BIOGRAPHICAL SKETCH

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NAME: Leon G. Fine

eRA COMMONS USER NAME (credential, e.g., agency login): Leon

POSITION TITLE: Chair, Department of Biomedical Sciences
Director, Graduate Research Education
Vice Dean for Research & Graduate Research Education

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Cape Town, Cape Town, South Africa	M.B., Ch.B.	1966	
Tel Hashomer Hospital and Tel Aviv University Medical School, Israel	Internship and Residency in Internal Medicine	1967-70	Internal Medicine
Albert Einstein College of Medicine, Bronx, New York	Fellowship in Nephrology	1972-74	Nephrology
American Board of Internal Medicine	Diplomate	1974	Internal Medicine
American Board of Nephrology	Diplomate	1976	Nephrology
Professional Colleges:			
UK	FRCP, FRCP(Glasg	1986 1993	
	Fellow of the Academy of Med.Sci.	1999	
USA	FACP	1978	

A. PERSONAL STATEMENT

I serve as Chair of the Department of Biomedical Sciences and Director of Graduate Research Education at Cedars-Sinai Medical Center. I am a former Dean of the University College of London, and immediate past Harveian Librarian at the Royal College of Physicians. I was Chief of the Division of Nephrology at UCLA from 1978 to 1991. My research has been focused on cellular mechanisms of renal hypertrophy, renal fibrosis and scarring, hypoxia-mediated mechanisms of kidney disease progression and a vasculogenic hypothesis for halting disease linked to regeneration of solid organs, As chief of Nephrology I oversaw a research enterprise, which included faculty at all levels as well as a series of NIH-funded physician scientist awards. I was recipient of a number of RO1 grants and was holder of a T32 training program grant, which included four UCLA campuses. I joined the staff of Cedars-Sinai in 2007, having completed my term as Chairman of the Department of Medicine and Dean of the Faculty of Clinical Sciences at University College London (UK) from 1991 to 2002.. As Chief of Medicine and Dean, I was responsible for oversight of career development of junior

faculty across multiple disciplines, wrote formal review processes for evaluating progress, and instituted plans for optimizing success in peer-reviewed funding, research networking, and scientific visibility of clinical research scientists. I also presided over a PhD program in the Department of Medicine and a number of Masters degree programs in the School of Medicine. As the Chair of the Department of Biomedical Sciences at Cedars-Sinai, my role is to advance the academic research enterprise, support development of translational and clinical investigators, and provide researchers in the basic biomedical sciences with physician partnerships to accelerate the translation of basic science discoveries towards clinical evaluation and, eventually, clinical practice. Towards this end, I have already achieved several key objectives.
Specifically, I have: 1) established the first graduate program at Cedars-Sinai, the PhD Program in Biomedical Sciences and Translational Medicine (2) developed and deployed a new Clinical Scholars program, which aims to foster development of promising young physician-scientists into independently-funded academic clinical and translational research careers through a program that includes a 1 year didactic curriculum, mentoring, and institutional financial support for research and 3) established a post-doctoral scientist program.

Clinical and Scientific Research institute (CTSI): I have served as a representative of the Cedars-Sinai campus on the CTSI for 5 years and anticipate that I will continue to serve in this capacity. I have served as curriculum chair of the TPTS program ((previously K32) and have contributed to the educational and training mission of the CTSI, in particular, the mentoring of young investigators towards KL2 awards. The Clinical scholars program at Cedars-Sinai additionally provides competitive funding through CSMC-CTSI clinical scholars grants, which provide funding for starting investigators to initiate studies and to gather preliminary data for subsequent K award applications. The integration of multiple campuses under the sponsorship of the CTSI in the educational field, has broadened considerably the opportunities for trainees in obtaining mentoring and guidance of the highest caliber in multiple fields of interest and to engage in innovative team science in the most exciting way.

B. POSITIONS AND HONORS

B. Positions and Honors

1974-75 **Instructor in Medicine,** Albert Einstein College of Medicine, Bronx, New York, USA
1975-76 **Assistant Professor of Medicine,** Albert Einstein College of Medicine, Bronx, New York, USA
1976-78 **Assistant Professor of Medicine,** University of Miami School of Medicine, Miami, Florida, USA
1978-82 **Associate Professor of Medicine,** University of California, Los Angeles, Los Angeles, CA, USA
1982-91 **Professor of Medicine,** University of California, Los Angeles, Los Angeles, California, USA
1991-06 **Professor of Medicine,** University College London, London, UK
2007- **Emeritus Professor,** University College London, London, UK
2007- **Professor of Medicine**, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA
2008- **Professor of Biomedical Sciences**, Cedars-Sinai Medical Center, Los Angeles, USA

