Richard E. Ostlund

# CURRICULUM VITAE

**RICHARD EMIL OSTLUND, JR. M.D.** 20 May 2016

Professor of Medicine
Washington University School of Medicine

May 20, 2016


**BUSINESS ADDRESS:**

Core Laboratory for Clinical Studies
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## EDUCATION and WORK EXPERIENCE:

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|---|---|
| 1962-1966 | University of Utah, Salt Lake City, Utah<br>B.S. in Chemistry 1966 |
| 1966-1970 | University of Utah College of Medicine<br>M.D. 1970 |
| 1970-1971 | Intern in Medicine<br>Duke University, Durham, North Carolina |
| 1971-1972 | Resident in Medicine<br>Duke University, Durham, North Carolina |
| 1972-1974 | Research Associate<br>Laboratory of Molecular Biology<br>National Cancer Institute<br>Dr. Ira Pastan |

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|---|---|
| 1974-1976 | Fellow in Endocrinology and Metabolism<br>Washington University<br>Drs. David M. Kipnis and William H. Daughaday |
| 1976-1981 | Assistant Professor of Medicine<br>Metabolism Division, Department of Internal Medicine<br>Washington University<br>Director Tissue Culture Facility<br>Diabetes and Endocrinology Center |
| 1981-1995 | Associate Professor of Medicine<br>Metabolism Division, Department of Medicine<br>Washington University<br>Director Tissue Culture Facility<br>Washington University Diabetes Center |
| 1985-1995 | Director, Metabolism Clinic<br>Washington University |
| 1990-1994 | Director, Program in Diabetes and Lipid Metabolism<br>The Jewish Hospital of St. Louis at Washington University. |
| 1995-Current | Professor of Medicine<br>Metabolism Division<br>Washington University |
| 2008-Current | Director, Core Laboratory for Clinical Studies |

**CERTIFICATION:**

National Board of Medical Examiners, 1971
American Board of Internal Medicine, 1974, 2004
American Board of Endocrinology and Metabolism, 1976, 2004

**SOCIETY MEMBERSHIPS:**

American Diabetes Association
Endocrine Society
American Oil Chemists Society
Alpha Omega Alpha
Phi Beta Kappa
Phi Kappa Phi
Tau Kappa Alpha

**AWARDS and HONORS:**

W.D. Bonner Chemistry Award, 1966

James Bush Memorial Research Award, 1968

Elliott P. Joslin Research and Development Award of the American Diabetes Association, 1976-77

Teacher of the Year, 1991, Jewish Hospital of St. Louis

Best paper, American Oil Chemists Society, 2003.

Reviewer for NIH and Veterans' Administration: Metabolism Study Section, site visitor for diabetes centers and program projects, consultant to Clinical Trials Review Group, Reviewer for VA merit awards

Reviewer for Journal of Clinical Investigation, Journal of Lipid Research, Arteriosclerosis, Atherosclerosis, Diabetes, Diabetes Care, Metabolism, American Journal of Clinical Nutrition, Journal of Clinical Endocrinology and Metabolism, Gastroenterology.

**GRANT SUPPORT:**

Past support:

American Diabetes Association
American Heart Association
National Institutes of Health R01, K01, P01, and Phase I and Phase II Small Business Innovation Research awards 1977-present.
Merck, Novartis, Roche, Pfizer, Monsanto

Current NIH Support:

R01 HL 108160 R. Ostlund (PI)
Reverse Cholesterol Transport in Humans
This research seeks to relate parameters of whole body cholesterol metabolism, measured by mass spectrometry, to metabolic variables, biomarkers and carotid intima-media thickness. The techniques used were developed at Washington University.

P60-DK20579 R. Ostlund, Core Director.
Washington University Diabetes Research and Training Center Immunoassay Core.
This is a facility dedicated to diabetes-related testing for University and external investigators.

**PATENTS**

1. Lange, L.G. III, Ostlund, R.E., Bosner, M.S. U.S. Patent 5,432,058. Method for measuring human cholesterol absorption using metabolically stable isotopes. Issued July 11, 1995. Assigned to CV Therapeutics, Inc, Palo Alto, CA. A mass spectrometric method is described which uses dual stable isotopic cholesterol tracers to measure percent cholesterol absorption in human subjects without exposure to radioactive materials.

