BIOGRAPHICAL SKETCH

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NAME: David J Salant

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POSITION TITLE: Professor of Medicine

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 the Witwatersrand School of Medicine.	MBBCh	11/1969	Medicine
Johannesburg Hospitals, South Africa.	FCP(SA)	12/1973	Internal Medicine
Boston University Medical Center, Boston, MA.	Postdoc	12/1978	Renal Immunology

A. Personal Statement

I have endeavored, with the help of NIH support for nearly four decades, to understand the pathogenesis of kidney diseases by careful and in-depth analysis of experimental models of human diseases. This led to several significant observations, some of which were paradigm shifting, including the documentation that immune deposits in experimental membranous nephropathy form in situ and are not trapped as circulating immune complexes and cause podocyte injury through complement activation and formation of the membrane attack complex. Skills developed through the identification of podocyte antigens by advanced imaging techniques and mass spectrometry in experimental models ultimately led to the identification of the main target antigen (PLA2R) and a minor target antigen (THSD7A) in human membranous nephropathy both of which were shown to be expressed on human podocytes by confocal microscopy. Since my appointment in 2018 as Vice-Chair for Research in the Department of Medicine, I have continued to work closely with my colleagues Drs. Laurence Beck and Weining Lu that have active research programs in experimental and human diseases affecting the glomerular filtration barrier. I am also co-investigator on a NIDDK-funded project to determine if zinc-finger transcription factor Krüppel-Like Factor 4 (KLF4) mediated inhibition of STAT3 signaling is required for the maintenance of podocyte integrity and prevention of aberrant proliferation of parietal epithelial cells (PI Sandeep Mallipattu, Stony Brook Medicine).

I have trained 39 postdoctoral and graduate students in the last 30 years. Twenty-five of them currently hold full-time academic positions. I served as program director of the institutional training grant Research Training in Nephrology (T32 DK07053-45) from 1987-2018. Trainees have served as first author on 47 or as co-author on most of the rest of my peer-reviewed publications. I have been thesis advisor to seven doctoral and masters candidates and served on several thesis committees at Boston University, Harvard Medical School, and elsewhere. I have also served on several national training organizations, including the Executive Committee of Nephrology Training Program Directors and Education Committee of the American Society of Nephrology, and I chaired the Nephrology Board of the American Board of internal Medicine. I am also the chair of our deparmental appointments and promotions committee. I devoted 10 percent of my time to administration of our institutional training grant but substantially more time training and mentoring research fellows, junior faculty and students. I remain as enthusiastic today about working with this extraordinarily committed and

accomplished group of trainees as I was in 1987 when I took over the directorship of our nephrology training program.

Citations:

Benzing T, **Salant D**. Insights into Glomerular Filtration and Albuminuria. N Engl J Med. 2021;384(15):1437-1446. DOI: 10.1056/NEJMra1808786

B. Positions and Honors

Positions and Employment

1970-1973	Intern and Resident (Internal Medicine). Johannesburg Hospital.
1974-1977	Consultant Physician (Int. Med.)/Attending Nephrologist. Johannesburg Hospital.
1975-1976	Lecturer (part-time). Dept. Physiology, Univ. Witwatersrand Medical School.
1977-1978	Research Fellow, Nephrology, Boston University School of Medicine, Boston.
1979-1983	Assistant Professor of Medicine, Boston University School of Medicine.
1983-1988	Associate Professor of Medicine Boston University School of Medicine.
1979-present	Attending Physician, Boston Medical Center (formerly Boston City and University Hospitals).
1987-2019	Chief, Renal Section, Boston University Medical Campus.
1988-present	Professor of Medicine, Boston University School of Medicine.
1990-2018	Director, Research Training Grant in Renal Disease.
1992-present	Faculty, Boston University Graduate School.
1992-present	Professor of Pathology and Laboratory Medicine, Boston Univ. School of Medicine.
2018-present	Vice Chair for Research, Department of Medicine, Boston University School of Medicine

