow, Department of Bioengineering, University of Washington
1990-1993	Postdoctoral Research Associate, Rosenstiel Research Center, Brandeis University
1994-1996	Research Fellow, Department of Medicine, Harvard Medical School
1996-1999	Instructor, Department of Medicine, Harvard Medical School
1999-2001	Assistant Professor, Department of Medicine, Harvard Medical School
2001-2008	Assistant Professor, Department of Medicine, Dartmouth Medical School
2009-present	Assistant Staff, Lerner Research Institute, Cleveland Clinic Foundation
2009-present	Assistant Professor, Lerner College of Medicine, Case Western Reserve University, and Department of Physiology and Biophysics, Case Western Reserve Medical School (CWRU).

RESEARCH FUNDING

Past:	1992-1994	American Heart Association Research Fellowship
	1997-1998	National Institutes of Health Training Grant
	1998-2001	American Heart Association Scientist Development Grant – Principal Investigator
	2000-2004	NIH SCOR grant, Co-Investigator
	2002-2006	NIH R01 Grant – Principal Investigator
	2006-2006	Hitchcock Foundation - Principal Investigator

2006-2008	NIH R01 Grant - Co-Investigator (PI – Michael Simons)
2007-2011	Mentor, American Heart Association Scientist Development Grant (awarded to Dr. Miao-liang Liu)

PROFESSIONAL SOCIETIES

1. American Society of Cell Biology
2. American Heart Association
3. North American Vascular Biology Organization

PROFESSIONAL SERVICE

Editorial Boards (Ad-hoc Reviewer):

1. Molecular Biology of the Cell.
2. Atherosclerosis, Thrombosis and Vascular Biology.
3. The Journal of Cellular Biochemistry.
4. American Journal of Physiology, Cell Physiology.
5. The Journal of Cell Science.
6. Trends in Cell Biology.
7. Circulation Research.
8. Biochimica et Biophysica Acta.
9. American Journal of Pathology.
10. Journal of Molecular and Cellular Cardiology.
11. Molecular Cancer.
12. PLoS ONE.
13. Blood.
14. FEBS letters.
15. The Journal of Biochemistry

Grant Review:

1. Institutional Development Grant, North Carolina Biotechnology Center, 2001.
2. The Wellcome Foundation, United Kingdom, 2007.
3. The American Heart Association, Region I, 2008.
4. The Israel Science Foundation, 2010.
5. NIH Interdisciplinary Molecular Science and Training IRG

Review for Professional Societies:

1. The American Heart Association, abstract reviewer for the Scientific Sessions, 2008.

TEACHING AND MENTORSHIP

Mentees:

- | | |
|-----------|---|
| 1998–2000 | David Seo, M.D., Resident; currently: Instructor, Duke Medical School |
| 1998–2001 | Masahiro Murakami, M.D., Ph.D., Research Fellow; currently: Instructor, Yale School of Medicine |
| 1999–2001 | Mitsuru Horiba, M.D., Research Fellow; currently: Attending Physician, Nagoya University, Japan |

- 2002–2003 Esther Lutgens, M.D., Ph.D., Research Associate; currently: Assistant Professor, Maastricht University
- 2002–2008 Miao-liang Liu, M.D., M.Sc., Instructor
- 2003–2006 Anna Salikhova, Ph.D., Postdoctoral Research Associate
- 2007–2008 Alexandra Rodman, undergraduate trainee; currently, Stony Brook University Medical School
- 2009–present Sudesh Agrawal, Ph.D., Research Associate
- 2009–present Chaunsen Wu, M.D., Ph.D., Postdoctoral Fellow
- 2009 Mariya Pogrebetskaya, undergraduate trainee
- 2009–2010 Sandeep Sarkari, undergraduate trainee
- 2010 Yihharn Hwang, undergraduate trainee
- 2011 Meredith McGuire, undergraduate trainee
- 2011 Sailesh Gowind, undergraduate trainee
- 2011 Michael Zdrzinski, Cleveland Clinic Lerner College of Medicine, lab rotation
- 2011 Yue Zhao, Molecular Medicine Graduate Program, journal club preparation
- 2011–present Junning Yang, Ph.D., Postdoctoral Fellow
- 2011–present Himabindu Reddy Seerapu, Ph.D., Postdoctoral Fellow

Classroom Teaching

1. Program in Experimental and Molecular Medicine, course 102: cell migration, 2007-2008.
2. Introduction to Angiogenesis, Cardiology Fellows' seminars, Cleveland Clinic Foundation, 2011.