2. Ostlund, R.E., Jr. and Sherman, W.R. U.S. Patent 5,550,166. Pinitol and derivatives thereof for the treatment of metabolic disorders. Issued August 27, 1996. Assigned to Washington University and licensed to Humanetics Corporation, Minneapolis, MN. The preparation and use of pinitol, a sugar derived from soybean processing, to treat insulin resistance, dyslipidemia and hyperlipidemia is described.

3. Ostlund, R.E. and Sherman, W.R. U.S. Patent 5,827,896. Pinitol and derivatives thereof for the treatment of metabolic disorders. Issued October 27, 1998. Assigned to Washington University and licensed to Humanetics Corporation, Minneapolis, MN. This is a continuation in part of U.S. patent 5,550,166 (#2 above). The use of pinitol to lower plasma free fatty acids is described.

4. Ostlund, R.E., Jr. U.S. Patent 5,932,562. Sitostanol formulation to reduce cholesterol absorption and method for preparing and use of same. Issued August 3, 1999. Assigned to Washington University and licensed to Lifeline Technologies, Inc., St. Louis, MO. A method to formulate plant sterols with lecithin and other emulsifiers to increase bioavailability for reduction of cholesterol absorption is described and supported by clinical studies.

5. Ostlund, R.E., Jr. U.S. Patent 6,063,776. Sitostanol formulation with emulsifier to reduce cholesterol absorption and method for preparing and use of same. Issued 5-16-00. Assigned to Washington University and licensed to Lifeline Technologies, Inc., St. Louis, MO. This describes the use of sodium stearoyl lactylate and lower concentrations of phospholipids to promote bioactivity of sitostanol.

6. Ostlund, R.E., Jr. 1999. Sitostanol formulation with emulsifier to reduce cholesterol absorption. Patent Cooperation Treaty (PCT) WO 99/60869. This is an international publication of patent material contained in previous US patents 5,932,562 and 6,063,776.

7. Ostlund RE, Jr. 2005. Formulacion de sitostanol con emulsificador para reducir la absorcion de colesterol. Mexican patent 232770.

8. Ostlund RE, Jr. 2006. Sitostanol formulation with emulsifier to reduce cholesterol absorption. Canadian patent 2332983.

9. Ostlund RE, Jr. 2006. Sitostanol formulation with emulsifier to reduce cholesterol absorption. Japanese patent 3755064.

10. Ostlund RE, Jr. 2008. Formulação sitostanol com emulsificante para reduzir a absorção do colesterol. Brazilian patent PI9910719-8 A.

11. Ostlund RE, Jr. 2008. Sitostanol formulation with emulsifier to reduce cholesterol absorption. European patent EP 1082029 B1.

12. Ostlund RE, Jr. 2008. Formulación de sitostanol con emulsionante para reducir la absorción de colesterol. Spanish patent EP 1082029.
13. Ostlund RE, Jr. 2008. Formulazione di sitostanolo con emulsionante per ridurrel'assorbimento del colesterolo. Italian patent 1082029.

14. Ostlund RE, Jr. 2008. Prostedek v pevn, avak ve vod rozpustn form pro snen absorpce cholesterol. Czech Republic patent 299194.

15. Ex Parte Reexamination Certificate (8352nd), United States Patent 6,063,776 C1. Issued June 28, 2011. This patent upholds the claims of patent #5 and adds additional claims.

**SMALL COMPANY FORMATION**

Patent 1 was part of the supporting scientific base for the venture capital funding and 1996 initial public offering of CV Therapeutics, Inc. (Nasdaq symbol CVTX). CV Therapeutics became a component of the Nasdaq Biotechnology Index and was acquired by Gilead Sciences in 2009. My method for measuring cholesterol absorption was used to evaluate the first company product, the drug CVT-1, a synthetic inhibitor of cholesterol esterase.

Working with the Washington University Office of Technology Management, a startup company, Lifeline Technologies, Inc., was incorporated in May, 1998, with Richard E. Ostlund, Jr. and Curtis A. Spilburg as founders. A closely-held private company, Lifeline has as its goal the development of bioactive formulations of plant sterols as dietary supplements, foods, and drugs to reduce serum cholesterol. Washington University has assigned exclusive rights to my work on the bioavailability of plant sterols (patent # 4 and continuations in part) to Lifeline in a royalty-bearing license agreement. The company has raised capital from private individuals and Shoreline Venture Partners, Menlo Park, California. It has been the recipient of an NIH Small Business Innovation Research Grant. Lifeline is currently developing commercial phytosterol products in north and south America in partnership with international companies.

