#### **CURRICULUM VITAE**

Name: Lee Alan Witters

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**Place of Birth**: Canton, Ohio

#### **Education**:

1965 A.B. Oberlin College

1969 M.D. University of Rochester School of Medicine and Dentistry

1992 M.A. Dartmouth College (honorary)

#### **Postdoctoral Training:**

#### Internship and Residencies:

1969-1971	Clinical Fellow in Medicine, Harvard Medical School
1969-1970	Intern in Medicine, Beth Israel Hospital, Boston, MA
1970-1971	Assistant Resident in Medicine, Beth Israel Hospital
Research Fellowships:	
1965-1969	Research Associate, Department of Medicine, University of Rochester
	School of Medicine and Dentistry
1971-1973	Clinical Associate, National Heart and Lung Institute Molecular Disease
	Branch (with Donald S. Fredrickson), National Institutes of Health
1973-1975	Research Fellow in Medicine, Harvard Medical School
	and Massachusetts General Hospital

#### **Academic Appointments**:

1973-1975	Research Fellow in Medicine, Harvard Medical School
1975-1978	Instructor in Medicine, Harvard Medical School
1978-1981	Assistant Professor of Medicine, Harvard Medical School
1981-1982	Honorary Research Fellow, Department of Biochemistry,
	University of Dundee, Scotland
1982-1984	Associate Professor of Medicine, Harvard Medical School
1984-1986	Associate Professor of Medicine, Dartmouth Medical School

1984-1999	Chief, Endocrine-Metabolism Division, Department of
	Medicine, Dartmouth Medical School
1985-1986	Associate Professor of Biochemistry, Dartmouth Medical School
1986-	Professor of Medicine, Dartmouth Medical School
1986-	Professor of Biochemistry, Dartmouth Medical School
1987-	Eugene W. Leonard 1921 Professor of Medicine & Biochemistry,
	Dartmouth Medical School
1993-1999	Director, Endocrinology Program, Norris Cotton Cancer Center,
	Dartmouth Medical School
1996-1999	Adjunct Professor of Biological Sciences, Dartmouth College
1999-2003	Director, Humanitates Vitae (Human Biology Program), Dartmouth College
1999-	Professor of Biological Sciences, Dartmouth College

# **Hospital Appointments**:

1973-1975	Clinical and Research Fellow in Medicine, Massachusetts
	General Hospital
1975-1978	Assistant in Medicine, Massachusetts General Hospital
1979-1983	Assistant Physician, Massachusetts General Hospital
1983-1985	Associate Physician, Massachusetts General Hospital
1984-1999	Chief, Endocrine-Metabolism Division, Dartmouth Medical School
1984-	Attending Physician, Dartmouth-Hitchcock Medical Center
1985-	Consultant in Medicine, Medical Services, Massachusetts
	General Hospital

Awards and Honors:	
1965	Graduated with Honors in Chemistry, Oberlin College
1969	Graduated with Distinction in Research, University of
I	Rochester School of Medicine and Dentistry
1974-1976 I	Fellow, The Medical Foundation of Boston, Inc.
1977-1979 I	Research and Development Awardee, American Diabetes Association
1978-1983 I	Research Career and Development Awardee, U.S. Public Health Service
1981-1982 I	Fellow, John Simon Guggenheim Foundation
1997-1998 I	Faculty Advisor of the Year (for service to the Nathan Smith
	Premedical Society), Dartmouth College
1999-2000	Teacher of the Year in the Basic Sciences, Dartmouth Medical School
2001 I	Excellence in Medical Education Award, DMS, Awarded by DMS
	Class of 2004
2002 I	Faculty Speaker, Dartmouth College Commencement Class Day (elected by
	Class of 2002)
2002 I	Elected as Honorary member, Golden Key International Honour Society:
1	keynote speaker at member induction ceremony
2003 I	Elected as Distinguished Member, National Society of Collegiate Scholars;
1	keynote speaker at member induction ceremony
2004 I	Professor of the Year, Dartmouth College, named by Order of Omega
2004 I	Profiles in Excellence Teaching Award (by Student Assembly), Dartmouth College

