Curriculum Vitae - William A. Frazier, PhD

Primary Position: Professor of Biochemistry and Molecular Biophysics

Office Address: Department of Biochemistry and Molecular Biophysics
2901 South Building, Campus Box 8231
Washington University School of Medicine
660 S. Euclid
St. Louis, MO 63110

Phone: (314)-362-3348 (office),

E-Mail: frazier@wustl.edu

Place of Birth: Lancaster, PA

Education
Johns Hopkins University, B.A. 1969
Washington University School of Medicine, Biochemistry, Ph. D. 1973

Postdoctoral
Washington University School of Medicine, R. A. Bradshaw, 1973
Univ. of California, San Diego Medical School, S. H. Barondes, 1974-76

Academic Appointments

Assistant/Associate Professor of Biochemistry (1976-1984)
Professor of Biochemistry and Molecular Biophysics (1985-2010)
Professor of Cell Biology (1987-2010)
Professor of Biomedical Engineering (2000-2010)
Member, Cardiovascular Research Group, Vascular Biology Interest Group (1998-2010)
Member, Diabetes Research Training Center (2008-2011)
Member, Siteman Cancer Center (2006-present)

Other Positions

Founder and President, Vasculox, Inc. St. Louis, MO (2006-2009)
Consultant to Vasculox, Inc. St. Louis, MO (2009-present)
Co-founder YourBevCo, LLC. St. Louis, MO (2013)
Founder and owner, Frazier Bioscience Consulting, LLC

Professional Societies

American Society for Cell Biology

American Heart Association

Awards and Honors

Maryland State Senatorial Scholarship, Johns Hopkins University;

Postdoctoral Fellowship, Sloan Foundation,

American Heart Association, Established Investigator.

Current Research Funding:

HL054390-12: CD47 is a thrombospondin receptor. Frazier, PI

CA097250-06: Role of Beta-3 Integrin in skeletal metastases, Weilbaecher, PI

CA176880-01 Tumor-toxic CD47mAb therapy for leukemia: a proof of concept study. Phase 1 STTR (Vasculox, Inc.) Frazier, PI.

Previous Research Funding:

HL095172-01: Development of a humanized anti-CD47 antibody for treatment of tissue ischemia, phase I STTR (Vasculox, Inc.) Frazier, PI

Washington University OTM Bear Cub Award: Selection of an anti-CD47 mAb for humanization. Frazier, PI

Institute of Clinical Translational Sciences: Identification of phosphorylated sites in BNIP3, Frazier, PI

Siteman Cancer Center Pilot Project Award: Anti-CD47 mAbs as adjuvants to tumor radiotherapy. Frazier, Co-PI

GM057573-01 to -09: CD47/IAP modulation of immune cell functions. 04-01-98 to 03-31-07.

CA065872-01 to -10: Regulation of angiogenesis by thrombospondin. 01-01-95 to 12-31-04.

Recent seminars:

"CD47: A New Therapeutic Target in Cancer and Cardiovascular Disease"
University of Delaware, May 20, 2011.

"CD47 regulates NO signaling and impacts mitochondrial density and function"
University of Alabama-Birmingham, February 22, 2011.

"Thrombospondin and its receptors in vascular pathophysiology"
Cleveland Clinic, June 17, 2005.

"A key to the enigma of thrombospondin-1 function in the cardiovascular system"
Univ. of Alabama, Birmingham, School of Medicine, Nov. 9, 2007.
Univ. of North Carolina, School of Medicine, Nov 14, 2007.

"CD47: A novel target in cardiovascular therapy".
Genentech, South San Francisco, Dec 18, 2008.
Harvard University School of Medicine, April 17 2009
Univ. of Pittsburgh School of Medicine, April 23, 2009
Oklahoma Medical Research Foundation, Dec 15, 2009

Recent Conference Presentations:

Gordon Conference on Atherosclerosis, June 2003, speaker.

ATVB San Francisco, May 2004, speaker.

FASEB summer conference, Matricelular proteins, Calloway Gardens, GA. Plenary speaker 2004.

Gordon Conference on Atherosclerosis, June 2005, speaker.

Symposium on proteomics, Beckman Institute, Irvine, CA, April, 2006. Plenary speaker.

FASEB Summer Conference, Thrombospondins and other matricellular proteins in tissue organization and homeostasis. Tucson AZ, June 2007, Invited plenary speaker.

ASCB National Meeting, CD47 and Thrombospondin-1 limit mitochondrial biogenesis. San Francisco, CA Dec. 2008, Minisymposium speaker.

Gordon Research Conference, Biology of Aging. CD47 limits mitochondrial biogenesis and exacerbates cardiovascular aging. Ventura CA Feb. 2009, Session speaker.