PUBLICATIONS


1. Miles, M.H., Eyring, E.M., Epstein, W.W., Ostlund, R.E. 1965. Fast reactions involving hydrogen bonding in 2,2-disubstituted malonic acids. J. Phys. Chem. 69:467-476.

2. Downes, H., Perry, R.S., Ostlund, R.E., Karler, R. 1970. A study of the excitatory effects of barbiturates. J. Pharmacol. Exp. Ther. 175:692-651.

3. Orfanakis, N.G., Ostlund, R.E., Bishop, C.R., Athens, J.W. 1970. Normal blood leukocyte concentration values. Am. J. Clin. Pathol. 53:647-651.

4. Ostlund, R.E., Bishop, C.R., Athens, J.W. 1971. Evaluation of non-steady-state neutrophil kinetics during endotoxin-induced granulocytosis. Proc. Soc. Exp. Biol. Med. 137:763-767.

5. Ostlund, R.E., Pastan, I., Adelstein, R.S. 1974. Myosin in cultured fibroblasts. J. Biol. Chem. 249:3903-3907.

6. Willingham, M.C., Ostlund, R.E., Pastan, I. 1974. Myosin is a component of the cell surface of cultured cells. Proc. Natl. Acad. Sci. USA 71:4144-4148.

7. Ostlund, R.E., Pastan, I. 1975. Fibroblast tubulin. Biochemistry 14:4064-4068.

8. Ostlund, R.E., Pastan, I. 1976. The purification and quantitation of myosin from cultured cells. Biochim. Biophys. Acta. 453:37-47.

9. Ostlund, R.E., Leung, J.T., Kipnis, D.M. 1977. Muscle actin filaments bind pituitary secretory granules in vitro. J. Cell Biol. 73:78-87.

10. Ostlund, R.E. 1977. Contractile proteins and pancreatic beta-cell secretion. Diabetes 26:245-254.

11. Ostlund, R.E., Jr., Leung, J.T., Kipnis, D.M. 1978. Myosins of secretory tissues. J. Cell. Biol. 77:827-836.

12. Ostlund, R.E., Jr., Leung, J.T., Hajek, S.V., Winokur, T., Melman, M. 1978. Acute stimulated hormone release from cultured $GH_3$ pituitary cells. Endocrinology 103:1245-1252.

13. Ostlund, R.E., Jr., Pfleger, B., Schonfeld, G. 1979. Role of microtubules in low density lipoprotein (LDL) processing by cultured cells. J. Clin. Invest. 63:75-84.

14. Ostlund, R.E., Jr., Leung, J.T., Hajek, S.V. 1979. Biochemical determination of tubulin-microtubule equilibrium in cultured cells. Anal. Biochem. 96:155-164.

15. Ostlund, R.E., Jr. 1981. Structure and function of islet cells. Granule releasing system. In, Handbook of Diabetes, Vol. 2, Islet cell function/insulin action, ed. M. Brownlee, Garland STPM Press, New York. pp 27-40.

16. Ostlund, R.E., Jr., Leung, J.T., Hajek, S.V. 1980. Regulation of microtubule assembly in cultured fibroblasts. J. Cell Biol. 85:386-391.

17. Witztum, J.L., Williams, J.C., Ostlund, R.E., Jr., Sherman, L., Siccard, G., Schonfeld, G. 1980. Successful plasmapheresis in a four-year old child with homozygous familial hypercholesterolemia. J. Pediatr. 97:615-618.

18. Patsch, W., Witztum, J., Ostlund, R.E., Jr., Schonfeld, G. 1980. Structure, immunology, and cell reactivity of low density lipoprotein (LDL) from umbilical vein of a newborn type II homozygote. J. Clin. Invest. 66:123-129.

19. Ostlund, R.E., Jr., Tucker, R.W., Leung, J.T., Okun, N., Williamson, J.R. 1980. The cytoskeleton in Chediak-Higashi syndrome fibroblasts. Blood 56:806-811, 1980.

