BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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O'BRIEN Terrence X. (M.D.)	POSITION TITLE Staff Cardiologist; Director, Echocardiography Laboratory (VAMC); Professor of Medicine, and Cell Biology and Anatomy; Director, Cardiovascular Clinical Research (MUSC)
eRA COMMONS USER NAME OBRIENTE	

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Stanford University, Palo Alto, CA	B.S.	1980	Chemistry and Biology
Stanford University, Palo Alto, CA	M.S.	1980	Biology
University of California, San Diego, CA	M.D.	1984	Medicine
University of Texas Southwestern Medical Center, Dallas, TX	Residency	1984-1987	Internal Medicine
University of California, San Diego, CA	Clinical	1988-1990	Clinical Cardiology
University of California, San Diego, CA	Research	1990-1993	Molecular Cardiology

A. Positions and Honors

Positions and Employment

1987-1988 Clinical Assistant Professor of Medicine, University of Texas Southwestern, Dallas, Texas
1990-1992 Instructor in Medicine; University of California Medical Center San Diego, California
1990-1993 Associate Investigator; Veterans Administration Medical Center, San Diego, California
1991-1993 Research Fellowship, Molecular Biology, Bugher Foundation, American Heart Association
1992-1993 Clinical Assistant Professor of Medicine, University of California, San Diego, CA
1993-2000 Assistant Professor of Medicine and Cell Biology and Anatomy, MUSC, Charleston, SC
1993-Present Staff Physician-Cardiology, RHJ-VAMC, Charleston, SC
1995- Present Director, Echocardiography Laboratory, RHJ-VAMC, Charleston, SC
1998- Present Faculty, Molecular & Cellular Biology & Pathobiology Program, MUSC, Charleston, SC
2000-2007 Associate Professor of Medicine and Cell Biology and Anatomy, MUSC, Charleston, SC
2001- Present Medical Director, MUSC Cardiology at East Cooper (Outreach Clinic)
2003- Present Director, Cardiovascular Clinical Research, MUSC, Charleston, SC
2007- Present Professor of Medicine (Cardiology) and Cell Biology and Anatomy, MUSC, Charleston, SC

Other Experience and Professional Memberships

- Member, Charleston Research Institute Board of Directors, 2006- Present
- Member, VA Merit Review Cardiology Study Section (Chair 2007-8), 2005-2008
- Associate Editor, Cardiology Section, American Journal of the Medical Sciences, 2006 - present
- American Heart Association
- American College of Cardiology
- Heart Failure Society of America
- American Society of Echocardiography
- International Heart Research Society
- American Medical Association

Honors

1976-1980 Stanford University Four-Year Academic Undergraduate Scholarship
1977-1980 California State Academic Scholarship, Stanford University
1980-1984 Regents Scholarship, University of California, San Diego, School of Medicine
1992 Trainee Investigator Award for Research, American Federation for Clinical Research
1990-1993 Associate Investigator Career Development Award, Veterans Administration
1991-1993 Bugher Fellowship in Molecular Biology, American Heart Association
1995-1999 Research Associate Award, Ralph H. Johnson Veterans Affairs Medical Center, Charleston, SC
1999 Young Investigator Award, American Heart Association Conference, Salt Lake City, Utah
2001- Present Tenure, Medical University of South Carolina
2006 Golden Apple Teaching Award Nomination, AMSA, MUSC

