

BIOGRAPHICAL SKETCH

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NAME Breyer, Richard M.	POSITION TITLE		
eRA COMMONS USER NAME breyerrm	Professor of Medicine and Pharmacology		
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
University of Michigan, Ann Arbor, MI	B.S.	1978	Microbiology
Massachusetts Institute of Technology, Cambridge, MA	S.M.	1982	Biology
Massachusetts Institute of Technology, Cambridge, MA	Ph.D.	1988	Biochemistry

A. Personal Statement

My expertise is in the area of prostaglandin receptor physiology and pharmacology. I have over 20 years experience in characterizing PG receptor binding and signaling as well as evaluating physiology and pathophysiology in mouse models. My lab has focused on the role of hypertension and diabetes in renal disease using mouse models and has more than 10 years experience with a variety of models. We have developed mouse knockout models for each of the PG receptors as well as novel antagonists for EP1 and EP3 receptors. I will provide expertise concerning all aspects of PG receptor characterization both in vivo and in cell culture models. I also have a background in protein structure and function and have a longstanding interest in determining the three dimensional structure of the PGE₂ receptors, and our laboratory is pursuing structural analysis of PG receptors.

B. Positions and Honors.

Positions and Employment

1982-1984 Research Assistant, Repligen Corporation, Cambridge, Massachusetts
1988-1990 Postdoctoral Fellow, Biologie Moléculaire des Récepteurs, Institut Pasteur Paris, France
1990-1991 Postdoc. Fellow, Laboratoire d'Immuno-Pharmacologie Moléculaire, Institut Cochin de Génétique Moléculaire Paris, France
1991-1997 Assistant Professor, Department of Medicine, Division of Nephrology, and Department of Pharmacology, Vanderbilt University, Nashville, Tennessee
1997-2004 Associate Professor, Department of Medicine, Division of Nephrology and Department of Pharmacology, Vanderbilt University, Nashville, Tennessee
2004-present Professor, Department of Medicine, Division of Nephrology and Department of Pharmacology, Vanderbilt University, Nashville, Tennessee
2006-present Professor of Biochemistry
2006-2011 John B. Youmans Professor of Medicine,
2011-present Ruth King Scoville Professor in Medicine

Other Experience and Professional Memberships

1978 Phi Beta Kappa, University of Michigan
1987-1988 Centocor Research Fellow, Predoctoral Fellowship
1988-1989 Fondation de la Recherche Médicale, Postdoctoral Fellowship
1989-1990 Association pour la Recherche sur le Cancer, Postdoctoral Fellowship
1990-1991 Agence Nationale sur le SIDA, Postdoctoral Fellowship

Honors

1992 National Kidney Foundation Young Investigator Award

C. Selected peer-reviewed publications

Most relevant to the current application

1. Downey, J.D., Saleh, S.A., Bridges, T.M., Morrison, R.D., Daniels, J.S., Lindsley, C.W. and **Breyer RM** (2013) Development of an in vivo active, dual EP1 and EP3 selective antagonist based on a novel acyl

sulfonamide bioisostere *Bioorg. & Med Chem Lett* 23(1):37-41 PMID: PMC3534858.

- Hoggatt J, Mohammad KS, Singh P, Hoggatt AF, Chitteti BR, Speth JM, Hu P, Poteat BA, Stilger KN, Ferraro F, Silberstein L, Wong FK, Farag SS, Czader M, Milne GL, **Breyer RM**, Serezani CH, Scadden DT, Guise TA, Srour EF, Pelus LM (2013) Differential stem- and progenitor-cell trafficking by prostaglandin E. *Nature* **495**, 365–369 PMID: PMC3606692.
- Bartlett, CE, Boyd, KL, Harris, RC, Zent, R, **Breyer RM** (2012) EP1 Disruption Attenuates End-Organ Damage in a Mouse Model of Hypertension. *Hypertension*, 60,1184-1191. PMID: PMC3478772.
- Chen L, Miao Y, Zhang Y, Dou D, Liu L, Tian X, Yang G, Pu D, Zhang X, Kang J, Gao Y, Wang S, Breyer MD, Wang N, Zhu Y, Huang Y, **Breyer R.M.** and Guan Y (2012) Inactivation of the E-Prostanoid 3 Receptor Attenuates the Angiotensin II Pressor Response via Decreasing Arterial Contractility. *Arterioscler Thromb Vasc Biol.* 2012;**32** (12):3024-32. PMID: PMC3565847
- Kennedy, C.R., Zhang, Y., Brandon, S, Guan, Y., Coffee K., Funk, C.D., Magnuson, M.A., Oates, J.A., Breyer, M.D. & **Breyer, R.M.** (1999). Salt-sensitive hypertension and reduced fertility in mice lacking the prostaglandin EP₂ receptor. *Nature Medicine*, 5(2), 217-220. PMID:9930871.