20. Ostlund, R.E., Jr., Hajek, S.V., Levy, R.A., Witztum, J.L. 1981. Analysis of lipids and endothelial and smooth muscle cells of umbilical cord in familial homozygous hypercholesterolemia. Metabolism 30:285-289.

21. Ostlund, R.E., Jr., Levy, R.A., Witztum, J.L., Schonfeld, G. 1982. Familial hypercholesterolemia: Evidence for a newly recognized mutation determining increased fibroblast receptor affinity but decreased capacity for low density lipoprotein in two siblings. J. Clin. Invest. 70:823-831.

22. Semenkovich, C.F., Ostlund, R.E., Jr., Levy, R.A., Osa, S.R. 1982. Low density lipoprotein (LDL) receptor activity in homozygous familial hypercholesterolemia fibroblasts. J. Biol. Chem. 257:12857-12865.

23. Patsch, W., Ostlund, R., Kuisk, I., Levy, R., Schonfeld, G. 1982. Characterization of lipoprotein in a kindred with familial hypercholesterolemia. J. Lipid Res. 23:1196-1205.

24. Brajtburg, J., Leberg, S., Bolard, J., Kobayashi, G.S., Levy, R.A., Ostlund, R.E., Jr., Medoff, G. 1984. Interaction of plasma proteins and lipoproteins with amphotericin B. J. Infect. Dis. 149:986-997.

25. Levy, R.A., Ostlund, R.E., Jr., Brajtburg, J. 1985. The effects of amphotericin B on lipid metabolism in cultured human skin fibroblasts. In Vitro. 21:26-31.

26. Semenkovich, C.F., Ostlund, R.E., Jr., Yang, J., Reaban, M.E. 1985. Demonstration of functional low-density lipoprotein receptors by protein blotting in fibroblasts from a subject with homozygous receptor-negative familial hypercholesterolemia. J. Lab. Clin. Med. 106:47-52.

27. Ostlund, R.E., Jr., Yang, J.W. 1985. Effect of cholesterol and growth factors on the proliferation of cultured human skin fibroblasts. Exp. Cell Res. 161:509-516.

28. Levy, R.A., Ostlund, R.E., Jr., Goldberg, A.C., Grundy, S.M. 1986. Long-term changes in cholesterol biosynthesis and the effect of plasmapheresis therapy in a hypercholesterolemia homozygote. Metabolism 35:415-418.

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30. Semenkovich, C.F., Ostlund, R.E., Jr. 1986. The low density lipoprotein receptor on human peripheral blood monocytes and lymphocytes: Visualization by ligand blotting and immunoblotting techniques. J. Clin. Endocrinol. Metab. 62:1279-1287.

31. Ostlund, R.E., Jr. 1987. Immunosorbent Chemistry: A study of agarose-based column sorbents for the removal of low-density lipoprotein (LDL) from blood. Artif. Organs 11:366-374.

32. Semenkovich, C.F., Ostlund, R.E., Jr. 1987. Estrogens induce low-density lipoprotein receptor activity and decrease intracellular cholesterol in human hepatoma cell line Hep G2. Biochemistry 26:4987-4992.

33. Ostlund, R.E., Jr. 1988. Removal of apolipoprotein B from dog whole blood by ex vivo hemoadsorption on antibody-agarose beads. Artif. Organs 12:491-496.

34. Semenkovich, C.F., Ostlund, R.E., Jr., Schechtman, K.B. 1989. Plasma lipids in patients with type I diabetes mellitus. Influence of race, gender, and plasma glucose control: Lipids do not correlate with glucose control in black women. Arch. Intern. Med. 149:51-56.

35. Ostlund, R.E., Jr., Reaban, M. 1989. Effect of exercise training on plasma cholesterol and cholesterol kinetics in adult female rats. Atherosclerosis 75:7-11.

36. Ostlund, R.E., Jr., Semenkovich, C.F., Schechtman, K.B. 1989. Quantitative relationship between plasma lipids and glycohemoglobin in type I diabetes mellitus: Longitudinal study of 212 patients. Diabetes Care 12:332-336.