Thesis Committees:

1. Devi Prasad Ramakrishnan, CWRU Molecular Medicine Program. Ph.D. thesis on "Role of VEGF(165)b in p53 mediated inhibition of angiogenesis in cardiac failure with prolonged hypertrophy". Qualifying examination committee, 2010.
2. Denise Chang, Lerner College of Medicine of Case Western Reserve University. M.D. thesis on "The Functional Role of Kindlin-3 in Integrin-Mediated Responses of Endothelial Cells", 2010-2011.

COMMITTEE SERVICE

1. Steering Committee, Graduate Program in Experimental and Molecular Medicine, Dartmouth Medical School, 2006-2007.
2. Faculty recruitment, Translational Medicine position, Dartmouth Medical School 2005-2006.
3. Interviewer of candidates for the Graduate Program, Cleveland Clinic Lerner College of Medicine, 2009.
4. Interviewer of candidates for Case Western Reserve Medical School, M.D. and MD/PhD program, 2009-2010.
5. Departmental Representative, animal user committee, Lerner Research Institute, 2011.

BIBLIOGRAPHY

Original Reports

1. Perl, M., **A. Horowitz**, and S. Sideman. A Comprehensive Model for the Simulation of the Left Ventricle Mechanics; Part 1: Model Description and Simulation Procedure. *Med. Biol. Engng. Comp.* 24 :145-149, 1986.

2. **Horowitz, A.**, M. Perl, and S. Sideman. A Comprehensive Model for the Simulation of the Left Ventricle Mechanics; Part 2: Implementation and Results Analysis. *Med. Biol. Engng. Comp.* 24: 150-156, 1986.
3. Perl, M., and **A. Horowitz**. Mechanical Model for the Simulation of Ischemia and Infarction of the Left Ventricle. *Med. Biol. Engng. Comp.* 25: 284-288, 1987.
4. **Horowitz, A.**, I. Sheinman, Y. Lanir, M. Perl, and S. Sideman. Nonlinear Incompressible Finite Element for Simulating Loading of Cardiac Tissue; Part I: Two Dimensional Formulation for Thin Myocardial Strips. *ASME J. of Biomech. Engng.* 110: 57-61, 1988.
5. **Horowitz, A.**, S. Sheinman, and Y. Lanir. Nonlinear Incompressible Finite Element for Simulating Loading of Cardiac Tissue; Part II: Three Dimensional Formulation for Thick Ventricular Wall Segments. *ASME J. of Biomech. Engng.* 110: 62-68, 1988.
6. **Horowitz, A.**, Y. Lanir, F. C. P. Yin, M. Perl, I. Sheinman, and R. K. Strumpf. Three Dimensional Structural Constitutive Law for the Passive Myocardium. *ASME J. of Biomech. Engng.* 110: 200-207, 1988.
7. **Horowitz, A.**, M. P. H. Wussling, and G. H. Pollack. Effect of Small Releases on Force during Sarcomere-isometric Tetani in Frog Muscle Fibers. *Biophys. J.* 63: 3-17, 1992.
8. **Horowitz, A.**, and K. M. Trybus. Inhibition of Smooth Muscle Myosin's Activity and Assembly by an Anti-rod Monoclonal Antibody. *J. Biol. Chem.* 267: 26091-26096, 1992.
9. **Horowitz, A.**, M. Perl, and S. Sideman. Geodesics as a Mechanically Optimal Fiber Geometry for the Left Ventricle. *Basic Res. Cardiol.* 88 (suppl. 2): 68-74, 1993.
10. **Horowitz, A.**, and G. H. Pollack. Force-length Relation of Isometric Sarcomeres in Fixed-end Tetani. *Am. J. Physiol. (Cell Physiol.)* 264: C19-C26, 1993.
11. Pollack, G. H., **A. Horowitz**, M. Wussling, and K. Trombitas. Shortening-induced Tension Enhancement: Implication for Length-Tension Relations. *Adv. Exp. Med. Biol.* 332: 678-688, 1993.
12. **Horowitz, A.**, K. M. Trybus, D. S. Bowman, and F. S. Fay. Antibodies Probe for Folded Monomeric Myosin in Relaxed and Contracted Smooth Muscle. *J. Cell. Biol.* 126 :1195-1200, 1994.
13. **Horowitz, A.**, O. Clément-Chomienne, M. P. Walsh, T. Tao, H. Katsuyama, and K. G. Morgan. Effects of Calponin on Force Generation by Single Smooth Muscle Cells. *Am. J. Physiol.* 270(*Heart Circ. Physiol.* 39): H1858-H1863, 1996.
14. **Horowitz, A.**, O. Clément-Chomienne, M. P. Walsh, and K. G. Morgan. ϵ Isozyme of Protein Kinase C Induces a Ca^{2+} -Independent Contraction in Vascular Smooth Muscle. *Am. J. Physiol.* 271 (*Cell Physiol.* 40): C589-C594, 1996.
15. Walsh, M. P., **A. Horowitz**, O. Clément-Chomienne, J. E. Andrea, and K. G. Morgan. Protein Kinase C Mediation of Ca^{2+} -Independent Contractions of Vascular Smooth Muscle. *Biochem. Cell Biol.*, 74: 485-502, 1996.
16. Itoh, H., P. R. Nelson, L. Mureebe, **A. Horowitz**, and C. Kent. The Role of Integrins in Saphenous Vein Vascular Smooth Muscle Cell Migration. *J. Vasc. Surgery*, 25: 1061-1069, 1997.
17. **Horowitz, A.**, and M. Simons. Regulation of Syndecan-4 Phosphorylation in Vivo. *J. Biol. Chem.*, 273: 10914-10918, 1998.

