

BIOGRAPHICAL SKETCH

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NAME M. ERIC GERSHWIN		POSITION TITLE PROFESSOR OF MEDICINE	
eRA COMMONS USER NAME MEGERSHWIN			
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>	YEAR(s)	FIELD OF STUDY
Syracuse University, Syracuse, New York	A.B. (summa cum laude)	1966	Zoology
Stanford University, Palo Alto, CA	M.D.	1971	Medicine

A. Positions and Honors.

1963 Biochemistry Research in NSF Program, University of California, Davis.
1963-1965 Genetics Research, Syracuse University, under the auspices of NSF.
1965 (sum) Institute of Arctic Biology, University of Alaska.
1966-1971 Clinical Pharmacology Research, Stanford Medical School.
1971-1973 Internship and Residency, Tufts-New England Medical Center, Boston, MA.
1973-1975 Clinical Associate, Immunology, NIH, Bethesda, MD.
1975-1977 Assistant Professor of Medicine (Rheumatology and Clinical Immunol.), Univ. of California, Davis.
1976-1979 Director, Tissue Typing Laboratory, University of California, Davis.
1977-1981 Associate Professor of Medicine, Division of Rheumatology/Allergy and Clinical Immunology, University of California, Davis.
1981-2003 Professor of Medicine, Div. of Rheumatology/Allergy and Clin. Immunol., Univ. of California, Davis.
1982-present Chief, Division of Rheumatology/Allergy and Clinical Immunology, University of California, Davis.
1985-1986 Visiting Scientist, Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia.
2003-present Distinguished Professor of Medicine, University of California at Davis.

Honors/Memberships:

Phi Beta Kappa, 1966; Pi Mu Epsilon, 1966; Witco Chem. Award in Organic Chem., Syracuse University, 1964, 1965, 1966; Stanford Award for Outstanding Student Research, 1968; Associate of American Colleges Recognition in Trop. Med., 1970; Rbt. Shelton Alumni Scholar Award, Stanford Univ., 1971; Alpha Omega Alpha, 1971; University of California Faculty Award for Biomedical Research, 1979; Chair, Division of Comp. Immunol. 1984-1986 (ASZ); ASCI, 1984; UC Award for Biomedical Research, 1985; Guggenheim Fellowship, 1985-1986; Oettinger Award, 1988; NIH General Medicine Study Section (A) 1990-1992; Chairperson, 1992-1994; American Association of Physicians (AAP), 1994; Jack and Donald Chia Professor of Medicine, 1994; Consultant, Center for Excellence, Japan Ministry of Education, 2004; Medal of the University of Milan, 2005.

B. Selected peer-reviewed publications (in chronological order).

Kita, H., Z.-X. Lian, J. Van de Water, X.S. He, S. Matsumura, M. Kaplan, V. Luketic, R.L. Coppel, A.A. Ansari and M.E. Gershwin. Identification of HLA-A2-restricted CD8⁺ cytotoxic T cell responses in PBC: T cell activation is augmented by immune complexes cross-presented by dendritic cells. *Journal of Experimental Medicine* 195:113-123, 2002.

Hashimoto, Y., E. Montecino-Rodriguez, M.E. Gershwin and K. Dorshkind. Impaired development of T lymphoid precursors from pluripotent hematopoietic stem cells in New Zealand Black mice. *Journal of Immunology* 168:81-86, 2002.