2007-2008 Awarded “Best Doctors in America” peer recognition

B. Selected peer-reviewed publications (publications selected from 46 peer-reviewed publications)

1. Ross RS and **O'Brien TX**. The mouse that roared: Cardiovascular applications of transgenic technology. Heart Failure, 8: 109-120, 1992.
2. Lee KJ, Ross RS, Rockman HA, Harris AN, **O'Brien TX**, Van Bilsen M, Shubeita HE, Kandol R, Brem G, Price J, Evans SM, Zhu H, Franz WM, Chien KR. Myosin light chain-2-luciferase transgenic mice reveal distinct regulatory programs for cardiac and skeletal muscle specific expression of a single contractile protein gene. J Bio Chem, 267: 15875-15885, 1992.
3. Chien KR, Zhu H, Knowlton KU, Miller-Hance W, Van-Bilsen M, **O'Brien TX**, Evans SM. Transcriptional regulation during cardiac growth and development. Ann Rev Physio, 55: 77-95, 1993.
4. **O'Brien TX**, Lee K., Chien KR. Positional specification of the ventricular myosin light chain-2 gene in the primitive murine heart tube. Proc Natl Acad Sci USA, 90:5157-5161, 1993.
5. Evans SM and **O'Brien TX**. Expression of the helix-loop-helix factor Id during mouse embryonic development. Dev Biol, 159: 485-499, 1993.
6. Chien KR, Knowlton KU, Lee KJ, Ross RS, Rockman HA, **O'Brien TX**. Molecular analysis of cardiac growth and development in transgenic mouse model systems. In: Idiopathic Dilated Cardiomyopathy, Figulla et al. (Eds.), Springer-Verlag Berlin Heidelberg, 1993.
7. Kubalak SW, Miller-Hance WC, **O’Brien TX**, Dyson, Chien KR. Chamber specification of atrial myosin light chain-2 expression precedes septation during murine cardiogenesis. J Bio Chem, 269:16961-70, 1994.
8. Thompson JT, Rackley MS, and **O’Brien TX**. Up-regulation of the cardiac homeobox gene Nkx2.5 (CSX) in feline right ventricular pressure overload. Am J Physiol 274: H1569-H1573, 1998.
9. **O’Brien TX**, Schuyler GT, Rackley, MS, Thompson JT. F1-ATP synthase -subunit and cytochrome c transcriptional regulation in right ventricular hemodynamic overload and hypertrophically stimulated cardiocytes. J Mol Cell Card. 31:167-178, 1999.
10. Gramling-Babb, P and **O’Brien, TX**: Recent advances in dobutamine stress echocardiography. Clin Cardiol 23: 560-570, 2000.
11. Brown AM and **O’Brien TX**. Upcoming therapies for congestive heart failure. Clinical Cornerstones, 3: 36-44, 2000.
12. Thompson JT and **O’Brien TX**. Cardiovascular Genetic Diseases. In: Taylor GJ, ed. Primary Care Management of Heart Disease, Mosby, p. 481-488, 2000.
13. Paul SC and **O’Brien TX**. Chest x-ray and vascular studies. In: Taylor, GJ, ed. Primary Care Management of Heart Disease. Mosby, pp. 77-84, 2000.
14. Mitchell, GF, Tardif, JC, Arnold, JMO, Marchiori, G, **O’Brien TX**, Dunlap, MA, Pfeffer, MA: Pulsatile Hemodynamics in Congestive Heart Failure. Hypertension, 38:1433-1439, 2001.
15. Muller JG, Thompson JT, Rackley MS, McQuinn TC, Menick DR, **O’Brien TX**. Co-regulation of Nkx2-5 and serum response factor induced activation of the cardiac sodium-calcium exchanger promoter. J Mol Cell Card, 34:807-821, 2002.
16. Harris BS, **O’Brien TX**, Gourdie RG. Coronary arteriogenesis and differentiation of periarteriolar Purkinje fibers in chick: Is there a link? Texas Heart Journal, 29:262-270, 2002.
17. Gourdie RG, Harris BS, Bond J, **O’Brien TX**, Mikawa T, Sedmera D, Thompson RP. His-Purkinje lineages and development. In: Development of the cardiac conduction system. John Wiley and Sons. Novartis Symposia Series 250. 122-134, 2003.
18. Gourdie RG, Harris BS, Bond J, Justus C, Hewett K, **O’Brien TX**, Thompson RP, Sedmera D. Development of the cardiac pacemaking and conduction system. Birth Defects Research, 69:46-57, 2003.
19. Teunissen BE, Jansen AT, van Amersfoorth SC, **O’Brien TX**, Jongsma HJ, Bierhuizen MF. Analysis of the rat connexin 43 promoter in neonatal cardiomyocytes. Gene, 322:123-36, 2003.
20. Jay PY, Harris BS, Maguire CT, Buerger A, Wakimoto H, Tanaka M, Kupershmidt S, Roden DM, Schultheiss TM, **O'Brien TX**, Gourdie RG, Berul CI, Izumo Nkx2-5 mutation causes anatomic hypoplasia of the cardiac conduction system. J Clin Invest. 113:1130-7, 2004.
21. Gourdie RG, Kubalak SW, **O’Brien TX**, Chien KR, Mikawa T. Development of Pacemaking and Cardiac