18. **Horowitz, A.**, and M. Simons. Phosphorylation of the Cytoplasmic Tail of Syndecan-4 Regulates Activation of Protein Kinase Ca. *J. Biol. Chem.*, 273: 25548-25551, 1998.
19. **Horowitz, A.**, M. Murakami, and M. Simons. Phosphatidylinositol-4,5-bisphosphate Mediates the Interaction of Syndecan-4 with Protein Kinase C. *Biochem.*, 38: 15871-15877, 1999.
20. **Horowitz, A.**, E. Tkachenko, and M. Simons. Fibroblast Growth Factor-specific Modulation of Cellular Response by Syndecan-4. *J. Cell Biol.*, 157: 715-725, 2002.
21. Murakami, M., **A. Horowitz**, S. Tang, J.A. Ware, and M. Simons. PKCd Regulates PKCa in a syndecan-4 dependent manner. *J. Biol. Chem.*, 277: 20367-20371, 2002.
22. Liu, M., and **A. Horowitz**. A PDZ motif as a critical determinant of Rho guanine exchange factor function and cell phenotype. *Mol. Biol. Cell*, 17: 1880-1887, 2006.
23. Chittenden, T.W., F. Claes, A.A. Lanahan, K.L. Moodie, M. Autiero, R.T. Palac, E.V. Tkachenko, A. Efenbein, M. Drinane, E. Dedkov, R. Tomanek, W. Li, J. Singh, **A. Horowitz**, M. Mulligan-Kehoe, Z.W. Zhuang, J.D. Pearlman, P. Carmeliet and M. Simon. Synectin-dependent regulation of arterial branching. *Dev. Cell.*, 10: 783-795, 2006.
24. Naccache, S. N., T. Hasson, and **A. Horowitz**. Binding of Internalized Receptors to the PDZ domain of GIPC/synectin recruits myosin VI to endocytic vesicles. *PNAS*, 103: 12735–12740, 2006.
25. Salikhova, A., L. Wang, A. A. Lanahan, M. Simons, D. Mukhopadhyay, and **A. Horowitz**. Vascular Endothelial Growth Factor and Semaphorin Induce Neuropilin-1 Endocytosis via Separate Pathways. *Circ. Res.*, 103: e71-e79, 2008.
26. Garnaas, M. K., M. Liu, K. Li, J. Baraban, **A. Horowitz***, and R. Ramchandran*. Syx, a novel RhoA guanine exchange factor, is essential for angiogenesis *in vivo*. (* - **co senior author**). *Circ. Res.*, 103: 710-716, 2008.
27. Ernkvist, M., N. Luna-Persson, S. Audebert, P. Lecine, I. Sinha, M. Liu, A. Bratt, K. Aase, A. Majumdar, **A. Horowitz**, J. Borg, and L. Holmgren. The Amot/Patj/Syx signaling complex spatially controls RhoA GTPase activity in migrating endothelial cells. *Blood*, 113: 244-253, 2009.
28. Rodríguez-Manzaneque, J. C., D. Carpiroc, M. C. Plaza-Calonge, A. X. Torres-Collado, S. N. Thaïc, M. Simons, **A. Horowitz** and M. L. Iruela-Arispe. Cleavage of syndecan-4 by adamts1 provokes defects in adhesion. *Int. J. Biochem. Cell Biol.* 41: 800-810, 2009.
29. Wu, C., S. Agrawal, A. VasANJI, S. Sarkaria, J. Xie, B. M. Liu, Anand-Apte, and **A. Horowitz**. Rab13-dependent trafficking of RhoA is required for directional migration and angiogenesis. *J. Biol. Chem.*, 286: 23511–23520, 2011.
Yi Fan, Y., A. Arif, Y. Gong, J. Jia, S. M. Eswarappa¹, B. Willard¹, **A. Horowitz**, L. M. Graham, M. S. Penn, and P. L. Fox. Stimulus-dependent phosphorylation of profilin-1 in angiogenesis. In press, *Nat. Cell Biol.*
30. Ngok, S., R. Geyer, S. Agrawal, A. Kourtidis, L. J. Lewis-Tuffin, K. L. Moodie³, D Huveltdt, C. Wu, M. Liu, R. Marx, J. M. Baraban, P. Storz, **A. Horowitz***, and P. Z. Anastasiadis*. VEGF and Angiopoietin-1 exert opposing effects on cell junctions by regulating the CRB complex associated Rho GEF Syx (* - **co senior author**). Under review, *J. Cell Biol.*, 2012.
31. Seerapu, H. R., Agrawal, S., and **A. Horowitz**. Neuropilin-1 regulates focal adhesion turnover in response to VEGF-A. In preparation, 2012.