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- Kita, H., S. Matsumura, X.S. He, A.A. Ansari, Z.X. Lian, J. Van de Water, R.L. Coppel, M.M. Kaplan, and M.E. Gershwin. Analysis of TCR antagonism and molecular mimicry of an HLA-A0201-restricted CTL epitope in PBC. *Hepatology* 36:918-926, 2002.
- Kita, H., O.V. Naidenko, M. Kronenberg, A.A. Ansari, P. Rogers, X.S. He, F. Koning, T. Mikayama, J. Van de Water, R.L. Coppel, M. Kaplan, and M.E. Gershwin. Quantitation and phenotypic analysis of natural killer T cells in PBC using a human CD1d tetramer. *Gastroenterology* 123:1031-1043, 2002.
- Kimura, Y., P.S.C. Leung, T.P. Kenny, J. Van de Water, M. Nishioka, A.S. Giraud, J. Neuberger, G. Benson, R. Kaul, A.A. Ansari, R.L. Coppel, and M.E. Gershwin. Differential expression of intestinal trefoil factor in biliary epithelial cells of PBC. *Hepatology* 36:1227-1235, 2002.
- Matsumura, S., H. Kita, X.S. He, A.A. Ansari, Z.X. Lian, J. Van de Water, K. Yamamoto, T. Tsuji, R.L. Coppel, M. Kaplan, and M.E. Gershwin. Comprehensive mapping of HLA-A*0201-restricted CD8 T-cell epitopes on PDC-E2 in PBC. *Hepatology* 36:1125-1134, 2002.
- Fukushima, N., G. Nalbandian, J. Van de Water, K. White, A.A. Ansari, P. Leung, T. Kenny, S.G. Kamita, B.D. Hammock, R.L. Coppel, F. Stevenson, H. Ishibashi, and M.E. Gershwin. Characterization of recombinant monoclonal IgA anti-PDC-E2 autoantibodies derived from patients with PBC. *Hepatology* 36:1383-1392, 2002.
- Leung, P.S.C., C. Quan, O. Park, J. Van de Water, M.J. Kurth, M.H. Nantz, A.A. Ansari, R.L. Coppel, K.S. Lam, and M.E. Gershwin. Immunization with a xenobiotic 6-bromohexanoate bovine serum albumin conjugate induces antimitochondrial antibodies. *Journal of Immunology* 170:5326-5332, 2003.
- Lian, Z-X., T. Okada, X.S. He, H. Kita, Y-J. Liu, A.A. Ansari, K. Kikuchi, S. Ikehara, and M.E. Gershwin. Heterogeneity of dendritic cells in the mouse liver: Identification and characterization of four distinct populations. *Journal of Immunology* 170:2323-2330, 2003.
- Shimoda, S., M. Nakamura, H. Ishibashi, A. Kawano, T. Kamihira, N. Sakamoto, S. Matsushita, A. Tanaka, H.J. Worman, M.E. Gershwin and M. Harada. Molecular mimicry of mitochondrial and nuclear autoantigens in PBC. *Gastroenterology* 124(7):1915-1925, 2003.
- Wu, C.-T., J.P. Eiserich, A.A. Ansari, R.L. Coppel, S. Balasubramanian, C.L. Bowlus, M.E. Gershwin and J. Van de Water. Myeloperoxidase-positive inflammatory cells participate in bile duct damage in PBC through nitric oxide-mediated reactions. *Hepatology* 38:1018-1025, 2003.
- Selmi, C., D.L. Balkwill, P. Invernizzi, A.A. Ansari, R.L. Coppel, M. Podda, P.S. Leung, T.P. Kenny, J. Van de Water, M.H. Nantz, M.J. Kurth, and M.E. Gershwin. Patients with PBC react against a ubiquitous xenobiotic-metabolizing bacterium. *Hepatology* 38:1250-1257, 2003.
- Kamihira, T., S. Shimoda, K. Harada, A. Kawano, M. Handa, E. Bab, K. Tsuneyama, M. Nakamura, H. Ishibashi, Y. Nakanuma, M.E. Gershwin and M. Harada. Distinct costimulation dependent and independent autoreactive T-cell clones in PBC. *Gastroenterology* 125:1379-1387, 2003.
- Bruggraber, S.F., P.S. Leung, K. Amano, C. Quan, M.J. Kurth, M.H. Nantz, G.D. Benson, J. Van de Water, V. Luketic, T.E. Roche, A.A. Ansari, R.L. Coppel and M.E. Gershwin. Autoreactivity to lipoate and a conjugated form of lipoate in PBC. *Gastroenterology* 125:1705-1713, 2003.
- Amano, K., P.S.C. Leung, Q. Xu, J. Marik, C. Quan, M.J. Kurth, M.H. Nantz, A.A. Ansari, K.S. Lam, M. Zeniya, R.L. Coppel, and M.E. Gershwin. Xenobiotic-induced loss of tolerance in rabbits to the mitochondrial autoantigen of PBC is reversible. *Journal of Immunology* 172: 6444-6452, 2004.
- Matsumura, S., J. Van de Water, P. Leung, J.A. Odin, K. Yamamoto, G.J. Gores, K. Mostov, A.A. Ansari, R.L. Coppel, Y. Shiratori, and M.E. Gershwin. Caspase induction by IgA antimitochondrial antibody: IgA-mediated biliary injury in PBC. *Hepatology* 39:1415-1422, 2004.
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- Lian, Z.X., K. Kikuchi, G.X. Yang, A.A. Ansari, S. Ikehara, and M.E. Gershwin. Expansion of bone marrow IFN- α -producing dendritic cells in New Zealand Black (NZB) mice: high level expression of TLR9 and secretion of IFN- α in NZB bone marrow. *Journal of Immunology* 173:5283-5289, 2004.

