

BIOGRAPHICAL SKETCH

NAME FitzGerald, Garret A.		POSITION TITLE McNeil Professor in Translational Medicine and Therapeutics	
eRA COMMONS USER NAME 1GARRET1		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 (if applicable)	YEAR(s)	FIELD OF STUDY
University College, Dublin, Ireland	M.B., B.Ch.	1974	Medicine
School of Hygiene, University of London	M.Sc.	1979	Statistics
University College, Dublin, Ireland	M.D. (Thesis)	1980	Pharmacology

A. Personal Statement

I have been funded by the NIH since 1980 to elucidate the importance of prostaglandins and related bioactive lipids in cardiovascular function. We invested substantially in mass spectrometry to quantify biosynthesis of these evanescent compounds. Using this approach, we were the first to provide evidence for platelet activation during the ischemic episodes of unstable angina and, more surprisingly, platelet activation coincident with therapeutic thrombolysis. We showed proof of concept of antiplatelet therapy as an adjuvant for thrombolytic drugs, influencing directly the design of the randomized trial that established the additive benefit of aspirin with streptokinase, ISIS-2. We characterized the dose dependent suppression by aspirin of thromboxane and prostacyclin in humans; determined that low dose aspirin acted on platelets predominantly in the presystemic circulation; specified and formulated the dose and release rates of aspirin necessary to confine its action presystemically and showed that this formulation suppressed thromboxane, while sparing completely the vascular capacity to form prostacyclin. More recently, we showed that ibuprofen could interact pharmacodynamically to undermine the antiplatelet effects of low dose aspirin. Our work contributed substantially to the emerging utility of isoprostanes as indices of oxidant stress. We were the first to propose a cardiovascular hazard from non steroidal anti-inflammatory drugs (NSAIDs) consequent to suppression of COX-2 derived prostacyclin and proceeded to obtain data congruent with this mechanism using multiple novel mouse models. We were the first to identify a molecular clock in the cardiovascular system; to show that a clock could be phase shifted by ligation of a hormone receptor and to implicate directly the molecular elements of the clock in regulation of blood pressure and thrombogenesis and in glucose homeostasis.

Presently, work in our laboratory includes (i) elucidation of the role of prostaglandins D₂ and F_{2α} and mPGES-1 in cardiovascular biology and the development of drugs targeting these pathways; (ii) elucidation of the role of peripheral clocks in cardiometabolic function and (iii) examination of the interaction of alcohol with n-3 dietary fatty acids. A major effort is leadership of the Personalized Therapeutics of NSAID Consortium which is planning to integrate basic and clinical investigation in the development and evaluation of algorithms predictive of analgesic response and cardiovascular risk from this common class of drugs.

B. Positions and Honors**Positions and Employment**

1974-1977	Residency, St. Vincent's and Mater Hospitals, Dublin
1977-1979	Research Fellow, Clinical Pharmacology, Royal Postgraduate Medical School, London
1980-1987	Fellowship/Faculty Positions, Medicine & Pharmacology, Vanderbilt University School of Medicine
1987-1991	Director, Division of Clinical Pharmacology, Vanderbilt University School of Medicine
1991-1994	Professor and Chairman, Department of Medicine and Therapeutics, University College Dublin
1994-present	Professor, Medicine and Pharmacology, University of Pennsylvania, Philadelphia, Pennsylvania
1996-present	Chair, Department of Pharmacology, University of Pennsylvania
2004-present	Director, Institute for Translational Medicine and Therapeutics, University of Pennsylvania

Other Professional Activities

1981-present American Association for the Advancement of Science (1998 elected Fellow)

1982-present	Fellow of the Royal College of Physicians, Ireland
1984-1990	NIH Biochemistry II Study Section: Member (1986-90); Chairman (1989-90)
1986-present	ASCI (86), AAP (89), IOM (09), FRS (12).
1990-present	Editorial Boards: Art Throm (1990-97; 2002-04); J Biol Chem (1993-99); Circulation (1993-present); JPET (1993-2000); JCI (2002-present); Trends in CV Med (1992-present); Systems Biology and Medicine (2008-present); Science Trans. Med. (2011 – present)
1997-present	AHA Arteriosclerosis, Thrombosis and Vascular Biology Council: (past Chair) FDA Science Board; NIH CSR Council of Councils; IOM Drug Forum; LeDucq Foundation SAB; PCAST working group on drug development; DZHK EAB (chair); Calibr SAB.
1998-present	Barnhart, Berson, Bishop, Bradshaw, Budnitz, BPS, Epstein, DaPazzi, Fisher, Gilmartin, Goodman, Green, Gruber, Habermann, Halushka. Harvey, Kearney, Leahey, Pickering, Riker, Ross, Samson, von Euler and Wilkinson Lectures