Reviews

1. **Horowitz, A.**, Bergh-Menice, C. B., Laporte, R., and Morgan, K. G. Mechanisms of Smooth Muscle Contraction. *Physiol. Rev.* 76: 967-1003, 1996.
2. Simons, M., and **A. Horowitz**. Syndecan-4-mediated signaling. *Cell. Signal.* 13: 855-862, 2001.
3. **Horowitz, A.**, and Simons, M. Branching Morphogenesis. *Circulation Research* 103: 784-795, 2008.
4. **Horowitz, A.**, Plekhg5, Molecule Pages, Nature, February 2010 (www.signaling-gateway.org).
5. **Horowitz, A.**, Angiomotin, Molecule Pages, Nature, September 2010 (www.signaling-gateway.org).
6. **Horowitz, A.**, and Seerapu, H. R., Regulation of VEGF signaling by membrane traffic. *Cell. Signal.* 24: 1810–1820, 2012.

Editorials

1. **Horowitz, A.**, Imaging of growth factor-augmented angiogenesis after myocardial infarction: glimmers of a spatiotemporal pattern? *J. Mol. Cell Cardiol.* 48: 1036-1038, 2010.
2. Wu, C., and **Horowitz, A.** Membrane traffic as a coordinator of cell migration and junction remodeling. *Communicative & Integrative Biology* 4: 703-705, 2011.