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- Selmi C, Ross SR, Ansari AA, Invernizzi P, Podda M, Coppel RL, and M.E. Gershwin. Lack of immunological or molecular evidence for a role of mouse mammary tumor retrovirus in primary biliary cirrhosis. *Gastroenterology* 127(2):493-501, 2004.
- Kimura, Y., C. Selmi, P.S.C. Leung, T.K. Mao, J. Schauer, M. Watnik, S. Kuriyama, M. Nishioka, A.A. Ansari, R.L. Coppel, P. Invernizzi, M. Podda, and M.E. Gershwin. Genetic polymorphisms influencing xenobiotic metabolism and transport in patients with primary biliary cirrhosis. *Hepatology* 41:55-63, 2005.
- Kamihira, T., S. Shimoda, M. Nakamura, T. Yokoyama, Y. Takii, A. Kawano, M. Handa, H. Ishibashi, M.E. Gershwin and M. Harada. Biliary epithelial cells regulate autoreactive T cells: implications for biliary-specific diseases. *Hepatology* 41:151-159, 2005.
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- Amano, K., P.S.C. Leung, R. Rieger, C. Quan, X. Wang, J. Marik, Y.F. Suen, M.J. Kurth, M.H. Nantz, A.A. Ansari, K.S. Lam, M. Zeniya, E. Matsuura, R.L. Coppel and M.E. Gershwin. Chemical xenobiotics and mitochondrial autoantigens in primary biliary cirrhosis: Identification of antibodies against a common environmental, cosmetic, and food additive, 2-octynoic acid. *Journal of Immunology* 174:5874-5883, 2005.
- Kikuchi, K., Z.X. Lian, G.X. Yang, A.A. Ansari, S. Ikehara, M. Kaplan, H. Miyakawa, R.L. Coppel and M.E. Gershwin. Bacterial CpG induces hyper-IgM production in CD27(+) memory B cells in primary biliary cirrhosis. *Gastroenterology* 128:304-312, 2005.
- Yang, G.X., Z.X. Lian, K. Kikuchi, Y.J. Liu, A.A. Ansari, S. Ikehara, and M.E. Gershwin. CD4- plasmacytoid dendritic cells (pDCs) migrate in lymph nodes by CpG inoculation and represent a potent functional subset of pDCs. *Journal of Immunology* 174:3197-3203, 2005.
- Kaplan, M.M. and M.E. Gershwin. Primary biliary cirrhosis. *New England J Medicine* 353:1261-1272, 2005.
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- Invernizzi, P., M. Miozzo, C. Selmi, L. Persani, P.M. Battezzati, M. Zuin, S. Lucchi, P.L. Meroni, B. Marasini, S. Zeni, M. Watnik, F.R. Grati, G. Simoni, M.E. Gershwin and M. Podda. X chromosome monosomy: A common mechanism for autoimmune diseases. *Journal of Immunology* 175:575-578, 2005.
- Invernizzi, P., C. Selmi, I.R. Mackay, M. Podda and M.E. Gershwin. From bases to basis: linking genetics to causation in primary biliary cirrhosis. *Clinical Gastroenterology and Hepatology* 3:401-410, 2005.
- Gershwin, M.E., C. Selmi, H.J. Worman, E.B. Gold, M. Watnik, J. Utts, K.D. Lindor, M.M. Kaplan J.M. Vierling and the USA PBC Epidemiology Group. Risk factors and comorbidities in primary biliary cirrhosis: a controlled interview-based study of 1032 patients. *Hepatology* 42:1194-1202, 2005.
- Mao T.K., Z.X. Lian, C. Selmi, Y. Ichiki, P. Ashwood, A.A. Ansari, R.L. Coppel, S. Shimoda, H. Ishibashi and M.E. Gershwin. Altered monocyte responses to defined TLR ligands in patients with primary biliary cirrhosis. *Hepatology* 42:802-808, 2005.
- Yang, G., Z. Lian, K. Kikuchi, Y. Moritoki, A. Ansari, Y. Liu, S. Ikehara and M.E. Gershwin. Plasmacytoid dendritic cells of different origins have distinct characteristics and function: Studies of lymphoid progenitors versus myeloid progenitors. *J. of Immunology* 175:7281-7287, 2005.
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- Cheng, I.R. Mackay, M.E. Gershwin and W.M. Ridgway. NOD.c3c4 congenic mice develop autoimmune biliary disease that serologically and pathogenetically models human primary biliary cirrhosis. *Journal of Experimental Medicine* 1-11, 2006.
- Wesierska-Gadek, J., E. Penner, P.M. Battezzati, C. Selmi, M. Zuin, E. Hitchman, H.J. Worman, M.E. Gershwin, M. Podda and P. Invernizzi. Correlation of initial autoantibody profile and clinical outcome in primary biliary cirrhosis. *Hepatology* 43:1135-1144, 2006.
- Rieger, R., P.S.C. Leung, M.R. Jeddloh, M.J. Kurth, M.H. Nantz, K.S. Lam, D. Barsky, A.A. Ansari, R.L. Coppel, I.R. Mackay and M.E. Gershwin. Identification of 2-nonyoic acid, a cosmetic component, as a potential trigger of primary biliary cirrhosis. *J. of Autoimmun* 27:7-16, 2006.
- Aoki, C.A., C.M. Roifman, Z.-X. Lian, C.L. Bowlus, G.L. Norman, Y. Shoenfeld, I.R. Mackay and M.E. Gershwin. IL-receptor alpha deficiency and features of primary biliary cirrhosis. *Journal of Autoimmunity* 27:50-53, 2006.
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- Shimoda, S., F. Ishikawa, T. Kamihira, A. Komori, H. Niuro, E. Baba, K. Harada, K. Isse, Y. Nakanuma, H. Ishibashi, M.E. Gershwin and M. Harada. Autoreactive T-cell responses in primary biliary cirrhosis are proinflammatory whereas those of controls are regulatory. *Gastroenterology* 131:606-618, 2006.
- Wakabayashi, K., Z.-X. Lian, Y. Moritoki, R.Y. Lan, K. Tsuneyama, Y.-H. Chuang, G.-X. Yang, W. Ridgway, Y. Ueno, A.A. Ansari, R.L. Coppel, I.R. Mackay and M.E. Gershwin. IL-2 receptor $\alpha^{-/-}$ mice and the development of primary biliary cirrhosis. *Hepatology* 44:1240-1249, 2006.
- Buxbaum, J, P. Qian, C. Khuu, B.L. Shneider, D.I. Daikh, M.E. Gershwin, P.M. Allen and M.G. Peters. Novel model of antigen-specific induction of bile duct injury. *Gastroenterology* 131(6):1899-906, 2006.
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- Oertelt, S., R. Rieger, C. Selmi, P. Invernizzi, A.A. Ansari, R.L. Coppel, M. Podda, P.S. Leung and M.E. Gershwin. A sensitive bead assay for antimitochondrial antibodies: Chipping away at AMA-negative primary biliary cirrhosis. *Hepatology* 45:659-665, 2007.
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- Gershwin, M.E. and I.R. Mackay, eds. *Lymphocytes and Liver: Domestic bliss or dangerous liaisons?* *Seminars in Liver Disease* 27:129-230, 2007.