Honors

1983-1985	Faculty Development Award, Pharmaceutical Manufacturers Association Foundation
1985-1990	Established Investigator, American Heart Association
1989-1991	William Stokes Professor of Experimental Therapeutics
1992	First International Prize for Aspirin Research (Bayer)
1994-2004	Robinette Foundation Professor of Cardiovascular Medicine
2000-2007	Elmer Bobst Professor of Pharmacology
2004	PhRMA Foundation Award for Excellence in Clinical Pharmacology
2004	D.Sc. (Hon.) University of Edinburgh, U.K.; D.Sc. (Hon.) University College Dublin, Ireland
2005	Coakley Medal (UCD); Robert Boyle Medal (RDS/Irish Times)
2006	William Harvey Medal (Harvey Inst); Cameron Prize (Edinburgh))
2007-present	McNeil Professor in Translational Medicine and Therapeutics
2007	M.D. (Hon.) Johann Wolfgang Goethe-University, Frankfurt, Germany
2009	American Heart Association Distinguished Scientist; J. Allyn Taylor Prize (W. Ontario).
2010	Phillips Award (American College of Physicians); Pharmacia ASPET Award
2011	Jakob Herz Prize (Erlangen); Outstanding Achievement Award, Eicosanoid Research Foundation; Oscar P. Hunter Award in Therapeutics (ASCPT)
2012	Lucian Award (McGill)
2013	D.Sc. (Hon) King's College, London, UK; Scheele Award (Swedish Acad. Pharmaceutical Science); Schottenstein Prize (OHSU); Lefoulon Delalande Grand Prix (Inst. de France)

C. Selected peer-reviewed publications (Google Scholar) *h index* 112; 57,661 citations (Pre- and post-doctoral trainees are underlined.)

1. FitzGerald GA, Oates JA, Hawiger J, Maas RL, Roberts LJ, Brash AR. (1983) Endogenous biosynthesis of prostacyclin and thromboxane and platelet function during chronic administration of aspirin in man. *J Clin Invest* 71: 676-688. [PMCID: PMC436917](#)
2. Pedersen AK, FitzGerald GA. (1984) Dose related kinetics of aspirin: Presystemic acetylation of platelet cyclooxygenase. *N Engl J Med* 311: 1206-1211. [Free Full Text](#)
3. Fitzgerald DJ, Roy L, Catella F, FitzGerald GA. (1986) Platelet activation in unstable coronary disease. *N Engl J Med* 315: 983-989. [Free Full Text](#)
4. McAdam BF, Catella-Lawson F, Mardini IA, Kapoor S, Lawson JA, FitzGerald GA. (1999) Systemic biosynthesis of prostacyclin by cyclooxygenase (COX)-2. *Proc Natl Acad Sci USA* 96: 272-277. [PMCID: PMC15129](#)
5. McNamara P, Seo S-B, Rudic RD, Sehgal A, Chakravarti D, FitzGerald GA. (2001) Regulation of CLOCK and MOP4 by nuclear hormone receptors in the vasculature: A humoral mechanism to reset a peripheral clock. *Cell* 105: 877-889. [Free Full Text](#)
6. Catella-Lawson F, Reilly MP, Kapoor SC, Cucchiara AJ, DeMarco S, Tournier B, Vyas SN, FitzGerald GA. (2001) Cyclooxygenase inhibitors and the antiplatelet effects of aspirin. *N Engl J Med* 345: 1809-1817. [Free Full Text](#)
7. Cheng Y, Austin SC, Rocca B, Koller BH, Coffman TM, Lawson JA, FitzGerald GA. (2002) Role of prostacyclin in the cardiovascular response to thromboxane A₂. *Science* 296: 539-541. [Free Full Text](#)
8. Egan KM, Lawson JA, Fries S, Koller B, Rader DJ, Smyth EM, FitzGerald GA. (2004) COX-2 Prostacyclin confers atheroprotection on female mice. *Science* 306: 1954-1957. [Free Full Text](#)

