

CURRICULUM VITAE

VASSILIS I. ZANNIS

Address: 150 Hartman Road, Newton, MA 02168
Date of Birth: November 18, 1940
Place of Birth: Chios, Greece
Citizenship: Naturalized US Citizen

Education:

1964 Second Deck Officer, Merchant Marine College, Athens, Greece
1968 B.S., University of Athens, Greece
1975 Ph.D., University of California, Berkeley (Biochemistry)

Postdoctoral Training:

Research Fellowships:

1975-1977 Postdoctoral Fellow, Department of Medicine, University of California, San Francisco
1977-1978 Research Associate, Department of Chemistry, Massachusetts Institute of Technology, Cambridge
1978-1979 Research Fellow, Department of Pediatrics, Harvard Medical School, Boston
1978-1979 Research Fellow, Metabolism Div., Dept. of Medicine, Children's Hospital Medical Center, Boston
1979-1981 Research Fellow, The Medical Foundation, Inc., Boston

Academic Appointments:

1979-1982 Research Associate, Department of Pediatrics, Harvard Medical School, Boston
1982-1984 Assistant Professor of Pediatrics-Biochemistry, Dept. Pediatrics, Harvard Medical School, Boston
1984-1987 Director, Section of Molecular Genetics, Associate Professor of Medicine & Biochemistry, Boston University Medical School
1987- Director, Section of Molecular Genetics, Professor of Medicine & Biochemistry, Boston University Medical School

Hospital Appointments:

1979-1984 Research Associate, Metabolism Division, Department of Medicine, Children's Hospital Medical Center, Boston

Other Professional Positions and Major Visiting Appointments:

1968-1969 Research and Teaching Assistant, Department of Food Chemistry, University of Athens, Greece
1969-1975 Teaching Assistant (five quarters) and Research Assistant (remainder of time), Dept. of Biochemistry, University of California, Berkeley
1982-1984 Adjunct Assistant Member, Memorial Sloan Kettering Cancer Center, New York
1984- Instructor, Department of Oral Biology, Harvard Medical School, Boston
1986- Professor of Biochemistry and Medicine, University of Crete Medical School, Crete, Greece

Awards and Honors:

- 1964 Merchant Marine College: First in class
- 1968 University of Athens, Department. of Chemistry: First in class
- 1983 Established Investigator Award of the American Heart Association

Memberships, Offices and Committee Assignments in Professional Societies:

- 1981 Biophysical Society
- 1981 American Chemical Society
- 1981 Electrophoresis Society
- 1981 Fellow, Council on Arteriosclerosis, American Heart Association
- 1982 American Institute of Nutrition
- 1983 American Society of Biological Chemistry and Molecular Biology

Major Current Research Interests:

1. Structure-function analysis of human apolipoproteins by *in vitro* mutagenesis of the genes and analysis of the properties of the variant proteins.
2. Transcription factors and mechanisms involved in the regulation of the human apolipoprotein genes.
3. Genetic variation in human apolipoproteins, identification of aberrant DNA and protein forms in diseases associated with high plasma cholesterol.
4. Post-translational modifications of human apolipoproteins and functional significance.
5. Effect of dietary factors on apolipoproteins as they relate to the pathogenesis of atherosclerosis.

A. Description of Ongoing Research Projects

Lipoproteins are macromolecular complexes of lipids and apolipoproteins, which are involved in cholesterol transport and cholesterol homeostasis. During the past 15 years our laboratory has cloned most of the apolipoprotein cDNAs and/or genes and has described genetic variations in apolipoproteins that are associated with human diseases. We have also identified the regulatory elements which are involved in the regulation of transcription of the apoA-I, apoA-II, apoA-IV, apoB, apoCII and apoCIII genes and several factors bound to them, and have assessed their importance for hepatic and intestinal transcription. Currently, we have two major research objectives:

I. Mechanisms of transcriptional regulation of the apolipoprotein genes *in vivo* and *in vitro*. This includes *a)* elucidation of the role of hormone nuclear receptors and factors bound to the apoCIII enhancer on the transcriptional regulation of the apoA-I, apoCIII, and apoA-IV gene cluster; *b)* elucidation of the importance of the hormone nuclear receptors and apoCIII enhancer for apolipoprotein gene regulation *in vivo* using *in vivo* footprinting, antisense methodologies, and transgenic mice. The combined *in vitro* and *in vivo* approaches may provide new insights on the mechanisms responsible for apolipoprotein gene regulation that may affect the plasma apolipoprotein and lipoprotein levels.

II. Elucidation of the structure-function relationship of human apoA-I and apoE. *a)* by *in vitro* mutagenesis of the corresponding genes and analysis of the properties of the protein products; and *b)* by using transgenic methodologies. ApoA-I is involved in the reverse transport of cholesterol and the activation of the enzyme LCAT. ApoE is responsible for the clearance of lipoprotein remnants and recently has been implicated in Alzheimer's disease. Pertinent questions are: domains of the two

proteins involved in lipid and receptor binding, in activation of enzymes, as well as the role of apoE in the pathogenesis of Alzheimer's disease.

B. Description of Dr. Zannis' Position in the Boston University Cardiovascular Institute Brochure

A Professor of Medicine and Biochemistry, he was recruited to the Whitaker Cardiovascular Institute in 1984 to head the new Section of Molecular Genetics. He has overseen the growth of the section to the current level which includes two associate professors (Dr. Nelson Ruiz-Opazo and Dr. Victoria Herrera), and two assistant professors (Dr. Margarita Hadzopoulou-Cladaras and Dr. Eleni Zanni). Drs. Zannis and Ruiz-Opazo are Established Investigators of the American Heart Association.