C. Research Support.

Overall Research Goals and Responsibilities. To oversee a program focused on dissecting the mechanisms of autoimmunity in primary biliary cirrhosis. This includes a program involving seven postdoctoral fellows, two graduate students and a technician. This program began in 1986 while I was on sabbatical at the Hall Institute in Melbourne, Australia and cloned PDC-E2, the major mitochondrial autoantigen of PBC.

Research Projects Ongoing or Completed for the last 3 years:

Active

DK 39588 Merit award. (Gershwin)

4/1/01 to 3/1/11

NIH NIDDKK. Mechanisms and Pathogenesis of Primary Biliary Cirrhosis. Aim: To determine the autoreactive epitopes in patients with antibodies to pyruvate dehydrogenase. To clone T cells from the liver of patients with PBC and map epitopes. To study the issues of spreading determinants and molecular recognition of biliary cells. No overlap.

DK037003 (Gershwin).

08/01/03 to 07/31/07

NIH. Xenobiotics in Primary Biliary Cirrhosis. This application focuses on whether environmental exposure to xenobiotics and, in particular, halogen substituted organic compounds such as chlorofluorohydrocarbon

substitutes can form protein adducts through acyl halide intermediates and lead to the production of AMAs. No overlap. This is the current application under review.

DK074768 (Gershwin)

7/1/06 to 6/30/11

NIH. Pathogenesis of Autoimmunity in a Murine Model of Primary Biliary Cirrhosis. This application focuses on a spontaneous model of PBC in a congenic strain of NOD mice and is a consortium effort with Cambridge University and the University of Pittsburgh. No overlap.

Pending

DK056839 (Gershwin)

7/1/07 to 6/30/12

NIH. Epidemiology of PBC: A Genome-Wide Association Study. The application focuses on a genome-wide analysis of patients with PBC compared to controls. No overlap.