9. Wang D, Patel V, Gao E, Rong Z, Levin M, Yu Z, Ferrari V, Lu MM, Xu J, Zhang H, Hui Y, Lawson J, Yi Y, FitzGerald GA. (2009) Cardiomyocyte cyclooxygenase -2 influences cardiac rhythm and function. Proc Natl Acad Sci 106: 7548-7552. [PMCID: PMC2670242](#)
10. Song W., Stubbe J., Ibrahim S., Alamuddin N., Paschos G., Ricciotti E., Prempeh M., Lawson J.A., Wilensky R.L. and FitzGerald G.A. (2012) Niacin evokes COX-1 derived PGD2 in mice and humans. J. Clin. Invest. 122(4):1459-68. [PMCID: PMC3314457](#)
11. Yu Z., Critchon I., Tang S.Y., Hui Y., Pure E. and FitzGerald G.A. (2012) Disruption of the 5 – lipoxygenase pathway attenuates atherogenesis consequent to COX-2 deletion in mice. Proc. Natl. Acad. Sci. 109(17):6727-32. [PMCID: PMC3340044](#)
12. Yu Y., Ricciotti E., Scalia R., Grant G., Yu Z., Xiong Y., Landesberg G., Wu W., Funk C.D., FitzGerald G.A. (2012) Vascular COX-2 modulates blood pressure and thrombogenesis. Sci. Trans. Med. 4(132):132ra54. [PMCID-Journal in Process](#) [Free Full Text](#)
13. Paschos G., Ibrahim S., Song W., Kunieda T., Grant G., Reyes T.M., Bradfield C., Vaughan C.H., Eiden M., Masoodi M., Griffin J.L., Wang F., Lawson J.A. and FitzGerald G.A. (2012) Obesity in mice with adipocyte-specific deletion of clock component Bmal1 Nat. Med. 18(12):1768-77. [PMCID in Process, NIHMSID # 504877](#)
14. Grosser T., Fries S., Lawson J.A., Kapoor S.C., Grant, G.R. and FitzGerald G.A. (2012) Resistance and pseudo-resistance; an unintended consequence of enteric coated aspirin. Circulation 127:377-385 [PMCID: PMC3552520](#) [Available on 2014/1/22]
15. Musiek E.S., Lim, M.M., Yang G., Bauer A.Q., Qil L., Roh J.H., Ortiz-Gonzalez X., Dearborn J.T., Culver J.P., Herzog E.D., Hogenesch J.B., Wozniak D.F., Dikranian K., Giasson B.I., Weaver D.R., Holtzman D.I. and FitzGerald G.A. (2013) Circadian clock proteins regulate neuronal redox homeostasis and neurodegeneration. J. Clin. Invest. (in press) .

C. Research Support

Ongoing Research Support

UL1 TR000003 FitzGerald (PI)

09/30/06 – 06/30/16

NIH/NCRR

Institutional Clinical and Translational Science Award (CTSA)

The major goal is to develop interdisciplinary structures designed to foster and facilitate research and education in the emerging discipline of translational medicine.

Role: PI

1U54HL117798 FitzGerald (PI)

08/01/12 - 05/31/17

NIH/NHLBI

Personalization of Therapeutic Efficacy and Risk

This proposal structure is perhaps the most comprehensive approach ever proposed to the progressive personalization of a class of drugs. This approach is designed to salvage the value and mitigate the risk of NSAIDs. If successful, it will delineate a strategy that can then be applied to many other drugs.

Role: PI

P01 HL062250 FitzGerald (PI)

09/30/09 – 06/30/14

NIH/NHLBI

Signal Transduction in Atherosclerosis

The major goal is the elucidation of signaling mechanisms in diverse cells which contribute to atherogenesis.

Role: PI

R01 HL097800 Hogenesch/FitzGerald (Co-PIs)

09/01/09 - 08/31/13

NIH/NHLBI

Multiscale Analysis of Inter-clock Communication

To determine whether molecular clocks in the periphery communicate with each other and the master clock

Role: Co-PI

R13 RR026129 FitzGerald (PI) 04/01/09 - 03/31/14

NIH/NCRR

ITMAT 2009 - Global Approaches to Translational Research

To seek partial support for an international meeting on translational research.

Role: PI

Completed Research Support (Last 3 years)

P50 HL054500 Bennett (PI) 02/01/06 – 1/31/11

NIH/NHLBI

SCCOR in Mechanisms of Normal and Abnormal Platelet Homeostasis

Mechanism Based Resistance to Aspirin (FitzGerald, Project Director)

The major goal of this project is to investigate the phenomenon of aspirin resistance.

Role: Project Director

P50 HL083799 FitzGerald (PI) 04/01/06 – 03/31/11

NIH/NHLBI

SCCOR in Lipids as Modulators of the Response to Vascular Injury

The major goal of this project is to characterize the role of lipids in the response to vascular injury.

Role: PI

UL1 RR024134 FitzGerald (PI) 09/17/09 - 09/26/11

ARRA supplement for workforce development

NIH/NCRR

Institutional Clinical and Translational Science Award

This grant is to expand the scope of training in epidemiology to encompass clinical trial expertise

Role: PI

UL1 RR024134 FitzGerald (PI) 09/14/09 – 09/13/11

ARRA Supplement for translational research

NIH/NCRR

Institutional Clinical and Translational Science Award

This grant is designed to explore the factors that contribute to variance in the analgesic efficacy of NSAIDs.

Role: PI

R24 GM088004-01 FitzGerald (PI) 04/01/10 - 01/31/11

NIH/NIGMS

Personalization of Therapeutic Efficacy and Risk

The major goal is to assemble a multidisciplinary consortium to address personalization of medicine.

Role: PI

BSF FitzGerald/Danenberg (Co-PIs) 10/01/08 - 09/30/12

United States- Israel Binational Science Fdn

C-reactive protein (CRP) and cyclooxygenase (COX) mediated pathways in vascular pathophysiology

The major goal is to determine if CRP mediates effects via eicosanoids

Role: Co-PI