Dr. Herrera is a Syntex scholar. Prior to his recruitment to the Institute, Dr. Zannis had made novel contributions in the lipoprotein field which include apolipoprotein synthesis, post-translational modifications and genetic variations, the genetics of apolipoprotein E and its involvement in type III hyperlipoproteinemia, the cloning of cDNAs and/or genes for apoA-I, apoE, and apoCIII. At Boston University, Dr. Zannis, Dr. Cladaras and colleagues completed the cDNA structure of apoB and apoA-IV and have studied the structure and functions of several apolipoproteins and the regulation of expression of their genes.

C. Research Interests in Lay Terms

Lipoproteins are complexes of lipids and proteins that carry cholesterol and other lipids in the bloodstream. The protein components are called apolipoproteins. They are synthesized in our liver and intestine and distribute cholesterol and other lipids to different organs and cells in our body. Their function is to either deliver or remove cholesterol from cells. Some proteins on the cell surface (called receptors) and other proteins (called enzymes) present in our plasma participate in this process. When the apolipoproteins or the receptors or some of the other proteins are changed (mutated), then cholesterol and/or triglycerides accumulate in our bloodstream. This in turn causes clogging of the arteries, atherosclerosis, in human patients and experimental animals.

Dr. Zannis' research has focused on the structure and functions of the proteins that carry cholesterol in the bloodstream. Starting in the late 1970's he characterized changes in some of these proteins (mutations) that are associated with high plasma cholesterol. Subsequently he isolated (cloned) the genes of most of these proteins and he is now studying how these proteins work in a test tube, in human cells, or in the entire animal. He is also studying what controls the synthesis of these proteins. In some instances it is beneficial to increase or decrease the production of some of these proteins to reduce the risk of cardiovascular disease. For instance, high levels of one of these proteins, the apoA-I, protect from atherosclerosis and heart disease. Also, high levels of another protein, the apoE, protect from atherosclerosis, whereas mutations absence of this protein causes very high plasma cholesterol in humans and experimental animals and results in atherosclerosis and heart disease.

Another interesting story is the discovery, back in 1980, that apoE has three major subtypes in humans: the apoE2, apoE3 and apoE4, which are inherited. People who have the apoE2 form are prone to atherosclerosis and heart disease. Surprisingly, people who have the E4 form have three times higher risk than normal in developing Alzheimer's disease. Using test tube and animal experiments, we are trying to figure out how apoE functions normally and how the apoE functions are altered in Alzheimer's disease.

D. Potential Benefit to the Public

1. The discovery of changes (mutations) in proteins, which can cause high plasma cholesterol, permits early diagnosis of the carriers by new protein and DNA tests that are 100% accurate.

2. Some of the new genes that have been isolated may in the near or distant future be used for manufacturing proteins or protein derivatives that have beneficial pharmacological properties or in gene therapy.
3. Understanding how we can control the synthesis of certain proteins, for instance apoA-I and apoE, may lead to the development of new drugs for the prevention and/or treatment of cardiovascular disease.
4. Understanding how apoE functions may help in the development of new drugs for slowing down or the prevention of Alzheimer's disease.

Previous Research Interests:

1. Enzyme mechanisms
2. Enzymology with emphasis on proteolytic enzymes and enzymes of purine metabolism.
3. Human inborn errors of metabolism.

Teaching Experience:

1. 1981 to 1997: I taught in the courses of Advanced Biochemistry (HST141 and Biochemistry 700b) at Harvard Medical School.
2. 1984 to 1999: I taught in undergraduate and graduate courses of Biochemistry and Molecular Biology (ME760, ME766, MED ME556 and GMS BI778) at Boston University Medical School.
3. 1985-1999: I organized and taught the course Molecular Basis of Human Disease and Biochemistry I at University of Crete Medical School.
4. 1994-1997: I taught in the Advanced Medical Genetics Program of Brandeis University

Research Publications

97 original peer-reviewed articles;
32 review and book chapters.

Research Support

Research has been supported throughout the years from the following sources:

- National Institutes of Health (NIH)
- National Science Foundation (NSF)
- American Heart Association (AHA)
- March of Dimes Birth Defects Foundation
- Hood Foundation
- American Egg Board
- American Diabetes Association
- Alzheimer's Association
- Medical Foundation of Boston

Administrative Experience:

- I. **1984-2000.** Organized and directed the Section of Molecular Genetics at Boston University.

Duties: Remodeling of the research laboratories, purchase of equipment, recruitment of junior faculty, establishment of molecular biology facilities and transfer of molecular biology expertise to other research laboratories of the medical school. Currently, the section has one associate professor and two assistant professors with independent funding. All three faculty have obtained career awards from the American Heart Association. The total research funds of the section exceed \$500,000 per year and the support by the university has been approximately \$30,000-50,000 per year.

The core laboratories for molecular and cellular biology were established with NIH funding for facilities and equipment. The facilities include tissue culture laboratories, fully equipped molecular biology laboratories, a DNA synthesizer and a peptide synthesizer and an *in situ* hybridization facility.

- II. **1985-1998.** Designed the research laboratories of the University of Crete School of Medicine in collaboration with the German architect, Professor Walter Gabelman in 1985. The laboratories have a total of 60,000 square feet of space and include core facilities and individual laboratories. I have participated in the Recruitment and Promotion Committee of approximately 80 faculty of different ranks to date in the medical school during the 1985-1998 period.