FASEB Summer Conference, Thrombospondins and other matricellular proteins. "Thrombospondin-1 and CD47: Role in aging and metabolic syndrome" Snowmass, CO, 2010. Invited speaker/session chair.
July 18-23, 2010.

13Th Midwest Platelet Conference, "Thrombospondin-1 and CD47: No free lunch on the

senior menu", UNC, Chapel Hill, NC. October 13-15, 2010.

American Society for Matrix Biology, "Matricellular regulation of mitochondria via CD47" Charleston, SC, October 24-27, 2010.

University Service

- Admissions committees for Biochemistry Department, Molecular Cell Biology Program and Biochemistry and Molecular Biophysics Program
- Steering committee for Molecular Cell Biology Graduate program and Biochemistry and Biophysics Graduate program (current)
- Founded "Membranes and Receptors" graduate course.
- Director, Molecular Biology and Biochemistry Graduate Program (1978-82)
- Past coursemaster of 1st year medical school biochemistry course.
- Committee on Academic Promotions and Review
- Chair of KECK postdoctoral fellowship selection committee (1996-2013).
- Director, Molecular Cell Biology Program (1995-98)
- Served on >30 PhD and MD/PhD student prelim committees, many as chair.
- Served on 26 thesis committees.
- Member of committee to restructure medical education at WUSM (1989-92).
- Member of Quad Departmental Seminar Committee (2008-2010)
- Mentoring committee for Biochemistry Department junior faculty
- Washington University Faculty Senate (1986-94)

Extramural Service

- Reviewer for NIH/CSR panels Neuro B, Cell Bio, Cell Bio B, Path A, Pathobiochem, and CDF4
- Reviewer for American Heart Association
- Promotion and Tenure committees for Harvard Medical School, University of Alabama, University of Wisconsin
- Congressional Liason Committee of American Society of Cell Biology
- Advisory Review Board, Mayo Clinic, Rochester MN
- Advisory Panel for Hope Heart Institute, Seattle, WA
- Review Panel for Intramural Division of Cancer Pathobiology, NCI, NIH

Graduate Student Trainees

Name	Time in lab	Current Position
James R. Bartles	1977-1982	Professor, Cell Biology, Northwestern
A. Christie King	1977-1982	Glaxo Smith Kline
Beth Hutchins	1980-1985	Senior Scientist, Schering-Plough Corp
Lori Paul	1982-1987	Biology teacher, St. Louis Community College
Carolyn Crankshaw	1988-1992	Scientist, Monsanto Corp., Pfizer, St. Louis
Ruiqin Zhong	1993-1997	University of Georgia, Athens Ga.
Jun Chung	1996-2000	Harvard University
Tejinder Rakhra	1997-2000	Unknown
Sarah Stuhlsatz	1999-2006	Staff Scientist, University of Oregon
Ming-Ping WU	2004-2008	OB/GYN Taiwan University Hospital
Ozge Uluckan	2006-2010	Post Doc, CNIO, Madrid Spain.
Katherine Linstrand	2010-present	

Postdoctoral Trainees

Lane J. Wallace	1978-1981	University of Ohio, Pharmacology
Nandini Kishore	1980-1983	Executive Director, Pfizer, St. Louis
Nancy Galvin	1981-1985	St. Louis University, Anatomy and Cell Biology
Gordon Jamieson	1982-1985	President, Translational Therapeutics, MA
Vishva Dixit	1983-1987	Vice President, Genentech, San Francisco, CA
Doris Haverstick	1984-1986	University of Virginia, Pharmacology
Minh Kosfeld	1990-1994	Unknown

Ai-Guo Gao	1993-1998	Senior Group Leader, Monsanto, St Louis
Nader Sheibani	1995-2000	Professor Ophthalmology, Univ of Wisconsin
Consuelo Munoz	1995-1997	Unknown
Xue-Qin Wang	1996-2001	University of Pennsylvania Medical School
John A. McDonald	1998-2004	Senior Scientist, Millipore Corp, St. Louis MO
Katherine Harris	2000-2002	Northwestern Univ, Technology Management
Partha Manna	2001-2005	Academic position in India
Anthony Vomund	2002-2007	Technical Rep, Midwest Scientific, St. Louis,
Dan Ye	2003-2007	Hospitalist, Cape Girardeau, MO
Donald Lawrence	2003-2007	Asst. Prof. Pathology, St. Louis University Med.
Per-Arne Oldenborg	2004-2006	Professor, University of Umea, Sweden
Loretta Pappan	2004-2008	Scientist, Edenspace, Manhattan, KS
Elfaridah Frazier	2007-2010	Clinical Scientist, Children's Hospital, St. Louis
Eric Christenson	2011-2012	Post Doc, National Institutes of Health