2006	Dean of Faculty Award for Undergraduate Mentoring and Advising,
	Dartmouth College
2006	Linda '82 and Paul Gridley Faculty Fellow Award (for faculty-student
	involvement; inaugural recipient), Dartmouth College
2010	Distinguished Educator Award, Dartmouth Medical School (voted by
	members of the class of 2012)
2010	Faculty Advisor of the Year (voted by Council of Student Organizations)
2010	Distinguished Educator Award, Dartmouth Medical School (voted by
	members of the class of 2013)
2011	Basic Science Teaching Award, Dartmouth Medical School (voted by
	graduating class of 2011)
2011	Distinguished Lecturer Award, Dartmouth Medical School (voted by
	members of the class of 2014)
2012	Elected to inaugural class Geisel School of Medicine Academy of Master
	Educators

#### **Licensure and Certification:**

1969- - Massachusetts License Registration No. 37796

1973- Diplomate, Internal Medicine, American Board of Internal Medicine

1975- Diplomate, Endocrinology and Metabolism, American Board of Internal Medicine

1984- New Hampshire License Registration No. 7006

#### Memberships, Offices and Committee Assignment in Professional Societies:

1965	Sigma Xi, Oberlin College
1969	Alpha Omega Alpha, University of Rochester
1977	Member, Professional Section, American Diabetes Association
1977	American Federation for Clinical Research
1982	Member, American Society for Clinical Investigation
1984	Member, American Association for the Advancement of Science
1984-1986	Member, Medical Science Review Committee, Juvenile Diabetes
	Foundation
1985-1989	Metabolism Study Section, National Institutes of Health
1988	American Society for Biochemistry and Molecular Biology
1991	The Biochemical Society (United Kingdom)
1999-2000	Chair and Vice Chair, Gordon Research Conference on 2 <sup>nd</sup> Messengers
	and Protein Phosphorylation

#### **Service to Biomedical Journals:**

Editor, Biochemical Journal 1995-2002

Reviewer for:

Journal of Biological Chemistry

Journal of Clinical Investigation

Science

European Journal of Biochemistry

New England Journal of Medicine

Diabetes

Endocrinology

Archives of Biochemistry and Biophysics

Molecular and Cellular Biology

**FASEB Journal** 

Journal of Cell Biology

Nature/Nature Medicine

#### **Major Research Interests:**

- 1. Hormonal and Nutritional Regulation of Lipogenesis
- 2. Cellular Responses to Metabolic Stress: the AMP-activated Protein Kinase
- 3. Molecular Mechanism(s) of Hormone Action

# Teaching Experience: Visiting Physician.

1971-1973	Visiting Physician, Georgetown University Hospital, Medical
	Services, Washington, D.C.
1973-1985	Attending Physician, Medical Services, Massachusetts General Hospital
1975-1985	Attending Physician, Endocrine Unit, Massachusetts General Hospital
1975-1985	Attending Physician, Diabetes Unit, Massachusetts General Hospital
1973-1985	Lecturer: Harvard Medical Endocrine Pathophysiology and
	Emergency Medicine Courses; MGH Internal Medicine
	and Endocrine Postgraduate Courses; regular lectureships
	at various medical schools and other hospitals
1985-	Attending Physician, Department of Medicine and Endocrine-
	Metabolism Division, Dartmouth-Hitchcock Medical Center
1985-	Lecturer in Endocrinology, Physiology and Biochemistry,
	Dartmouth Medical School
1996-	Lecturer, Department of Biological Sciences, Dartmouth College
1999-2003	Director and Faculty Member, Humanitates Vitae (the Human Biology
	Program at Dartmouth College)

# Major Clinical, Hospital, Medical School and College Service Responsibilities:

Physician, Diabetes Outpatient Clinic, Massachusetts General
Hospital plus inpatient consultation service
Attending Physician, Medical Ward Services, Massachusetts General
Hospital
Attending Physician, Endocrine Services, Massachusetts General Hospital
Member, Subcommittee for Review for Research Proposals,
Massachusetts General Hospital
Member, Committee on Research, Massachusetts General Hospital
Member, Internship Selection Committee, Medical Services,
Massachusetts General Hospital