Bibliography:

Original Reports:

1. **Zannis VI**. Ph.D. Thesis (1975) Investigations of the mechanism of action of chymotrypsin and papain. University of California, Berkeley, 1975.
2. **Zannis VI**, D Doyle, DW Martin Jr. (1978) Purification and characterization of human purine nucleoside phosphorylase. *J. Biol. Chem.* 253:504-510.
3. **Zannis VI**, JF Kirsch (1978) Effects of substituents on the rates of deacylation of substituted benzoyl papains. Role of the carboxylate residue in the catalytic mechanism. *Biochem.* 17:2669-2674.
4. Gudas LJ, **VI Zannis**, SM Clift, AJ Amman, GEJ Staal, DW Martin Jr. (1978) Characterization of mutant subunits of purine nucleoside phosphorylase. *J. Biol. Chem.* 253:8916-8924.
5. **Zannis VI**, LJ Gudas, DW Martin Jr. (1979) Characterization of the subunit of purine nucleoside phosphorylase from cultured normal human fibroblasts. *Biochem. Genet.* 17:621-630.
6. **Zannis VI**, LJ Gudas, DW Martin Jr. (1980) Characterization of the subunit composition of hypoxanthine-guanine phosphoribosyl transferase from human erythrocytes and cultured fibroblasts. *Biochem. Genet.* 18:1-19.
7. **Zannis VI**, JL Breslow (1980) Characterization of a unique human apolipoprotein E variant associated with type III hyperlipoproteinemia. *J. Biol. Chem.* 255:1759-1762.
8. **Zannis VI**, JL Breslow, AJ Katz (1980) Isoproteins of human apolipoprotein A-I demonstrated in plasma and intestinal organ culture. *J. Biol. Chem.* 255:8612-8617.
9. **Zannis VI**, PW Just, JL Breslow (1981) Human apolipoprotein E isoprotein subclasses are genetically determined. *Am. J. Hum. Genet.* 33:11-24.
10. **Zannis VI**, JL Breslow (1981) Human VLDL apoE isoprotein polymorphism is explained by genetic variation and post-translational modifications. *Biochem.* 20:1033-1041.
11. **Zannis VI**, JL Breslow, TR SanGiacomo, DP Aden, BB Knowles (1981) Characterization of the major apolipoproteins secreted by two hepatoma cell lines. *Biochem.* 20:7089-7096.
12. **Zannis VI**, D Kurnit, JL Breslow (1982) Hepatic apoA-I and apoE and intestinal apoA-I are synthesized in precursor isoprotein forms by organ cultures of human fetal tissues. *J. Biol. Chem.* 257:536-544.
13. **Zannis VI**, AM Lees, RS Lees, JL Breslow (1982) Abnormal apoA-I isoprotein composition in patients with Tangier disease. *J. Biol. Chem.* 257:4978-4986.
14. **Zannis VI**, JL Breslow, G Utermann, RW Mahley, KH Weisgraber, RJ Havel, JL Goldstein, MS Brown, G Schonfeld, WR Hazzard, CB Blum (1982) Proposed nomenclature of apoE isoprotein genotypes and phenotypes. *J. Lipid. Res.* 23:911-914.
15. Breslow JL, **VI Zannis**, TR SanGiacomo, JLHC Third, T Tracy, CJ Glueck (1982) Studies of familial type III hyperlipoproteinemia using as a genetic marker the apoE phenotype E2/2. *J. Lipid Res.* 23:1224-1235.
- 15a. Chirgwin JM, AE Przybyla, RJ MacDonald, WJ Rutter. 1979. *Biochemistry* 18:5294-5299.
- 15b. Thomas, P. 1983. *Methods Enzymol.* 100:255-266.
16. Breslow JL, D Ross, J McPherson, HW Williams, D Kurnit, A Nussbaum, SK Karathanasis, **VI Zannis** (1982) *Proc. Natl. Acad. Sci. USA* 79:6861-6865.
17. Breslow, J.L., J. McPherson, A.L. Nussbaum, H.W. Williams, F. Lofquist-Kahl, S.K. Karathanasis and V.I. Zannis (1983) Identification and DNA sequence of a human apolipoprotein E cDNA clone. *J. Biol. Chem.* 257:14639-14641 and 258:11422.
18. Karathanasis, S.K., R.A. Norum, V.I. Zannis and J.L. Breslow (1983) An inherited polymorphism in the human apolipoprotein A-I gene locus related to the development of atherosclerosis. *Nature* 301:718-720.