Entrepreneurial Activities

In November 2006 I founded **Vasculox, Inc** (a Delaware Corporation, www.vasculox.com) based on technology discovered jointly by myself and my long-time collaborator, David Roberts at NIH. The technology is embodied in US 12/444,364 and Canadian, Australian and European applications, Isenberg, J.S., Roberts, D.D. and Frazier, W.A. (inventors), Prevention of Tissue Ischemia: Related Methods and Compositions. (Held jointly by Washington University and NIH). This technology is based on our finding that TSP1 acting via CD47 constantly limits the NO-cGMP signaling pathway in all vascular cells. Alleviating this built-in brake on NO signaling has many potential benefits in treatment of cardiovascular diseases and ischemia arising from a number of causes. Just after founding Vasculox, I was fortunate to participate in the Kaufman Foundation FASTRAK entrepreneurship course offered by the Washington University Office of Technology Management.

Vasculox has obtained a license from NIH to commercialize a humanized anti-CD47 monoclonal antibody (mAb) for all cardiovascular indications covered in the above patent. Our technology has many potential applications and thus a major part of our start-up effort was directed at identifying the optimal first clinical target for our CD47mAb. The first clinical indication to be addressed with the Vasculox humanized mAb is organ transplantation, a setting in which severe ischemia-reperfusion injury (IRI) limits outcomes and also restricts the use of “extended criteria” or less than optimal organs. Organ transplantation is an orphan indication; there is a clear unmet medical need. Vasculox has worked with transplant surgeons at BJC Hospital (Washington University Medical School) to obtain proof of concept data in ex vivo and in vivo kidney and liver transplant models. Vasculox is also developing humanized antibodies against CD47 as novel therapeutics in leukemias and other cancers.

Vasculox has received STTR/SBIR grants (from NHLBI, NIDDK and NCI), funding from Biogenerator (a non-profit whose mission is to provide resources to St. Louis start-ups from local universities) and the Missouri Technology Corporation in the form of a Tech Launch grant and a Seed Capital Grant.

In 2013 I cofounded of Your Bev Co., a biotech start-up whose mission is to develop devices and processes for removal of noxious materials from beverages including gluten from beers and sulfites from wine. UrBev has received SPARK funding from BioGenerator.

Bibliography

Original Articles

1. Nason, A., Antoine, A.D., Ketchum, P.A., Frazier, W.A. III, and Lee, D.K. Formation of Assimilatory Nitrate Reductase by In vitro Inter-Cistronic Complementation in Neurospora crassa. Proc. Natl. Acad. Sci. USA 65. 137 (1970).

2. Ketchum, P.A., Cambier, H.Y., Frazier, W.A. III, Madansky, C.H., and Nason, A. In vitro Assembly of Neurospora Assimilatory Nitrate Reductase from Protein Subunits of a Neurospora Mutant and the Xanthine Oxidizing or Aldehyde Oxidase Systems of Higher Animals. Proc. Natl. Acad. Sci. USA 66, 1016 (1970).

3. Angeletti, R.H., Frazier, W.A. III, and Bradshaw, R.A. Structural Studies of 2.5 S Mouse Submaxillary Gland Nerve Growth Factor. Adv. Exp. Med. Biol. 32, 99-106 (1972).

4. Frazier, W.A., Angeletti, R.H., and Bradshaw, R.A. Nerve Growth Factor and Insulin. Science 176, 482 (1972).

5. Bradshaw, R.A., Frazier, W.A., and Angeletti, R.H. A Comparison of the Structural and Functional Properties of Nerve Growth Factor and Insulin. Chemistry and Biology of Peptides, Proc. of the 3rd American Peptide Symposium (J. Meienhofer, ed.) Ann Arbor Science Publishers, Inc., pp. 423- 439, 1972.

6. Frazier, W.A., Angeletti, R.H., Sherman, R., and Bradshaw, R.A. The Topography of 2.5 S Nerve Growth Factor: The Reactivity of Tyrosine and Tryptophan. Biochemistry 12, 3281-3293 (1973).

7. Frazier, W.A., Ohlendorf, C.E., Boyd, L.F., Aloe, L., Johnson, E.M., Ferrendelli, J.A., and Bradshaw, R.A. On the Mechanism of Action of Nerve Growth Factor and Cyclic AMP on Neurite Outgrowth in Embryonic Chick Sensory Ganglia: Demonstration of Independent Pathways of Stimulation. Proc. Natl. Acad. Sci. USA 70, 2448-2452 (1973).