Book chapters

1. **Horowitz, A.**, Directional cues in angiogenesis, Ch. 6, pp 147-173, in Modern Concepts in Angiogenesis, M. Simons and G. Rubanyi, eds. Imperial College Press, 2007.
2. **Horowitz, A.**, SYX/PLEKHG5, A RhoA Guanine Exchange Factor Involved in Cell Migration and Angiogenesis, in Encyclopedia of Signaling Molecules, S. Choi ed., Springer, in press, 2011.

Invited Presentations

1. Theory of Heart workshop, University of California at San Diego, 1989.
2. Mini symposium on Cell Adhesion and Signaling in Development and Disease, 38th Meeting of The American Society of Cell Biology, San Francisco, 1998.
3. Symposium on Phosphoinositide Signaling, Joint Meeting of the American Society of Biochemistry and Molecular Biology and the American Society for Pharmacology and Experimental Therapeutics, Boston, 2000.
4. Neuropilin-1 is internalized in Response to Semaphorin 3C in a Synectin dependent Manner. Scientific Sessions of the American Heart Association, Chicago, 2006.
5. Work in progress: 1. Is the Uptake of Neuropilin-1 essential for Semaphorin and VEGF signaling in Endothelial Cells? 2. Knockout of the RhoA Guanine Exchange Factor Syx specifically impairs Angiogenesis in the Mouse. UCLA, August 10, 2007.
6. Knockout of a Tight Junction-associated Guanine Exchange Factor blocks Angiogenesis in the Mouse. Mayo Clinic Jacksonville, October 19, 2007.
7. Inhibition of Endothelial Cell Migration by Semaphorin 3C Requires Neuropilin-1 Uptake via Lipid Rafts. Scientific Sessions of the American Heart Association, Orlando, 2007.
8. VEGF and Semaphorin Induce Neuropilin-1 Endocytosis via Separate Pathways. Keystone meeting on Molecular Mechanisms of Angiogenesis in Development and Disease, Vancouver, BC, Canada, January 2008.
9. Chair, Session on Pathological Angiogenesis, Keystone meeting on Molecular Mechanisms of Angiogenesis in Development and Disease, Vancouver, BC, Canada, January 2008.
10. Mouse and zebrafish models of angiogenesis-specific defects. Cleveland Clinic, February 2008.

11. Neuropilin-1 Endocytosis is Essential for its Signaling and Depends on its Ligand. Angiogenesis meeting, European School of Hematology, Paris, May 2008.
12. Guidance and sprouting mechanisms in angiogenesis. University College, London, May 2008.
13. Neuropilin-1 Endocytosis is essential for its signaling and depends on its ligand. Biology of Signaling in the Cardiovascular System Meeting, Cape Cod, 2008.
14. Moderator, Cardiovascular Seminar on Guidance signaling in the vascular system. Scientific Sessions of the American Heart Association, New Orleans, 2008.
15. Gordon Research Conference, Vascular Cell Biology, Ventura, CA, March 2009. Intercellular Communication during Vessel Sprouting.
16. Case Comprehensive Cancer program, 2009 retreat. Molecular Mechanisms of Vessel Sprouting and Guidance.
17. Developmental Vascular Biology Workshop, North American Vascular Biology Organization, February 2010. Trafficking of the RhoA guanine exchange factor PLEKHG5 regulates angiogenesis.
18. Experimental Biology 2010 meeting, April 2010. Vesicle trafficking of a RhoA guanine exchange factor regulates VEGF-driven directional migration.
19. Gordon Research Conference, Vascular Cell Biology, Ventura, CA, February 2011. Co-trafficking of Syx and RhoA integrates junction disassembly and cell migration in response to VEGF.
20. Beth Israel Deaconess Medical Center and Harvard Medical School, Center for Vascular Biology Research, Emerging Role of Membrane Traffic in Angiogenesis, January 2012.

Patents

1. Simons, M., and **A. Horowitz**. Stimulation of Angiogenesis via Syndecan-4 Cytoplasmic Domain Signaling Pathway. US patent 6,815,187 B1.
2. Simons, M., R. Volk, and **A. Horowitz**. Stimulation of Angiogenesis via Enhanced Endothelial Expression of Syndecan-4 Core Proteins. US patent 7,029,668 B1.