19. Zannis, V.I., S.K. Karathanasis, H. Keutmann, G. Goldberger and J.L. Breslow (1983) Intracellular and extracellular processing of human apoA-I. Secreted apoA-I isoprotein 2 is a propeptide. *Proc. Natl. Acad. Sci.* 80:2574-2578.
20. Fisher, E.A., C. Blum, V.I. Zannis and J.L. Breslow (1983) Independent effects of dietary saturated fat and cholesterol on plasma lipids, lipoproteins and apoE. *J. Lipid Res.* 24:1039-1048.
21. Karathanasis, S.K., J. McPherson, V.I. Zannis and J.L. Breslow (1983) Linkage of human apolipoprotein A-I and C-III genes. *Nature* 304:371-373.
22. Karathanasis, S.K., V.I. Zannis and J.L. Breslow (1983) Isolation and characterization of the human apolipoprotein A-I gene. *Proc. Natl. Acad. Sci.* 80:6147-6151.
23. Karathanasis, S.K., V.I. Zannis and J.L. Breslow (1983) A DNA insertion has occurred in the apolipoprotein A-I gene of patients with premature atherosclerosis. *Nature* 305:823-825.
24. Zannis, V.I., J. McPherson, G. Goldberger, S.K. Karathanasis and J.L. Breslow (1984) Synthesis, intracellular processing and signal peptide of human apoE. *J. Biol. Chem.* 259:5495-5499.
25. Nicolosi, R.J. and V.I. Zannis (1984) Apolipoprotein A-I of primates. *J. Lipid Res.* 25:879-887.
26. Karathanasis, S.K., V.I. Zannis and J.L. Breslow (1985) Isolation and characterization of two human apoC-III cDNA clone alleles. *J. Lipid Res.* 26:451-456.
27. Zannis, V.I., S.F. Cole, C. Jackson, D.M. Kurnit and S.K. Karathanasis (1985) Distribution of apoA-I, apoC-II, apoC-III and apoE mRNA in human tissues, time dependent induction of apoE mRNA by cultures of human monocyte-macrophages. *Biochemistry* 24:4450-4455.
28. Zannis, V.I., R.J. Nicolosi, E. Jensen, K.C. Hayes and J.L. Breslow (1985). Plasma and hepatic apoE isoproteins of nonhuman primates. Differences in apoE among human and new and old world monkeys. *J. Lipid Res.* 26:1421-1430.
29. Zannis, V.I., J.M. Ordovas, C. Cladaras, F.S. Cole, G. Forbes and E.J. Schaefer (1985) mRNA and apolipoprotein E synthesis abnormalities in peripheral blood monocyte macrophages in familial apolipoprotein E deficiency. *J. Biol. Chem.* 260:12891-12894.
30. Zanni, E.E., Z.F. Stephan, V.I. Zannis, J.L. Breslow and K.C. Hayes (1986) ApoE distribution in lipoproteins of Rhesus monkeys is modulated by dietary fat and cholesterol. *J. Nutrition* 116:1611-1619.
31. Karathanasis, S.K., I. Yunis and V.I. Zannis (1986) Structure, evolution and tissue-specific synthesis of human apolipoprotein A-IV. *Biochemistry* 25:3962-3970.
32. Zannis, V.I., J. vanderSpek and D. Silverman (1986) Intracellular modifications of human apolipoprotein E. *J. Biol. Chem.* 261:13415-13421.
33. Cladaras, C., M. Hadzopoulou-Cladaras, R. Avila, A. Nussbaum, R. Nicolosi and V.I. Zannis (1986) cDNA derived structure of a amino terminal domain of human apoB and size of apoB mRNA transcript. *Biochemistry* 25:5351-5357.
34. Cladaras, C., M. Hadzopoulou-Cladaras, R.T. Nolte, D. Atkinson and V.I. Zannis (1986) The complete sequence and structural analysis of human apolipoprotein B-100: Relationship between apoB-100 and apoB-48 forms. *The EMBO J.* 5:3495-3508.
35. Cladaras, C., M. Hadzopoulou-Cladaras, B. Felber, G. Pavlakis and V.I. Zannis (1987) The molecular basis of a familial apoE deficiency: an acceptor splice site mutation in the third intron of the deficient apoE gene. *J. Biol. Chem.* 262:2310-2315.
36. Zanni, E.E., V.I. Zannis, C. Blum, P. Herbert and J.L. Breslow (1987) Effect of egg cholesterol and dietary fats on plasma lipids, lipoproteins and apoproteins of human subjects fed natural diets. *J. Lipid Research* 28:518-527.
37. Makrides, S.C., N. Ruiz-Opazo, M. Hayden, A.L. Nussbaum, J.L. Breslow and V.I. Zannis (1988) Sequence and expression of Tangier apoA-I gene. *Eur. J. Biochem.* 173:465-471.

38. Ruiz-Opazo, N. and V.I. Zannis (1988) Expression of the human apolipoprotein A-I gene in rat myogenic L6E9 cells. DNA methylation and regulation of gene activity. *J. Biol. Chem.* 263:1739-1744.
39. Lenich, C., P. Brecher, S. Makrides, A. Chobanian and V.I. Zannis (1988) Apolipoprotein gene expression in the rabbit: abundance, size and distribution of apolipoprotein mRNA species in different tissues. *J. Lipid Res.* 29:755-764.
40. Hussain, M.M., N.L.R. Bucher, B. Faris, C. Franzblau and V.I. Zannis (1988) Tissue-specific post-translational modification of rat apoE synthesis of sialated apoE forms by neonatal rat aortic smooth muscle cells. *J. Lipid Res.* 29:915-923.
41. Mavrothalassitis, G., G. Tzimagiorgis, S.A. Mitsialis, V.I. Zannis, A. Plaitakis, J. Papamatheakis and N. Moschonas (1988) Isolation and characterization of cDNA clones encoding for human liver glutamate dehydrogenase: evidence for a small gene family. *Proc. Natl. Acad. Sci. USA* 85:3494-3498.
42. Roghani, A. and V.I. Zannis (1988) Alterations of the Gln residues of human proapoA-I by in vitro mutagenesis. Characterization of the normal and mutant protein forms. *Biochemistry* 27:7428-7435.
43. Roghani, A. and V.I. Zannis (1988) Mutagenesis of the glycosylation sites of human apoCIII: O-linked glycosylation is not required for apoCIII secretion and lipid binding. *J. Biol. Chem.* 263:17925-17932.
44. Makrides, S.C., R. Mulinari, V.I. Zannis and H. Gavras (1988) Regulation of renin gene expression in hypertensive rats. *Hypertension* 12:405-410.
45. Plaitakis, A., N. Moschonas, J. Papamatheakis and V.I. Zannis (1988) Glutamate dehydrogenase isoforms in the cerebellum of control subjects and patients with neurodegenerative disorders. DNA evidence for multiple gene encoding for human glutamate dehydrogenase. *Ann. Neurol.* 24:147-148.
46. Hussain, M.M., E.E. Zanni, M. Kelly and V.I. Zannis (1989) Synthesis, modification and flotation properties of rat hepatocyte apolipoproteins. *Biochim. Biophys. Acta* 101:90-101.
47. Zanni, E.E., A. Kouvatzi, M. Hadzopoulou-Cladaras, M. Krieger and V.I. Zannis (1989) Expression of apoE gene in Chinese hamster cells with a reversible defect in O-glycosylation. Glycosylation is not required for apoE secretion. *J. Biol. Chem.* 264:9137-9140.
48. Hussain, M.M. and V.I. Zannis (1989) Characterization of glutamate dehydrogenase isoproteins purified from the cerebellum of normal subjects and patients with degenerative neurological disorders and from human neoplastic cell lines. *J. Biol. Chem.* 264:20730-20735.
49. Hussain, M.M. and V.I. Zannis (1990) Intracellular modification of human apolipoprotein A-II (apoA-II) and sites of apoA-II mRNA synthesis: Comparison of apoA-II with apoCII and apoCIII isoproteins. *Biochemistry* 29, 209-217.
50. Flordellis, C.S., M. Castellano, R. Franco, V.I. Zannis and H. Gavras (1990) Expression of multiple $\alpha 2$ adrenoceptor-like mRNA species in rat tissues. *Hypertension* 15:881-887.
51. Bresnahan, M.R., C.S. Flordellis, D.K. Vassilatis, S.C. Makrides, V.I. Zannis and H. Gavras (1990) Expression of human alpha-2A adrenergic receptors in stable mouse C127 cell clones differing in the predominant mechanism of effector coupling. *Biochim. Biophys. Acta* 1052:439-445.
52. Kardassis, D., M. Hadzopoulou-Cladaras, D.P. Ramji, R. Cortese, V.I. Zannis and C. Cladaras (1990) Characterization of the promoter elements required for hepatic and intestinal interaction of the human apoB gene definition of the DNA binding site of a tissue specific transcriptional factor. *Mol. Cell. Biol.* 10:2653-2659.
53. Ogami, K., M. Hadzopoulou-Cladaras, C. Cladaras and V.I. Zannis (1990). Promoter elements required for hepatic and intestinal transcription of the human apoCIII gene. *J. Biol. Chem.* 265:9808-9815.
54. Kardassis, D., V.I. Zannis and C. Cladaras (1990) Purification and characterization of the nuclear factor BA1: A transcriptional activator of the human apoB gene. *J. Biol. Chem.* 265:21733-21740.