Honors, Awards and other Professional Activities

Clinical Investigator Award NIH (AM 00742)	1980-1983
Established Investigator Award, American Heart Association	1985-1990
American Society for Clinical Investigation	1987- present (emeritus)
Pathology A Study Section NIH	1989-1993
ABIM Subspecialty Board on Nephrology (Chairman 1998-2002)	1992-2002
NIDDK Special Emphasis Panels	1994-present
Visiting Professor of Molecular Physiology, Stanford University	1995
American Association of Physicians	1995-present
Editorial Board, Kidney International	1990-2012
Advisory Board, Journal of Renal Nutrition	1995-2000
Editorial Board, American Journal of Physiology (Renal)	1996-present
Editorial Board, Journal of the American Society of Nephrology	1997-2001, 2007-present
Associate editor, Journal of the American Society of Nephrology	2013-2017
Guest editor, Journal of the American Society of Nephrology	2018-present
Meira and Shaul Massry Visiting Professorship, UCLA, USC and UCD	2010
Jean Hamburger Award, International Society of Nephrology	2013
John P. Peters Award, American Society of Nephrology	2013
Fellow of the American Association for the Advancement of Science	2015
Donald W. Seldin Distinguished Award, National Kidney Foundation	2015
Innovator of the Year, Boston University	2015
Marilyn Farquhar Award, 11th International Podocyte Conference	2016
Edward N. Gibbs Lecture and Award, New York Academy of Sciences	2018

C. Contribution to Science

1. **Studies of membranous nephropathy**: The first was an unequivocal demonstration using isolated rat glomeruli that the target antigen in experimental membranous nephropathy is an intrinsic component of the glomerular capillary wall; later discovered by others to be megalin. The insights and technical expertise gained from experimental models allowed us to make the translational step to identify PLA2R as the target antigen in human membranous nephropathy and establish that autoantibodies to the antigen are commonly

found in 70-80% of patients with active disease. This latter discovery has been awarded international patents and led to licensing and approval of two commercial immunodiagnostic assays for MN by the United States FDA in 2014.

a. Couser WG, Steinmuller DR, Stilmant MM, **Salant DJ** and Lowenstein LM: Experimental glomerulonephritis in the isolated perfused rat kidney. J Clin Invest 62:1275-1287, 1978. PMCID: PMC371893
b. **Salant DJ**, Darby C and Couser WG: Experimental membranous glomerulonephritis in rats. Quantitative studies of glomerular immune deposit formation in isolated glomeruli and whole animals. J Clin Invest 66:71-81, 1980. PMCID: PMC371507
c. Beck, LH, Jr., Bonegio, RG, Lambeau, G, Beck, DM, Powell, DW, Cummins, TD, Klein, JB, **Salant, DJ**: M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy. N Engl J Med, 361**:** 11-21, 2009. PMCID: PMC2762083
d. Tomas NM*, Beck LH*, Meyer-Schwesinger C, Seitz-Polski B, Ma H, Zahner G, Dolla G, Hoxha E, Helmchen U, Dabert-Gay AS, Debayle D, Merchant M, Klein J, **Salant DJ**, Stahl RA, Lambeau G. Thrombospondin type-1 domain-containing 7A in idiopathic membranous nephropathy. N Engl J Med 371(24):2277-2287, 2014. PMC4278759