400 - 4000	
1985-1999	Chief, Endocrine-Metabolism Division, Department of Medicine,
	Dartmouth Medical School; Director, Endocrine Fellowship Program,
	Dartmouth Medical School; Attending Physician, DHMC
1986-1988	Member, Research and Development Committee, V.A. Hospital,
	White River Junction, VT
1985-1986	Chairman, Dean's Committee on Impact of Medical Center
	Relocation on Dartmouth Medical School
1986-	Co-Director, Endocrine Research Training Program, Dartmouth
	Medical School
1986-1987	Member, Search Committee for Pharmacology Chairman, Clinical
	Pharmacology
1987-1996	Member, Diabetes Advisory Committee, Mary Hitchcock Memorial
	Hospital
1987-1992	Chairman, Department of Medicine Faculty Promotions Committee,
	Dartmouth Medical School
1989-1990	Chairman, Rheumatology Chairman Search Committee, DMS
1989-1991	Chair/Co-Chairman, Department of Medicine Clinician-Scientist
	Search Committee, DMS
1990-1993	Member, DMS Research Committee
1991	Member, Dean's Committee on New Curricular Directions, DMS
1993-1997	Director, Endocrinology Program, Norris Cotton Cancer Center,
	Dartmouth Medical School
1997-1999	Director, Cell Signaling, Growth and Differentiation Program,
	Norris Cotton Cancer Center, Dartmouth Medical School
1997-	Faculty Advisor, The Nathan Smith Premedical Society,
	Dartmouth College
1997-	DMS Institutional Representation to the American Society for
	Clinical Investigation
1999-2002	Chair, Committee on Physician-Scientists, Dartmouth Medical School
2000-	Chair, Health Professions Advisory Committee, Dartmouth College
2001-2002	Member, Committee on Academic Advising, Dartmouth College
1999-	Member, Advisory Board, Diabetes Center, Massachusetts General Hospital
2002-2003	Member, Search Committee for DMS Dean
2002-2003	Member, College Course Steering Committee, Dartmouth College
2003-2006	Member, Committee on Instruction, Dartmouth College
2004-	Member, Dickey Center Faculty Steering Committee, Dartmouth College
2004-2006	Member, Dickey Center Global Health Initiative Steering Committee,
	Dartmouth College
2006-	Member, Committee on Classroom Technology, Academic Computing
	Division, Dartmouth College
2010-	Member, AB/MD Program Study Group, Dartmouth College
2010	Director, Health Professions Program, Dartmouth College (note: this is the
	year of my formal appointment, but I have been doing this <i>pro bono</i> since
	1997, along with my advisorship of the undergraduate Nathan Smith
	Society).

# **Bibliography:**

### Original Manuscripts

- 1. Witters, L. A., Alberico, L., and Avruch, J. (1976) Insulin regulation of glycogen synthase in the isolated rat hepatocyte. *Biochem. Biophys. Res. Comm.* 69: 977-1003.
- 2. Witters, L. A., Herbert, P. N., Shulman, R. S., Krauss, R. A., and Levy, R. I. (1976) Therapeutic failure in familial type II hyperlipoproteinemia. *Metabolism* 25: 1017-1025.
- 3. Witters, L. A., Ohman, J. L., Weir, G. C., Raymond, L., and Lowell, F. C. (1977) Insulin antibodies in the pathogenesis of insulin allergy and resistance. *Amer. J. Med.* 63: 703-709.
- 4. Witters, L. A., Avruch, J. (1978) Insulin regulation of hepatic glycogen synthase and phosphorylase. *Biochemistry* 17: 406-410.
- 5. Avruch, J., Witters, L. A., Alexander, M. C., and Bush, M. A. (1978) The effects of glucagon and insulin on cytoplasmic protein phosphorylation in hepatocytes. *J. Biol. Chem.* 253: 4754-4761.
- 6. Avruch, J., Witters, L. A., Alexander, M. C., Bush, M. A., and Crapo, L. M. (1979) Insulin and the phosphorylation of intracellular proteins. *Proc. ICN/UCLA Symp. Transmembrane Signalling* 31: 621-628.
- 7. Witters, L. A., Kowaloff, E. M., and Avruch, J. (1979) Glucagon regulation of protein phosphorylation: Identification of acetyl-CoA carboxylase as a substrate. *J. Biol. Chem.* 254: 245-249.
- 8. Witters, L. A. and Trasko, C. T. (1979) Regulation of hepatic free fatty acid metabolism by insulin and glucagon. *Amer. J. Physiol.* 237: E23-E29.
- 9. Witters, L. A., Moriarty, D., and Martin, D. B. (1979) Regulation of hepatic acetyl-CoA carboxylase by insulin and glucagon. *J. Biol. Chem.* 254: 6644-6649.
- 10. Alexander, M. C., Kowaloff, E. M., Witters, L. A., Dennihy, D. T., and Avruch, J. (1979) Purification of a hepatic 123,000 dalton hormone-stimulated 32P-peptide and its identification as ATP-citrate lyase. *J. Biol. Chem.* 254: 8052-
- 11. Avruch, J., Witters, L. A., Alexander, M. C., Kowaloff, E. M., and Palmer, J. L. (1979) Insulin-stimulated protein phosphorylation: A progress report. *Proc. 10th International Congr. Diabetes Federation* 500: 185-190.
- 12. Witters, L. A. and Vogt, B. (1981) A new method for the isolation of rat liver acetyl-CoA carboxylase. *J. Lipid Res.* 22: 364-369.
- 13. Segre, G. V., Perkins, A. S., Witters, L. A., and Potts, J. T. Jr. (1981) Metabolism of parathyroid hormone by isolated rat Kupffer cells and hepatocytes. *J. Clin. Invest.* 67: 449-457
- 14. Witters, L. A. (1981) Insulin stimulates the phosphorylation of acetyl-CoA carboxylase. *Biochem. Biophys. Res. Comm.* 100: 872-878.
- 15. Witters, L. A., Friedman, S. A., and Bacon, G. W. (1981) Microsomal acetyl-CoA carboxylase: evidence for association of enzyme polymer with liver microsomes. *Proc. Natl. Acad. Sci.* USA 78: 3639-3643.
- 16. Witters, L. A., Friedman, S. A., Tipper, J. P., and Bacon, G. W. (1981) Regulation of acetyl-CoA carboxylase by guanine nucleotides. *J. Biol. Chem.* 256: 8573-8578.