55. Hussain, M.M., A. Roghani, C. Cladaras, E.E. Zanni and V.I. Zannis (1991) Secretion of lipid poor nascent human apoA-I, apoCIII and apoE by cell clones expressing the corresponding genes. *Electrophoresis* 12:273-283.
56. Lenich, C.M., A.V. Chobanian, P. Brecher and V.I. Zannis (1991) Effect of dietary cholesterol and alloxan-diabetes on tissue cholesterol and apolipoprotein E mRNA levels in the rabbit. *J. Lipid Res.* 32:431-438.
57. Flordellis, C.S., D.E. Handy, M.R. Bresnahan, V.I. Zannis and H. Gavras (1991) Cloning and expression of a rat brain α_{2B} adrenergic receptor (α_2 adrenergic receptor subtypes/cDNA/[3 H] rauwolscine/antisense mRNA). *Proc. Natl. Acad. Sci. USA* 88:1019-1023.
58. Papazafiri, P., K. Ogami, D.P. Ramji, A. Nicosia, P. Monaci, C. Cladaras and V.I. Zannis (1991) Promoter elements and factors involved in hepatic transcription of the human apoA-I gene: Positive and negative regulators bind to overlapping sites. *J. Biol. Chem.* 266:5790-5797.
59. Ogami, K., D. Kardassis, C. Cladaras and V.I. Zannis (1991) Purification and characterization of a heat stable nuclear factor CIIB1 involved in the regulation of the human apoCIII gene. *J. Biol. Chem.* 266:9640-9646.
60. Herscovitz, H., M. Hadzopoulou-Cladaras, M.T. Walsh, C. Cladaras, V.I. Zannis and D.M. Small (1991) The expression, secretion and lipid binding characteristics of the Nterminal 17% of apolipoprotein B (apoB-17). *Proc. Natl. Acad. Sci. USA* 88:7313-7317.
61. Chambaz, J., P. Cardot, D. Pastier, V.I. Zannis and C. Cladaras (1991) Promoter elements and factors required for hepatic transcription of the human apoA-II gene. *J. Biol. Chem.* 266:11676-11685.
62. Cardot, P., J. Chambaz, C. Cladaras and V.I. Zannis (1991) ApoA-II gene regulation by the cooperation of factors binding to the proximal and distal regulatory elements. *J. Biol. Chem.* 266:24460-24470.
63. Kardassis, D., V.I. Zannis and C. Cladaras (1991) Organization of the regulatory elements and nuclear activities participating in the transcriptional activation of the human apoB gene. *J. Biol. Chem.* 267:2622-2632.
64. Herscovitz, H., D. Gantz, A.M. Tercyak, V.I. Zannis and D.M. Small (1992) Expression of human apolipoprotein E but not that of apolipoprotein A-I by mouse C127 cells is associated with increased lipid secretion. The secretion lipids are in the form of vesicles and discs. *J. Lipid Res.* 33:791-803.
65. Minnich, A., X. Collet, A. Roghani, C. Cladaras, R.L. Hamilton, C.J. Fielding and V.I. Zannis (1992) Site-directed mutagenesis and structure-function analysis of the human apolipoprotein A-I: relation between LCAT activation and lipid binding. *J. Biol. Chem.* 267:16553-16560.
66. Ladas, J.A.A., M. Hadzopoulou-Cladaras, D. Kardassis, P. Cardot, J. Cheng, V.I. Zannis and C. Cladaras (1992) Transcriptional regulation of human apolipoprotein genes apoB, apoCIII and apoA-II by members of the steroid hormone receptor superfamily HNF-4, ARP-1, EAR-2 and EAR-3. *J. Biol. Chem.* 267:15849-15860.
67. Cardot, P., J. Chambaz, D. Kardassis, C. Cladaras and V.I. Zannis (1993) Factors participating in the liver-specific expression of the human apoA-II gene and their significance for transcription. *Biochemistry* 32:9080-9093.
68. Kritis, A.A., E. Ktistaki, D. Barda, V.I. Zannis and I. Talianidis (1993) An indirect negative autoregulatory mechanism involved in hepatocyte nuclear factor-1 gene expression. *Nucl. Acids Res.* 21:5882-5889.
69. Lopez, J., A. Roghani, J. Bertrand, E.E. Zanni, A. Kalopissis, V.I. Zannis and J. Chambaz (1994) Intracellular early and late modifications of human apolipoprotein A-II. Effect of glutamine+1 to leucine substitution. *Biochemistry* 33:4056-4064.
70. Ktistaki, E., J.M. Lacorte, N. Katrakili, V.I. Zannis and I. Talianidis. (1994) Transcriptional regulation of the apolipoprotein A-IV gene involves synergism between a proximal hormone