37. Ostlund, R.E., Jr., Staten, M., Kohrt, W.M., Schultz, J., Malley, M. 1990. The ratio of waist-to-hip circumference, plasma insulin level, and glucose intolerance as independent predictors of the $HDL_2$ cholesterol level in older adults. N. Engl. J. Med. 322:229-234.

38. Keidar, S., Ostlund, R.E., Jr., Schonfeld, G. 1990. Apolipoprotein E-rich HDL in patients with homozygous familial hypercholesterolemia. Atherosclerosis 84:155-163.

39. Semenkovich, C.F., Ostlund, R.E., Jr., Olson, M.O.J., Yang, J.W. 1990. A protein partially expressed on the surface of HepG2 cells that binds lipoproteins specifically is nucleolin. Biochemistry 29:9708-9713.

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41. Ostlund, R.E., Jr. 1990. Ratio of waist-to-hip circumference, plasma insulin level, and glucose intolerance as independent predictors of $HDL_2$-cholesterol level in older adults. Lipid Digest 6:30-31.

42. Ostlund, R.E., Jr. 1992. Immunoadsorbents, in Encyclopedia of Immunology, ed. I.M. Roitt, P.J. Delves, Academic Press, London, pp. 776-778.

43. Ostlund, R.E., Jr., Staten, M.A., Kohrt, W.M., Obert, K.A., Daughaday, W.H. 1991. Insulin-like growth factor and apolipoprotein B. JAMA 266:1937-1938.

44. Levy, R.A., Ostlund, R.E., Jr., Schonfeld, G., Wong, P., Semenkovich, C.F. 1992. Cholesteryl ester storage disease: Complex molecular effects of chronic lovastatin therapy. J. Lipid Res. 33:1005-1015.

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47. Ostlund, R.E., Jr. 1993. A minimal model for human whole body cholesterol metabolism. Am. J. Physiol. 265(E28):513-520.

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50. Ostlund, R.E., Jr., McGill, J.B., Herskowitz, I., Kipnis, D.M., Santiago, J.V., Sherman, W.R. 1993. D-*chiro*-Inositol Metabolism in Diabetes Mellitus. Proc. Natl. Acad. Sci. 90:9988-9992.

51. Ostlund, R.E., Jr., Yang, J.W., Heath-Monnig, E., Semenkovich, C.F. 1994. Increased LDL receptor expression mediated through the IGF-I receptor in cultured fibroblasts. Molecular Endocrinology 8:904-909.

52. Myers, P.R., Wright, T.F., Tanner, M.A., Ostlund, R.E., Jr. 1994. The effects of native LDL and oxidized LDL on EDRF bioactivity and nitric oxide production in vascular endothelium. J. Lab. Clin. Med. 124:672-683.

53. Ameis, D., Brockmann, G., Knoblich, R., Merkel, M., Ostlund, R.E., Jr., Yang, J.Y., Coates, P.M., Cortner, J.A., Feinman, S.V., Greten, H. 1995. A 5' splice-region mutation and a dinucleotide deletion in the lysosomal acid lipase gene in two patients with cholesteryl ester storage disease. J. Lipid Research 36:241-250.

54. Ostlund, R.E., Jr., Sherman, W.R. Measurement of D-*chiro*-inositol in clinical studies. 1995. Diabetes Care 18:1074-1075.

55. Ostlund, R.E., Jr, Seemayer, R., Gupta, S., Kimmel, R., Ostlund, E.L., Sherman, W.R. 1996. A Stereospecific *myo*-Inositol/D-*chiro*-Inositol Transporter in HepG2 Liver Cells: Identification with 3-$^{3}$H-D-*chiro*-Inositol. J. Biol. Chem. 271:10073-10078.

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65. Ostlund, R.E., Jr., Spilburg, C.A., Stenson,W.F. 1999. Sitostanol administered in lecithin micelles potently reduces cholesterol absorption in human subjects. Am. J. Clin. Nutr. 70:826-831.

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85. Lin X, Yue P, Yan Xie, Davidson NO, Sakata N, Ostlund RE Jr, Chen Z, Schonfeld G. 2005. Reduced intestinal fat absorptive capacity but enhanced susceptibility to diet-induced fatty liver in mice heterozygous for apoB38.9 truncation. American Journal of Physiology 289:G146-152.

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There are fifteen issued patents in addition to these publications.