2. **Studies of the role of complement in membranous nephropathy**: After defining the mechanisms of immune deposition in the passive Heymann nephritis model of MN, we subsequently identified a new role for complement in glomerular injury in the same model, followed by the first demonstration that the complement membrane attack complex is the agent of injury and that podocytes are the target. This ultimately led to a collaborative study demonstrating that the IgG4 anti-PLA2R antibodies derived from patients with MN are capable of activating the lectin-binding pathway of complement and injuring podocytes in culture.
   a. **Salant DJ**, Belok S, Madaio MP and Couser WG: A new role for complement in experimental membranous nephropathy in rats. J Clin Invest 66:1339-1350, 1980. PMCID: PMC371620
   b. Groggel GC, Adler S, Rennke HG, Couser WG and Salant DJ: Role of the terminal complement pathway in experimental membranous nephropathy in the rabbit. J Clin Invest 72:1948-1957, 1983. PMID: 6227634 PMCID: PMC437035
   c. Cybulsky AV, Rennke HG, Feintzeig ID and **Salant DJ**: Complement-induced glomerular epithelial cell injury: The role of the membrane attack complex in rat membranous nephropathy. J Clin Invest 77:1096-1107, 1986. PMID: 3514672. PMCID: PMC424443
   d. Haddad G, Lorenzen JM, Ma H, de Haan N, Seeger H, Zaghrini C, Seeger H, Zaghrini C, Brandt S, Kölling, M, Wegmann U, Kiss B, Pál G, Gál P, Wuthrich RP, Wuhrer M, Beck LH, **Salant DJ**, Lambeau G, Kistler AD. Altered glycosylation of IgG4 promotes lectin complement pathway activation in anti-PLA2R1 associated membranous nephropathy. J Clin Invest Dec 2020. doi.org/10.1172/JCI140453. PMID: 33351779. PMC7919733

3. **Studies of podocyte injury**: Based on the discoveries in experimental models of proteinuria, I was among the first to suggest that podocyte injury is the primary cause of most if not all proteinuric kidney diseases. This has been borne out by a substantial literature of discovery of hereditary and acquired forms of glomerular disease characterized by proteinuria and podocyte injury. We performed a series of in vivo and in vitro studies that identified several cellular pathways activated in podocytes by complement-induced sublethal injury, including phospholipases and calcium flux, collagen gene activation and alterations in focal adhesion complexes and the podocyte slit diaphragm induced by nephrin-actin dissociation. Use of advanced imaging techniques and proteomic technology led to the identification of nephrin as the slit-diaphragm protein targeted by nephritogenic monoclonal antibody, mAb516 and several collaborative studies have examined cellular signaling pathways for the maintenance of podocyte integrity.
   a. Topham PS, Haydar SA, Kuphal R, Lightfoot JD, **Salant DJ**: Complement mediated injury reversibly disrupts glomerular epithelial cell actin microfilaments and focal adhesions. Kidney Int 55:1763-1775, 1999. PMID: 10231439
   b. Topham PS, Kawachi H, Haydar SA, Chugh S, Addona TA, Charron KB, Holzman LB, Shia MA, Shimizu F, **Salant DJ**: Nephritogenic monoclonal antibody 5-1-6 is directed at the extracellular domain of rat nephrin. J Clin Invest 104:1559-1566, 1999. PMID: 10587519. PMCID: PMC409863

c. Yuan H, Takeuchi E, Taylor GA, McLaughlin M, Brown D, **Salant DJ**. Nephrin dissociates from actin and its expression is reduced in early experimental membranous nephropathy. J Am Soc Nephrol 13:945-956, 2002. PMID: 11912254
d. Fan X, Li Q, Pisarek-Horowitz A, Rasouly HM, Wang X, Bonegio RG, Wang H, McLaughlin M, Mangos S, Kalluri R, Holzman LB, Drummond IA, Brown D, **Salant DJ**, Lu W. Inhibitory Effects of Robo2 on Nephrin: A Crosstalk between Positive and Negative Signals Regulating Podocyte Structure. Cell Rep 2:52-61, 2012. PMID: 22840396. PMCID: PMC3627357.