- response element and a distant enhancer located in the upstream promoter region of the apolipoprotein C-III gene. *Nucl. Acids Res.* 22:4689-4696.
71. Cardot, P., D. Pastier, J.M. Lacorte, M. Mangeney, V.I. Zannis and J. Chambaz. (1994) Purification and characterization of nuclear factors binding to the negative regulatory element D of human apolipoprotein A-II promoter: A negative regulatory effect is reversed by GABP, an Ets-related protein. *Biochemistry* 33:12139-12148.
 72. Herscovitz, H., A. Kritis, I. Talianidis, E. Zanni, V. Zannis and D.M. Small. (1995) Non-hepatic cells secrete the N-terminal 41% of apoB on HDL-sized lipoproteins containing triacylglycerol-rich core. *Proc. Natl. Acad. Sci.* 92:659-663.
 73. Talianidis, I., A. Tambakaki, J. Toursounova and V.I. Zannis. (1995) Complex interactions between SP1 bound to multiple distal regulatory sites and HNF-4 bound to the proximal promoter leads to the transcriptional activation of the liver-specific human apoCIII gene. *Biochemistry* 34:10298-10309.
 74. Tzamelis, I. and V.I. Zannis. (1996) Binding specificity and modulation of the apoA-I promoter activity by homo- and heterodimers of nuclear receptors. *J. Biol. Chem.* 271:8402-8415.
 75. Kritis, A.A., A. Argyrokastritis, S. Power, S. Cereghini, N. Katrakili, N.K. Moschonas, V.I. Zannis and I. Talianidis. (1996) Isolation and characterization of a third isoform of human hepatocyte nuclear factor 4. *Gene* 173:275-280.
 76. Kardassis, D., M. Laccotripe, I. Talianidis, and V.I. Zannis. (1996) Transcriptional regulation of the genes involved in lipoprotein transport. The role of proximal promoters and long range regulatory elements and factors in apolipoprotein gene region. *Hypertension* 27:980-1008.
 77. Kardassis, D., I. Tzamelis, M. Hadzopoulou-Cladaras, I. Talianidis and V.I. Zannis. (1997) Distal apoCIII regulatory elements F to J act as a general modular enhancer for proximal promoters that contain hormone response elements: Synergism between HNF-4 molecules bound to the proximal promoter and distal enhancer sites. *Arterioscler. Thromb. Vasc. Biol.* 17:222-232.
 78. Hatzivassiliou, E., P. Cardot, V.I. Zannis, and S.A. Mitsialis. (1997) Ultraspiracle, a *Drosophila* retinoic X receptor α homologue, can mobilize the human thyroid hormone receptor to transactivate a human promoter. *Biochemistry* 36:9221-9231.
 79. Laccotripe, M., S.C. Makrides, A. Jonas, and V.I. Zannis. (1997) The carboxyl-terminal hydrophobic residues of apolipoprotein A-I affect its rate of phospholipid binding and its association with high-density lipoprotein. *J. Biol. Chem.* 272:17511-17522.
 80. Aleshkov, A., C.R. Abraham, and V.I. Zannis. (1997) Interaction of nascent apoE2, apoE3, and apoE4 isoforms expressed in mammalian cells with amyloid peptide β (1-40). Relevance to Alzheimer's disease. *Biochemistry* 36:10571-10580.
 81. Xu, S., M. Laccotripe, X. Huang, A. Rigotti, V.I. Zannis, and M. Krieger. (1997) Apolipoproteins of HDL can directly mediate binding to the scavenger receptor SR-B1, an HDL receptor that mediates selective lipid uptake. *J. Lipid Res.* 38:1289-1298.
 82. Lacorte, J.-M., E. Ktistaki, A. Beigneux, V.I. Zannis, J. Chambaz, and I. Talianidis. (1997) Activation of CAAT enhancer binding protein δ (C/EBP δ) by interleukin-1 negatively influences apolipoprotein CIII expression. *J. Biol. Chem.* 272:23578-23584.
 83. Vorgia, P., V.I. Zannis, and D. Kardassis. (1998) A short proximal promoter and the distal hepatic control region-1 (HCR-1) contribute to the liver-specific expression of the human apoCII gene *in vitro*. Tissue specific enhancement by HCR-1 requires two proximal hormone response elements which have different binding specificities for orphan receptors HNF-4, ARP-1 and EAR-2. *J. Biol. Chem.* 273:4188-4196.
 84. Kardassis, D., E. Saccharidou and V.I. Zannis. (1998) Transactivation of the human apoCII promoter by orphan and ligand-dependent nuclear receptors. The regulatory element CIIC is a thyroid hormone response element. *J. Biol. Chem.* 273:17810-17816.