Additional recent publications of importance to the field (in chronological order):

- Natarajan C., Hata, A.N., Hamm, H.E., Zent, R. and **Breyer R.M.** (2013) Extracellular Loop II Modulates GTP Sensitivity of the Prostaglandin EP3 Receptor. *Mol. Pharmacol.* **83**(1):206-16. PMID: PMC3533480
- Shi J, Wang Q, Johansson JU, Liang X, Woodling NS, Priyam P, Loui TM, Merchant M, **Breyer R.M.**, Montine TJ and Andreasson K (2012) Inflammatory prostaglandin E(2) signaling in a mouse model of Alzheimer disease. *Ann Neurol.* **72**(5):788-98.PMID: PMC3509238
- Downey, J.D., Sanders, C.R. & **Breyer, R.M.** (2011). Evidence for the presence of a critical disulfide bond in the mouse EP3 γ receptor. *Prostaglandins & Other Lipid Mediators*, 94(1-2), 53-58. PMID:PMC3065360.
- Jewell, M.L., **Breyer, R.M.** & Currie, K.P. (2011). Regulation of calcium channels and exocytosis in mouse adrenal chromaffin cells by prostaglandin EP3 receptors. *Molecular Pharmacology*, 79(6), 987-996. PMID:PMC3102550.
- Smith, J.P., Haddad, E.V., Downey, J.D., **Breyer, R.M.** & Boutaud, O. (2010). PGE₂ decreases reactivity of human platelets by activating EP2 and EP4. *Thrombosis Research*, 126(1), e23-29. PMID:PMC2902561.
- Babaev, V.R., Chew, J.D., Ding, L., Davis, S., Breyer, M.D., **Breyer, R.M.**, Oates, J.A., Fazio, S. & Linton, M.F. (2008). Macrophage EP4 deficiency increases apoptosis and suppresses early atherosclerosis. *Cell Metabolism*, 8(6), 492-501. PMID:PMC2614698.
- Hata, A.N., Lybrand, T.P. & **Breyer, R.M.** (2005). Identification of determinants of ligand binding affinity and selectivity in the prostaglandin D₂ receptor CRTH2. *Journal of Biological Chemistry*, 280(37), 32442-32451. PMID:16030019.
- Yang, L., Yamagata, N., Yadav, R., Brandon, S., Courtney, R.L., Morrow, J.D., Shyr, Y., Boothby, M., Joyce, S., Carbone, D.P. & **Breyer, R.M.** (2003). Cancer-associated immunodeficiency and dendritic cell abnormalities mediated by the prostaglandin EP2 receptor. *Journal of Clinical Investigation*, 111(5), 727-735. PMID:PMC151895.
- Zhang, Y., Guan, Y., Schneider, A., Brandon, S, **Breyer, R.M.** & Breyer, M.D. (2000). Characterization of Murine Vasopressor and Vasodepressor Prostaglandin E₂ Receptors. *Hypertension*, 35(5), 1129-1134. PMID:10818076.
- Breyer, R.M.**, Emeson, R.B., Tamng, J.L., Breyer, M.D., Davis, L.S., Abromson, R.M. & Ferrenbach, S.M. (1994). Alternative Splicing Generates Multiple Isoforms of a Rabbit Prostaglandin E2 Receptor. *Journal of Biological Chemistry*, 269(8), 6163-6169. PMID:8119961.

D. Research Support

Projects Ongoing or Completed During the Last 3 Years

Ongoing

BX000616 VA Merit (R. Breyer)

10/01/2010 - 09/30/2014

Novel EP receptor antagonists for the treatment of hypertension and of diabetes

5/8ths support

Department of Veterans Affairs

To define the role of the EP1 and EP3 receptors mouse models of hypertension and diabetes using novel EP receptor antagonists

Role: Principal Investigator

Completed

NIH/NIDDK 5R01 DK037097-25 (R. Breyer)

09/15/08 - 08/31/12

“Molecular Mechanism of PGE2 Receptor Pressor Effects”

To define the role of the EP1 and EP3 receptors mouse models of hypertension and diabetes using targeted gene disruption.

Role: Principal Investigator

NIH/NIGMS - 5P50 GM015431-43 (Roberts)

07/03/06 - 06/30/11

“Research Center for Pharmacology and Drug Toxicology”

This grant examines the role of DP receptors in inflammation. We generated a DP targeted gene disruption to examine the effect of loss of DP receptor on mouse models of neuro-inflammation.

Role: Co-investigator, P.I Project 2

NIH/NIGMS 5R01 GM081816-03 (Sanders)

09/21/06 - 01/31/11

“Overcoming the Barriers to Structural Analysis of GPCRs”

The goal is to obtain additional high resolution structural information on G protein-coupled receptors.

Role: Co-investigator

NIH/NIAID - 5R01 AI059108-05 (R. Breyer)

02/01/05 - 01/31/11

“The Structure and Function of the CRTH2 PDG2 Receptor

To define the pharmacology of the CRTH2 receptor and investigate its role in mouse models of disease.

Role: Principal Investigator

NIH/NCI 5P50 CA090949-07 (Carbone)

09/26/07 - 03/31/10

“SPORE in Lung Cancer”

The goal is to define complex pathways and important intermediates in these pathways to help in the early detection and optimal treatment of patients with lung cancer.

Role: Co-investigator

NIH/NIMH 5R41 MH085768-02 (Baldwin)

09/30/08 - 08/31/10

“PET and SPECT Ligands for Imaging Neuronal Apoptosis”

The goal of this grant is to develop novel in vivo imaging agents.

Role: Co-investigator

NIH/NIDDK - 5R01 DK048831-14 (Yin)

04/15/04 - 02/28/09

“Biochemistry and Pharmacology of D2/E2 Isoprostanes”

The goal of this grant is to study formation of D and E –ring isoprostanes from radical oxidation of arachidonic acid.

Role: Co-investigator

NIH/NIEHS - 5P01 ES013125-03 (Porter)

06/01/07 - 05/31/09

“Lipid Peroxidation and Antioxidant Mechanisms”

The goal of this grant is to study lipid peroxidation.
Role : Co-investigator Project 2