4. **Studies of experimental glomerulonephritis**: I have also collaborated extensively with an international group of investigators to test a wide variety of inflammatory, profibrotic, cytopathic and cytoprotective pathways in our models of glomerulonephritis. Examples include the role of leukocytes and chemokines in glomerular injury and inflammation, post-inflammatory fibrogenesis, and DNA methylation in kidney fibrosis.
    a. Bechtel W, McGoohan S, Zeisberg EM, Muller GA, Kalbacher H, **Salant DJ**, Muller CA, Kalluri R, Zeisberg M: Methylation determines fibroblast activation and fibrogenesis in the kidney. Nat Med, 16**:** 544-550, 2010. PMCID: PMC3106179.
    b. Korte EA, Caster DJ, Barati MT, Tan M, Zheng S, Berthier CC, Brosius FC, Vieyra MB, Sheehan RM, Kosiewicz M, Wysoczynski M, Gaffney PM, **Salant DJ**, McLeish KR, Powell DW. ABIN1 Determines Severity of Glomerulonephritis via Activation of Intrinsic Glomerular Inflammation. Am J Pathol. 2017 Dec; 187(12):2799-2810. PMC5718094
    c. Dai Y, Chen A, Liu R, Gu L, Sharma S, Cai W, Salem F, **Salant DJ**, Pippin JW, Shankland SJ, Moeller MJ, Ghyselinck NB, Ding X, Chuang PY, Lee K, He JC. Retinoic acid improves nephrotoxic serum-induced glomerulonephritis through activation of podocyte retinoic acid receptor a. Kidney Int. 2017 Dec; 92(6):1444-1457. PMC5696080
    d. Caster DJ, Korte EA, Tan M, Barati MT, Tandon S, Creed TM, **Salant DJ**, Hata JL, Epstein PN, Huang H, Powell DW, McLeish KR. Neutrophil exocytosis induces podocyte cytoskeletal reorganization and proteinuria in experimental glomerulonephritis. Am J Physiol Renal Physiol. 2018 Sep 01; 315(3):F595-F606. PMC6172569

5. **Studies of experimental crescentic glomerulonephritis**:The model of accelerated nephrotoxic serum nephritis in mice was developed in my lab with funding by the NIH and has been employed in collaboration with several groups to investigate mechanisms and consequences of crescentic glomerulonephritis.
    a. Lloyd CM, Minto AW, Dorf M, Proudfoot M, **Salant DJ**, Gutierrez-Ramos J-C: RANTES and MCP-1 play an important role in the inflammatory phase of crescentic glomerulonephritis, but only MCP-1 is involved in crescent formation and interstitial fibrosis. J Exp Med 185:1371-1380, 1997.
    b. Bollée G, Flamant M, Schordan S, Fligny C, Rumpel E, Milon M, Schordan E, Sabaa N, Vandermeersch S, Galaup A, Rodenas A, Casal I, Sunnarborg SW, **Salant DJ**, Kopp JB, Threadgill DW, Quaggin SE, Dussaule J-C, Germain S, Mesnard L, Endlich K, Boucheix C, Belenfant X, Callard P, Endlich N, Tharaux PL. Epidermal growth factor receptor promotes glomerular injury and renal failure in rapidly progressive crescentic glomerulonephritis. Nat Med, 17:1242-1250, 2011 (Epub 09/29/2011). PMC3198052
    c. Estrada CC, Paladugu P, Guo Y, Pace J, Revelo MP, **Salant DJ**, Shankland SJ, D'Agati VD, Mehrotra A, Cardona S, Bialkowska AB, Yang VW, He JC, Mallipattu SK. Kruppel-like factor 4 is a negative regulator of STAT3-induced glomerular epithelial cell proliferation. JCI Insight. 2018;3(12). PMC6124441
    d. Kasinath V, Yilmam OA, Uehara M, Jiang L, Ordikhani F, Li X, Sala**nt DJ**, Abdi R. Activation of fibroblastic reticular cells in kidney lymph node during crescentic glomerulonephritis. Kidney Int. 2019 Feb; 95(2):310-320. PMC6342621

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