85. Hadzopoulou-Cladaras, M., S.N. Lavrentiadou, V.I. Zannis, and D. Kardassis. (1998) Transactivation of the ApoCIII promoter by ATF-2 and repression by members of the Jun family. *Biochemistry* 37:14078--14087
86. Lavrentiadou, SN., M. Hadzopoulou-Cladaras, D Kardassis and V.I. Zannis. (1999) Binding specificity and modulation of the human apoCIII promoter activity by heterodimers of ligand-dependent nuclear receptors. *Biochemistry* 38:964-975.
87. Pissios, P., H.-Y. Kan, S. Nagaoka, and V.I. Zannis. (1999) SREBP-1 binds to multiple sites and transactivates the human apoA-II promoter *in vitro*: SREBP-1 mutants defective in DNA binding or transcriptional activation repress the apoA-II promoter activity. *Arteriosclerosis, Thrombosis & Vascular Biology* 19:1456-1469.
88. Le Beyec, J., V. Chaffeton, H.-Y. Kan, P.-L. Janvier, C. Cywiner, F.-P Chatelet, A.D. Kalopissis, V. Zannis, J. Chambaz, M. Pinçon-Raymond and P. Cardot. (1999) The intergenic sequence -700/-310 upstream of the apoA-IV promoter and the -890/-520 apoCIII enhancer are sufficient to restrict gene expression in intestinal villus enterocytes along the cephalo-caudal and crypt-villus axis. *J. Biol. Chem.* 274:4954-4961.
89. Kan, H.-Y., P. Pissios, J. Chambaz, and V.I. Zannis. (1999) DNA binding specificity and transactivation properties of SREBP-2 bound to multiple sites on the human apoA-II promoter. *Nucl. Acids Res.* 27:1104-1117.
90. Aleshkov, S.B., X. Li, S.N. Lavrentiadou, and V.I. Zannis. (1999) Contribution of cysteine 158, the glycosylation site theonine 194, the amino- and carboxy-terminal domains of apolipoprotein E in the binding to amyloid peptide β (1-40). *Biochemistry* 38:8918-8925.
91. Liadaki, K.N., T. Liu, S. Xu, B.Y. Ishida, P.N. Duchateaux, J.P. Krieger, J. Kane, M. Krieger, V.I. Zannis. (2000) Binding of high density lipoprotein (HDL) and discoidal reconstituted HDL to the HDL receptor scavenger receptor class B type I. *J. Biol. Chem.* 275: 21262-21271
92. Kardassis, D., K. Pardali, V.I. Zannis. (2000) SMAD proteins transactivate the human apoCIII promoter by physically and functionally interacting with hepatocyte nuclear factor 4. *J. Biol. Chem.* 275:41405-41414
93. Kan HY, S Georgopoulos, VI Zannis. (2000) A hormone response element in the human apoCIII enhancer is essential for intestinal expression of the apoA-I and apoCIII genes and contributes to the hepatic expression of the two linked genes in transgenic mice. *J. Biol. Chem.*275:30423-30431.
94. Gorshkova, I.N., K. Liadaki, O. Gursky, D. Atkinson, V.I. Zannis. (2000) Probing the lipid-free structure and stability of apolipoprotein A-I by mutation. *Biochemistry* (submitted).
95. Kvdreos. K.E., K.W. van Diik. A. van der Zee. L.M. Havekes. V.I. Zannis. 2000. Domains of apolipoprotein E contributing to triglyceride and cholesterol homeostasis *in vivo*. *J. Clin. Invest.* (submitted)
96. Carraway M, H Herscovitz, V Zannis, DM Small. 2000. Specificity of lipid incorporation is determined by sequences in the N-terminal 37% of apoB. *Biochemistry* (in press)
97. Georgopoulos S, HY Kan, VI Zannis. 2000. The SP1 sites of the apoCIII promoter are required for the expression of the apoCIII gene as well as the intestinal expression of the apoE-I gene in transgenic mice. *Nucl. Acids Res.* 28:4919-4929
98. Herscovitz H, A Derksen, MT Walsh, CJ McKnight, DL Gantz, M Hadzopoulou-Cladaras, V Zannis, C Curry, DM Small. 2001. The N-terminal 17% of apoB binds tightly and irreversibly to emulsions modeling nascent very low density lipoproteins. *J. Lipid Res.* 42:51-59.

Reviews and Book Chapters:

1. Zannis, V.I., L.J. Gudas, D. Doyle and D.W. Martin, Jr. (1977) Purification and characterization of hypoxanthine-guanine phosphoribosyl transferase from cultured HTC cells. *Purine Metabolism in Man - Second Internal Symposium, Vienna.* New York: Plenum Press. 76A:162-171.

2. Zannis, V.I. and D.W. Martin, Jr. (1978) Use of two-dimensional gel electrophoresis for detection of post-translational protein modifications and in the study of genetic protein variants. Investigations of purine nucleoside phosphorylase and hypoxanthine-guanine phosphoribosyl transferase. In: Catsimpoolas, N., ed. *Electrophoresis*. Amsterdam: Elsevier North Holland. pp. 305-322.
3. Zannis, V.I. and J.L. Breslow (1980) Two-dimensional maps of human apolipoproteins in normal and diseased states. In: Radola, B.J., ed. *Electrophoresis*. Berlin, New York: Walter de Gruyter, Inc. pp. 437-473.
4. Breslow, J.L. and V.I. Zannis (1980) Biochemical and genetic studies of human apolipoprotein E. In: Fumagalli, R., Kritchevsky, D., Paoletti, R., eds. *Drugs affecting lipid metabolism*. Amsterdam: Elsevier/North Holland, pp. 61-71.
5. Zannis, V.I. and J.L. Breslow (1982) Apolipoprotein E. *Molecular and Cellular Biochemistry*. pp. 3-20.
6. Zannis, V.I., V. Rooney, P. Fraser and J.L. Breslow (1983) Use of electrophoretic techniques for detection of molecular defects of lipoprotein metabolism. In: Lewis, L.A., ed. *CRC Handbook of Electrophoresis*. Volume III. pp. 319-348.
7. Breslow, J.L., S.K. Karathanasis and V.I. Zannis (1983) Isolation of a cDNA clone for human apolipoprotein E. *NHLBI Workshop*. 136-147.
8. Zannis, V.I. and J.L. Breslow (1985) Genetic mutation affecting human lipoprotein metabolism. *Advances in Human Genetics*. 14:125-215 and 383-386.
9. Breslow, J.L. and V.I. Zannis (1986) Genetic variation in apolipoprotein E and type III hyperlipoproteinemia. *Arteriosclerosis Review*, Vol. 14 (A. Gotto and R. Paoletti, eds.), pp. 119-141.
10. Zannis, V.I. (1986) The molecular basis of beta thalassemia in: *Thalassemia: An Interdisciplinary Approach* (J.T. Chirban, ed.) University Press of America. pp. 59-77.
11. Zannis, V.I. (1986) Genetic polymorphism in human apolipoprotein E. *Methods in Enzymology* 128:823-851.
12. Karathanasis, S.K., V.I. Zannis and J.L. Breslow (1986) Characterization of the apolipoprotein A-I/C-III gene complex. *Methods in Enzymology*. 128:712-726.
13. Zannis, V.I., S.K. Karathanasis and J.L. Breslow (1986) Intra- and extracellular modifications in apolipoproteins. *Methods in Enzymology* 128:690-712.
14. Karathanasis, S.K., E. Salmon, I.A. Haddad and V.I. Zannis (1985) Nucleotide and corresponding amino acid sequences of human apoA-I, apoA-II, apoC-I, apoCII, apoCIII and apoE cDNA clones. In: *Biochemistry and Biology of Plasma Proteins* (A. Scanu and A. Spector, eds.), Vol. 11. pp. 475-493.
15. Zannis, V.I., M.M. Hussain, M. Hadzopoulou-Cladaras, A. Kouvatsi, D. Kardassis and C. Cladaras (1988) Molecular biology of human apolipoprotein B and related diseases. In: *Eicosanoids, Apolipoproteins, Lipoprotein Particles and Atherosclerosis*. Plenum Publishing Corporation (C.L. Malmendier and P. Alaupovic, eds.), pp. 107-121.
16. Zannis, V.I. (1989) Molecular biology of human apolipoproteins B and E and associated diseases of lipoprotein metabolism. In: *Advances in Lipid Research* Vol. 23, pp. 1-64, Academic Press, San Diego, CA.
17. Zannis, V.I., D. Kardassis, K. Ogami, M. Hadzopoulou-Cladaras and C. Cladaras (1990) Transcriptional regulation of the human apolipoprotein genes. In: *Advances in Experimental Medicine and Biology* (C.L. Malmendier, P. Alaupovic and Brewer, B.H., eds.), 285:1-23.
18. Zannis, V.I., C. Cladaras and E.E. Zanni (1991) Apolipoprotein and lipoprotein synthesis and modifications. *Current Opinion in Lipidology* 2:149-155.
19. Zannis, V.I., D. Kardassis, P. Cardot, M. Hadzopoulou-Cladaras, E.E. Zanni and C. Cladaras (1992) Molecular biology of the human apolipoprotein genes: Gene regulation and structure/function relationship. *Current Opinion in Lipidology* 3:96-113.