Conduction System Lineages. In: Molecular Basis of Cardiovascular Disease, 2nd Edition, (ed. KR Chien), W. B. Saunders, p225-237, 2004.

22. Jay PY, Harris BS, Buerger A, Rozhitskaya O, Maguire CT, Barbosky L, McCusty E, Berul CI, **O'Brien TX**, Gourdie RG, Izumo S. Function follows form: Cardiac conduction system defects in Nkx2.5 mutation. Anatomical Record, 280A:966-972,2004.
23. Harris BS, Jay PY, Rackley MS, Izumo S, **O'Brien TX**, Gourdie RG. Transcriptional regulation of cardiac conduction system. Anatomical Record, 280A:1036-1045,2004.
24. O'Brien, TX, Smith, DA. Congestive Heart Failure Overview. In: Emedicine Consumer Health. Emedicine, Inc., St. Petersburg, Fl, (www.emedicinehealth.com/Articles/10929-1.asp). January 7, 2005.
25. Harris BS, Gourdie RG, **O'Brien TX**. The atrioventricular conduction system and transcription factors Nkx2.5 and Msx2. Editorial, Journal of Cardiovascular Electrophysiology, 16:86-87, 2005.
26. Little WC, Zile M, Kitzman DW, Hundley WG, **O'Brien TX**, deGroof RC. The effects of Alagebrium Chloride ALT-711, a novel glucose cross-link breaker, in the treatment of elderly patients with diastolic heart failure. Journal of Cardiac Failure, 11:191-195, 2005.
27. Mitchell GF, Arnold MO, Dunlap ME, **O'Brien TX**, Marchiori G, Warner E, Granger CB, Desai S, Pfeffer MA. Pulsatile hemodynamic effects of candesartan in patients with chronic heart failure: The Charm Trial. European J. of Heart Failure, 8:191-7, 2005.
28. Harris BS, Spruill L, Edmonson AM, Rackley MS, Benson DW, ***O'Brien TX**, *Gourdie RG (*=co-senior authors). Differentiation of cardiac Purkinje fibers requires precise spatiotemporal regulation of Nkx2-5 expression. Developmental Dynamics. 235:38-49, 2006.
29. Udelson JE, McGrew FA, Flores E, Ibrahim H, Katz S, Koshkarian G, **O'Brien TX**, Kronenberg MW, Zimmer C, Orlandi C, Konstam MA. Multicenter, randomized, double-blind, placebo-controlled study on the effect of oral tolvaptan on left ventricular dilation and function in patients with heart failure and systolic dysfunction. Journal of the American College of Cardiology, 49:2151-2159, 2007.
30. Sidney DS, **O'Brien TX**. Pericarditis, constrictive. (www.emedicine.com) eMedicine Journal>Medicine>Cardiology, Vol. 9, July 5, 2008.
31. Bonnema DD, **O'Brien TX**, Pericarditis constrictive-effusive. (www.emedicine.com) eMedicine Journal>Medicine>Cardiology, Vol. 9, July 26, 2008.
32. **O'Brien TX** and Epps AR. Cardiovascular risk in women with high normal blood pressure. (editorial) Southern Med. J., In press, 2008.