PROFESSIONAL ACTIVITIES:
1978-91**Chief, Division of Nephrology,** Center for the Health Sciences, University of California, Los Angeles, Los Angeles, California, USA
1991-93 **Head, Department of Medicine and Chairman of the Board of Medicine**, University College London Medical School, London, UK (Formerly University College and Middlesex School of Medicine)
1994-98 **Head, Joint Department of Medicine and Chairman, Division of Medicine,** University College London Medical School and Royal Free Hospital School of Medicine, London, UK
1998-2002 **Chairman, Division of Medicine / Head, Department of Medicine,** Royal Free and University College Medical School, University College London, London, UK
2002-2006 **Dean, Faculty of Clinical Sciences**, Royal Free and University College Medical School, University College London
2007- **Chair, Department of Biomedical Sciences and Director of Graduate Research Education**
Cedars-Sinai Medical Center and David Geffen School of Medicine at UCLA, Los Angeles, CA
2011- **Vice Dean for Research and Graduate Research Education**
Cedars-Sinai Medical Center and David Geffen School of Medicine at UCLA, Los Angeles, CA

HONORS AND AWARDS:
1961 University of Cape Town: ***Class Medal in Chemistry***
1962 University of Cape Town: ***Class Medal in Physiology***
1964 University of Cape Town: ***Class Medal in Medicine***
1966 University of Cape Town: ***Graduate with Honors, Distinctions in 1st and 2nd Professional Examination University Gold Medal, Most Distinguished Graduate in Medicine***
1967 University of Cape Town: ***Myer Levinson and Crasnow Postgraduate Scholarships***
1969 University of Cape Town: ***Forman Fellowship***
1972-74 New York State Kidney Disease Institute: ***Fellowship***
1977-82 National Institutes of Health: ***Research Career Development Award***
1982 American Society for Clinical Inevstigation: Elected member
1986 University of Kansas: ***Edward J. Dillon Memorial Lecturer***
1987 Annual Meeting of American Urological Association: ***National Kidney Foundation Lecturer***
1988 University of Iowa: ***Lawrence H. Norby Visiting Professor of Nephrology***
1988 Association of American Physicians: Elected member
1988 National Institutes of Health: ***Senior Fellowship of the Fogarty International Center***
1990 Commemoration: 150 Years of Beneficiencia Portuguesa do Rio de Janeiro: ***Guest Lecturer***
1991 Royal College of Physicians and Surgeons, Glasgow: ***Burns Lecturer***
1992University of Toronto: ***Lance Lipton Visiting Professor***
1993 Association of Physicians of Great Britain and Ireland; President
1994 University of Miami: ***John R. Richardson Visiting Professor***
1995 Hadassah Hospital-Hebrew University Medical School: ***British Council Visiting Professor***
1995 Oporto University Faculty of Medicine ***Honorary Docent***
1996 Australian & New Zealand Society of Nephrology: ***Honorary Member***
1997 Swedish Society of Medicine: ***Medalist***
1999 Academy of Medical Sciences, UK: ***Founder Fellow***
2002 King's College London, ***Novartis Visiting Professor***

C. CONTRIBUTIONS TO SCIENCE

1. Nephron Adaptation and Chronic Renal Disease.

My contribution to the field of nephron adaptation in the chronically diseased kidney, was to establish an in vitro isolated perfused renal tubule system for separating those adaptations which are dependent upon extrinsic humoral factors, generated in the uremic environment (the dogma at the time), form those which are intrinsic to the surviving nephron population. These studies established the central role of intisic adaptations in tubular function including hypertrophy, and adaptations in sodium, phosphate, potassium adaptations in different nephron segments. They also demonstrated changes in end-organ responsiveness to hormones, such as vasopressin.

a. Fine LG, Bourgoignie JJ, Hwang KH & Bricker NS. On the influence of the natriuretic factor from patients with chronic uremia on the bioelectric properties and sodium transport of the isolated mammalian collecting tubule. **J Clin Invest** 58:590-597, 1976
b. Fine LG, Yanagawa N, Schultze RG, Tuck M & Trizna W. Functional profile of the isolated uremic nephron. Potassium adaptation in the rabbit cortical collecting tubule. J Clin Invest 64:1033-1043, 1979
c. Fine LG, Trizna W, Bourgoignie JJ & Bricker NS. Functional profile of the isolated uremic nephron. Role of compensatory hypertrophy in the control of fluid reabsorption by the proximal straight tubule. **J Clin Invest** 61:1508-1518, 1978
d. Fine LG, Schlondorff D, Trizna W, Gilbert RM & Bricker NS. Functional profile of the isolated uremic nephron. Impaired water permeability and adenylate cyclase responsiveness of the cortical collecting tubule to vasopressin. **J Clin Invest** 61:1519-1527, 1978

2. The Biology of Renal Hypertrophy.

My contribution to the understanding of the biology of tubular hypertrophy, which occurs as an adaptation of surviving nephrons in the chronically diseased kidney, was to establish an in vitro model of tubular cell hypertrophy. Using this model we demonstrated that increased Na-H exchange was an early event in cell growth and that basolateral Na-K ATPase activity and organelle growth is evident in hypertrophied cells. A cell-growth inhibitor. (later called TGF beta), converted a hyperplastic growth response to a hypertrophic response.