20. Zannis, V.I., D. Kardassis and E.E. Zanni (1993) Genetic mutations affecting human lipoproteins, their receptors and their enzymes. *Adv. Hum. Genetics* (H. Harris and K. Hirschorn, eds.) Plenum Press, NY. Vol. 21, pp. 145-319.
21. Zannis, V.I. and D. Kardassis (1992) Human apolipoprotein CI. *Human Protein Data*, VCH Publisher, A. Haerberli, ed., pp. 47-49.
22. Zanni, E. and V.I. Zannis (1992) Human apolipoprotein CII. *Human Protein Data*, VCH Publisher, A. Haerberli, ed., pp. 51-53.
23. Zannis, V.I., Cardot, P., Cladaras, C., Zanni, E., Chambaz, J., Talianidis, I., Zannis, V.I. and Kardassis, D. (1994) Transcriptional regulation of the human apolipoprotein genes. In: *Liver Gene Expression* (F. Tronche and M. Yaniv, eds.) R.G. Landes Biomedical Publishers, Austin, TX USA pp. 63-85.
24. Zannis, V., C. Cladaras and I. Talianidis (1995) Role of the hormone response elements (HRE) and the apoCIII enhancer in the transcriptional regulation of the genes involved in lipid transport. *Xth International Symposium on Atherosclerosis. Atherosclerosis* (F.P. Woodford, J. Davignon, A. Sniderman, eds.) Elsevier Publishing Company, pp. 400-408.
25. Zannis, V.I., M. Laccotripe, S.C. Makrides, D. Kardassis and E. Zanni (1996) Genetic factors contributing to cardiovascular disease. The role of apolipoproteins and their receptors. In: *Vascular Endothelium: Responses to Injury*. NATO ASI Series (J.D. Catravas, A.D. Callow and U.S. Ryan, eds.) Series A: Life Sciences, Vol. 281, pp. 69-128.
26. Kardassis, D., M. Laccotripe, I. Talianidis and V.I. Zannis. (1996) Transcriptional regulation of the genes involved in lipoprotein transport. The role of proximal promoters and long range regulatory elements and factors in apolipoprotein gene region. *Hypertension* 27:980-1008.
27. Zannis, V.I., E.E. Zanni, S.C. Makrides, D. Kardassis and S. Aleshkov. 1998. Role of apolipoprotein E in Alzheimer's disease. In: *NATO ASI Series, Life Sciences* (J.D. Catravas, ed.) Plenum Press, N.Y. 294:179-209.
28. Zannis, V.I. and J. Cohen. 2000. Old and new players in the lipoprotein system. *Current Opinion in Lipidology* 11:101-103.
29. Segrest, J.P., L. Li, G.M. Anantharamaiah, S.C. Harvey, K.N. Liadaki and V.I. Zannis. 2000. Structure and function of apolipoprotein A-I and high-density lipoprotein. *Current Opinion in Lipidology* 11:105-115.
30. Zannis, V.I., H.-Y. Kan, A. Kritis, E.E. Zanni and D. Kardassis. 2001. Transcriptional regulatory mechanisms of the human apolipoprotein genes *in vitro* and *in vivo*. *Current Opinion in Lipidology* 12:181-207.
31. Zannis, V.I., H.-Y. Kan, S. Georgopoulos, E.-M. Novak and D. Kardassis. 2001. Transcriptional regulation of pro- and anti-atherogenic genes. In: *Vascular Endothelium: Source and Target of Inflammatory Mediators* NATO ASI Series: Life Sciences (Catravas, J.D., A.D. Callow and U.S. Ryan, eds.) (in press)
32. Zannis, V.I., H.-Y. Kan, A. Kritis, E. Zanni and D. Kardassis. 2001. Transcriptional regulation of the human apolipoprotein genes. *Frontiers in Bioscience* (D. Hui, ed.) (in press).