- 17. Avruch, J., Alexander, M. C., Palmer, J. L., Pierce, M. W., Nemenhof, R. A., Blackshear, P. J., Tipper, J. P., and Witters, L. A. (1982) The role of insulin-stimulated protein phosphorylation in insulin action. *Fed. Proc.*41: 2629-2633.
- 18. Tipper, J. P. and Witters, L. A. (1982) In vitro phosphorylation and inactivation of rat liver acetyl-CoA carboxylase purified by avidin-affinity chromatography. *Biochim. Biophys. Acta* 715: 162-169.
- 19. Ingebritsen, T. S., Blair, J., Guy, P., Witters, L. A., and Hardie, D. G. (1983) The protein phosphatases involved in cellular regulation. 3. Fatty acid synthesis, cholesterol synthesis and glycolysis/gluconeogenesis. *Eur. J. Biochem.* 132: 275-281.
- 20. Holland, R., Witters, L. A., and Hardie, D. G. (1983) The effect of glucagon on acetyl-CoA carboxylase phosphorylation in hepatocytes. In: *Int. Symp. on Isolation, Characterization and Use of Hepatocytes*, R. A. Harris and N. W. Cornell (eds.), Elsevier Biomedical, New York, pp. 585-590.
- 21. Witters, L. A., Tipper, J. P., and Bacon, G. W. (1983) Stimulation of site-specific phosphorylation of acetyl coenzyme A carboxylase by insulin and epinephrine. *J. Biol. Chem.* 258: 5643-5648.
- 22. Tipper, J. P., Bacon, G. W., and Witters, L. A. (1983) Acetyl-CoA carboxylase protein kinase: isolation of two cAMP-independent kinases identical to casein kinase I and casein kinase II. *Arch. Biochem. Biophys.* 227: 386-396.
- 23. Holland, R., Witters, L. A., and Hardie, D. G. (1984) Glucagon inhibits fatty acid synthesis in isolated hepatocytes via phosphorylation of acetyl-CoA carboxylase by cyclic AMP- dependent protein kinase. *Eur. J. Biochem.* 140: 325-333.
- 24. Witters, L. A., Vater, C. E., and Lienhard, G. (1985) Phosphorylation of the glucose transporter in vitro and in vivo by protein kinase C. *Nature* 315: 777-778.
- 25. Witters, L. A. and Bacon, G. W. (1985) Protein phosphatases active on acetyl-CoA carboxylase phosphorylated by casein kinase I and II and the cAMP-dependent protein kinase. *Biochem. Biophys. Res. Comm.* 130: 1132-1138.
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- Witters, L. A., Colliton, J. W., McDermott, J. M., Zhang, F., and Glynn, B. P. (1986)
   Regulation of adipocyte metabolism by insulin and phorbol esters: potential role of protein kinase C. In: *Mechanisms of Insulin Action*, P. Belfrage (ed.), Elsevier Press, pp. 229-237.
- 29. Blackshear, P. J., Wen, L., Glynn, B. P., and Witters, L. A. (1986) Protein kinase C-stimulated phosphorylation in vitro of a Mr 80,000 protein phosphorylated in response to phorbol esters and growth factors in intact fibroblasts. *J. Biol. Chem.* 261:1459-1469.
- 30. Blackshear, P. J., Wen, L., Nemenoff, R., Gunsalus, J. R., and Witters, L. A. (1986) Growth factor activation of protein kinase C-dependent and independent pathways of protein phosphorylation in fibroblasts. Relevance to activation of protein kinase C in neuronal tissues. In: *Prog. Brain Res.*, G. H. Gispen and A. H. Routtenberg (eds.), Elsevier Sci. Pub., Amsterdam, Chapter 16, pp. 183-195.