The pattern of gene expression in early hypertrophy was fundamentally different from that in cell proliferation indicating that hypertphy is a unique form of growth and not an interrrupted phase of hyperplasia.

a. Fine LG, Badie-Dezfooly B, Lowe AG, Hamzeh A, Wells J & Salehmoghaddam S. Stimulation of Na-H antiport is an early event in hypertrophy of renal proximal tubular cells. **Proc Nat Acad Sci** (USA) 82:1736-1740, 1985
b. Fine LG, Holley RW, Nasri H & Badie-Dezfooly B. BSC-1 growth inhibitor transforms a mitogenic stimulus into a hypertrophic stimulus for renal proximal tubular cells: Relationship to Na^+/H^+ antiport activity. **Proc Nat Acad Sci** USA 82:6163-6166, 1985
c. Salehmoghaddam S, Bradley T, Mikhail N, Badie-Dezfooly B, Nord EP, Trizna W, Kheyfets R & Fine LG. Hypertrophy of basolateral Na-K-pump activity in the proximal tubule of the remnant kidney. **Lab Invest** 53:443-452, 1985
d. Kujubu DA, Norman JT, Herschman H & Fine LG. Primary response gene expression in renal hypertrophy and hyperplasia: evidence for different growth initiation processes. **Am J Physiol** 260:F823-F827, 1991

3. Gene Transfer in Mammalian Kidney.

My contribution to the field modification of renal function via gene transfer, was to demonstrate the feasibilty of direct gene transfer into tublular cells by direct injection. This was followed by selective modification of glomerular function by using the mesangial cell as a vector for transgene delivery, trapping these cell in the glomerular caplllary tuft. Using this approach we demonstrated expression that increased levels of TGF beta could suppress a mitogenic response in the glomerulus, a finding with obvious relevance to intervention on glomerulonephritis.

a. Woolf AS, Bosch R & Fine LG. Gene transfer into the Mammalian Kidney: First steps to Gene Therapy. **Kidney Int** 43:S116-S119, 1993
b. Kitamura M, Taylor S, Unwin R, Burton S, Shimizu F & Fine LG. Gene Transfer into the Rat Renal Glomerulus via a Mesangial Cell Vector: Site-specific Delivery, In Situ Amplification and Sustained Expression of an Exogenous Gene In Vivo. **J Clin Invest** 94:497-505, 1994
c. Kitamura M, Burton S, English J, Kawachi H & Fine LG. Transfer of a mutated gene encoding active transforming growth factor B_1 suppresses mitogenesis and IL-1 response in the glomerulus. **Kidney Int** 48:1747-1757, 1995
d. Kitamura M, Suto T, Yokoo T, Shimuzu F & Fine LG. Transforming growth factor -B_1 is the predominant paracrine inhibitor of macrophage cytokine synthesis produced by glomerular mesangial cells. **J Immunol** 156:2964-2971, 1996

4. Chronic Hypoxia Renal Disease Progression

My contribution to the understanding of why renal disease, once initiated, almost invariably go on to end-stage disease. We established the "chronic hypoxia hypothesis" which stated that impaired microvacular perfuisn leads to hypoxia which, in turn, is a fibrogenic stimulus. Scar formation ensues which further obliterates interstitial capillaries, which leads to ongoing hypoxia and scarring. As a corollary of this, we have recently proposed that regeneration of micro-vessels could be a unifying approach to preventing progressive loss of function and restoring function in solid organs.

a. Fine LG, Orphanides C & Norman J. Progressive Renal Disease: The chronic hypoxia hypothesis. **Kidney Int** 53(65):S74-S78, 1998
b. Norman JT & Fine LG. Intrarenal oxygenation in chronic renal failure. **Clin Exp Pharmacol Physiol**. 33:989-996, 2006
c. Fine LG and Norman JT. Chronic hypoxia as a mechanism of progression of chronic kidney diseases: from hypothesis to novel therapeutics. **Kidney International** 74: 867-872, 2008
d. Long DA, Norman JT and Fine LG. Restoring the renal microvasculature to treat chronic kidney. **Nat. Rev Nephrol** 8:242-250, 2012

Complete List of Published Work:

http://www.ncbi.nlm.nih.gov/sites/myncbi/1ZG4s6J7GJf5j/bibliograpahy/48032165/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

Completed

W81XWH-09-1-0644 08/01/09-07/31/11
USAMRMC.

Title: *Use of Molecular and In Vivo Imaging Modalities in Immunobiologic and Regenerative Preclinical Investigations*

The goal of this project is to utilize cutting-edge imaging modalities in three distinct research projects. Project 1 will investigate ways to disarm pathogens without threatening their survival per se. Project 2 will use the human sodium iodide symporter as a reporter gene for tracking cardiac stem cells and quantifying engraftment using PET or SPECT in small and large animal models. Project 3 will determine the safety and efficiency of mesenchymal stem cell-based vertebral fracture repair using molecular and small animal imaging technologies.

Role; PI