C. Research Support

Ongoing Research

VA BLRD Merit Review Award (O'Brien - PI) 04/01/2006-03/31/2009

The Cardiac Conduction System as Regulated by NKX2.5

This grant investigates the role of Nkx2.5 upon regulation of the cardiac conduction system throughout early life to adult life and how human disease-associated Nkx2.5 mutations disrupt these inductive patterns.
Role: PI

Bristol Myers Squibb and Sanofi-Synthelabo (O'Brien - PI) 05/01/2002- Initiation

Irbesartan in Heart Failure with Preserved Systolic Function. I-PRESERVE Clinical Trial

This long-term study of an angiotensin receptor antagonist is in the data analysis stage.
Role: PI

Encysive Pharmaceuticals (O'Brien - PI) 05/01/2006-Initiation

Sitaxsentan Sodium to Improve Exercise Tolerance in Subjects with Diastolic Heart Failure

The goal of this study is to support that Sitaxsentan is a highly selective endothelin-1 antagonist.
Role: PI

Amgen (O'Brien - PI) 02/01/2008-Initiation

A Double-Blind, Randomized, Placebo-Controlled, Multicenter Study to Assess the Efficacy and Safety of Darbepoetin Alfa Treatment on Mortality and Morbidity in Heart Failure Subjects with Symptomatic Left Ventricular Systolic Dysfunction and Anemia. The RED-HF Trial

The goal of this study is the same as the project title.

Role: PI

Cardiokine Biopharma (O'Brien - PI) 05/01/2008-Initiation
Clinical Trial at the RHJ-VAMC.
Treatment of Hyponatremia Based on Lixivaptan in NYHA Class III/IV Cardiac Failure. The BALANCE Trial
The goal is to prove that Lixivaptan is a more selective vasopressin 2 receptor antagonist that may be more effective in severe systolic heart failure associated with hyponatremia.
Role: PI

NIH-NHLBI Contractor (O'Brien - PI) 06/01/2008-Initiation
New England Research Institute, Inc.
Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist. The TOPCAT Trial
The goal is to determine if aldosterone inhibition improves mortality in diastolic heart failure.
Role: PI

Pending
None

Completed Research Support
NIH/NHLBI (#P01 HL48788) 08/01/1993-07/30/2008
Load-Induced Cardiac Hypertrophic Growth in the Adult Mammal
Project 3, Cardiac Na-Ca Exchanger: Hypertrophic Regulation
Role: Co-Investigator
Core E, Morphology and Molecular Imaging Core (O'Brien - PI)
This grant focuses upon the causes and consequences of cardiac hypertrophic growth. Dr. O'Brien is Director of the Imaging Core and will assist Dr. Menick in Project 3 with experimental design and interpretation.

Amylin Pharmaceuticals (O'Brien - PI) 02/01/2005-02/01/2007
A Phase 2, Randomized Double-Blind, Parallel-Group, Placebo-Controlled, Multicenter Study to Examine the Effects of AC2592 Administered by Continuous Subcutaneous Infusion in Subjects with Advanced Chronic Congestive Heart Failure

Pfizer Pharmaceuticals (O'Brien - PI) 05/01/2004-05/01/2006
A Randomized, Double-Blind, Multi Center Study Evaluating the Effects of Eplerenone vs Placebo on Ventricular Remodeling in Patients with Left Ventricular Systolic Dysfunction (EF<35%) and Mild to Moderate Heart Failure

Otsuka America (O'Brien - PI) 11/11/2003-09/30/2006
Multicenter, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Long-Term Efficacy and Safety of Oral Tolvaptan Tablets in Subjects Hospitalized with Worsening Congestive Heart Failure. The EVEREST Trial

Fujisawara Healthcare, Inc. (O'Brien - PI) 01/01/2004-03/01/2006
Protocol 03-0-162, A Phase 2, Dose Escalation Evaluation of the Pharmacokinetic and Hemodynamic Effects of Carperitide in Subjects with Congestive Heart Failure