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- 32. Witters, L. A. (1986) Protein kinases and phosphatases active on acetyl-CoA carboxylase. *Adv. Prot. Phosphatases* 3:201-224.
- 33. Witters, L. A. and McDermott, J. M. (1986) Regulation of acetyl-CoA carboxylase by ADP-ribosylation. *Biochemistry* 25:7216-7220.
- 34. Witters, L. A., Mendel, D. W., and Colliton, J. W. (1987) Modulation of acetyl-CoA carboxylase by inhibitors of IMP dehydrogenase. *Arch. Biochem. Biophys.* 252:130-135.
- 35. Allard, W. J., Gibbs, E. M., Witters, L. A., and Lienhard, G. E. (1987) The glucosetransporter in human fibroblasts is phosphorylated in response to phorbol ester but not in response to growth factors. *Biochim. Biophys. Acta* 929:288-295.
- 36. Witters, L. A. and Watts, T. D. (1988) An autocrine factor from Reuber hepatoma cells that stimulates DNA synthesis and acetyl-CoA carboxylase: Characterization of biologic activity and evidence for a glycan structure. *J. Biol. Chem.* 263: 8027-8036.
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- 38. Witters, L. A., Watts, T. D., Daniels, D. L., and Evans, J. L. (1988) Insulin stimulates the dephosphorylation and activation of acetyl-CoA carboxylase, *Proc. Natl. Acad. Sci.* USA 85: 5473-5477.
- 39. Witters, L. A., Watts, T. D., Gould, G. W., Lienhard, G. E., and Gibbs, E. M. (1988) Regulation of protein phosphorylation by insulin and an insulinomimetic oligosaccharide in 3T3-L1 adipocytes and Fao hepatoma cells. *Biochem. Biophys. Res. Comm.* 153, 992-998.
- 40. Vivier, P. M., Dietrich, A. J., and Witters, L. A. (1988) Management of elevated cholesterol levels by New Hampshire primary care physicians: Report of a survey. *Family Practice* 27, 167-172.
- 41. Evans, J. L., Quistorff, B., and Witters, L. A. (1989) Zonation of hepatic lipogenic enzymes identified by dual digitonin pulse perfusion. *Biochem.* J. 259:821-829.
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- 43. Iverson, A.J., Nordlund, A-C., and Witters, L.A. (1990), Immunologic Analysis of acetyl-CoA carboxylase mass, tissue distribution and subunit composition, *Biochem. J.*,269,365-371.
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- 46. Bianchi, A., Quistorff, B. and Witters, L.A. (1990), Hepatic Zonation of Insulin-Stimulated Tyrosine Phosphorylation, *FEBS Lett.*, 269, 435-439.
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- 50. Bianchi, A., Evans, J.L., Nordlund, A.-C.., Watts, T. D., and Witters, L. A. (1991) Acetyl-CoA carboxylase in Reuber hepatoma cells: covariation of enzyme activity, insulin regulation and neutral lipid content, *J. Cell. Biochem.*, 48, 86-97.
- 51 .Lynch, C. J., McCall, K. M., Billingsley, M. L., Hreniuk, S. P., Martin, L. F., Witters, L. A., and Vannucci, S. J. (1992) Pyruvate carboxylase in obesity. *Am. J. Physiol.* 262: E608-E618.
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  Application of Dual-Digitonin Pulse Perfusion to the Study of Hepatic mRNA Zonation, *Biochem. J*, 294, 809-812.
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- non-catalytic subunits are homologs of proteins that interact with the yeast SNF1 protein kinase, *J. Biol. Chem.*, 269, 29343-29346.
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