8. Frazier, W.A., Boyd, L.F., and Bradshaw, R.A. The Interactions of Nerve Growth Factor with Surface Membranes: Biological Competence of Insolubilized Nerve Growth Factor. Proc. Natl. Acad. Sci. USA 70, 2931-2935 (1973).

9. Frazier, W.A. Nerve Growth Factor: Studies on the Structure, Function and Mechanism. Ph.D. Thesis, Washington University, St. Louis, MO (1973).

10. Frazier, W.A., Boyd, L.F., and Bradshaw, R.A. Properties of the Specific Binding of ^{125}I-Nerve Growth Factor to Responsive Peripheral Neurons. J. Biol. Chem. 249, 5513-5519 (1974).

11. Frazier, W.A., Boyd, L.F., Szutowicz, A., Pulliam, M.W., and Bradshaw, R.A. Specific

Binding Sites for ^{125}I-Nerve Growth Factor in Peripheral Tissues and Brain. Biochem. Biophys. Res. Comm. 57, 1096-1103 (1974).

12. Frazier, W.A., Boyd, L.F., Pulliam, M.W., Szutowicz, A., and Bradshaw, R.A. Properties and Specificity of Binding Sites for ^{125}I-Nerve Growth Factor in Embryonic Heart and Brain. J. Biol. Chem. 249, 5918-5923 (1974).

13. Hogue-Angeletti, R.A., Frazier, W.A., Jacobs,J., Niall, H.D., and Bradshaw, R.A. Purification,Characterization and Partial Amino Acid Sequence of N. naja Nerve Growth Factor. Biochemistry 15, 26-34 (1976).

14. Server, A.L., Herrup, K., Shooter, E.M., Hogue-Angeletti, R.A., Frazier, W.A., and Bradshaw, R.A. Comparison of the Nerve Growth Factor Proteins from Cobra Venom (Naja naja) and Mouse Submaxillary Gland. Biochemistry 15, 35-39 (1976).

15. Szutowicz, A., Frazier, W.A., and Bradshaw, R.A. Subcellular Localization of Nerve Growth Factor Receptor in 13-Day Chick Embryo Brain. J. Biol. Chem. 251, 1516-1523 (1976).

16. Szutowicz, A., Frazier, W.A., and Bradshaw, R.A. Subcellular Localization of Nerve Growth Factor Receptors: Developmental Correlation in Chick Embryo Brain. J. Biol. Chem. 251, 1524-1528 (1976).

17. Frazier, W.A., Rosen, S.D., Reitherman, R.W., and Barondes, S.H. Purification and Comparison of Two Developmentally Regulated Lectins from Dictyostelium discoideum: Discoidin I and II. J. Biol. Chem. 250, 7714- 7721 (1975).

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25. Rosen, S.D., Kaur, J., Clark, D.L., Pardos, B.T., and Frazier, W.A. Purification and Characterization of Multiple Species (Isolectins) of a Slime Mold Lectin Implicated in Cell Cohesion. J. Biol. Chem. 254, 9408- 9415 (1979).

26. Wallace, L.J., and Frazier, W.A. Direct and Enzyme Mediated Photoaffinity Labeling of Membrane Associated Actin in Dictyostelium discoideum. J. Biol. Chem. 254, 10109-10114 (1979).

27. Bartles, J.R., and Frazier, W.A. Preparation of ^{125}I-Discoidin I and the Properties of Its Binding to Dictyostelium discoideum Cells. J. Biol. Chem. 255, 30-38 (1980).

28. Bartles, J.R., Santoro, B.C., and Frazier, W.A. Purification of a High- Affinity Discoidin I Binding Proteoglycan from Axenic D. discoideum Growth Medium. Biochim. Biophys. Acta 674, 372-382 (1981).

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I. Discoidin I Binds to Two Types of Receptors on Fixed Dictyostelium discoideum Cells. Biochim. Biophys. Acta 687, 121-128 (1982).

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38. Dixit, V.M., Grant, G.A., Frazier, W.A., and Santoro, S.A. Isolation of the Fibrinogen-Binding Region of Platelet Thrombospondin. Biochem. Biophys. Res. Comm. 119, 1075-1081 (1984).

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44. Dixit, V.M., Haverstick, D.M., O'Rourke, K.M., Hennessy, S.W., Grant, G.A., Santoro, S.A., and Frazier, W.A. A Monoclonal Antibody against Human Thrombospondin Inhibits Platelet Aggregation. Proc. Natl. Acad. Sci. USA 82, 3472-3476 (1985).

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of Human Thrombospondin Contain a Cell Attachment Site. J. Cell Biol.. 112, 1031-1040 (1991).

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