

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.

Photocopy this page or follow this format for each person.

NAME Christos S. Mantzoros, M.D.		POSITION TITLE Assistant Professor of Medicine, Harvard Medical School	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Athens University Medical School, Athens, Greece	M.D.	1989	Medicine
Athens University Medical School, Athens, Greece.	Sc.D.	1996	Medicine- Clinical Epidemiology
Harvard School of Public Health, Boston, MA	M.Sc.	1997	Clinical Epidemiology
Harvard Medical School, Boston, MA	M.M.Sc.	1997	Medical Sciences in Clinical Investigation

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

Professional Positions:

- 1990-1993 Intern, Junior and Senior Resident, Internal Medicine, Wayne State University, Program A, Detroit, MI
- 1993-1994 Clinical Fellow, in Endocrinology, Diabetes and Metabolism, Longwood Medical Area / Harvard Medical School Training Program, Boston, MA
- 1994-1996 Clinical and Research Fellow in Endocrinology, Diabetes and Metabolism, Longwood Medical Area / Harvard Medical School Training Program, Boston, MA
- 1995-1997 Clinical Investigator Training Program, Harvard Medical School / Massachusetts Institute of Technology, Division of Health Sciences and Technology.
- 1995-present Assistant in Medicine, Department of Internal Medicine, Mac Lean Hospital - Massachusetts General Hospital
- 1996-present Associate in Medicine, Beth Israel Deaconess Medical Center
- 1998-present Clinical Investigator, Beth Israel Deaconess Medical Center and Massachusetts Institute of Technology, General Clinical Research Center
- 2000-present Program Director, in Endocrinology, Diabetes and Metabolism, Beth Israel Deaconess Medical Center and Joslin Diabetes Center.

Awards and Other Professional Activities:

- 1984-1987 Papadakis Scholarship, Athens University, Athens, Greece
- 1985, 1986 German Foundation for Academic Exchanges (Deutscher Akademischer Austausch Dienst)
- 1994 American College of Physicians: Clinical Research Award, National Annual Meeting, Miami, FL
- 1995 CITP Award, Harvard / MIT, Division of Health Sciences and Technology
- 1996 10th International Congress of Endocrinology: Merck Senior Fellows Award, San Francisco, CA
- 1996 OHEP Certificate of Excellence in Medical Research (first place), Rochester, MI
- 1996 A. S. Onassis Award, Athens, Greece
- 1996 Advisory Committee on body composition, Food and Drug Administration, Washington, DC
- 1997 Clinical Associate Physician Award, National Institutes of Health
- 1997 Outstanding Professor and Scientist, USA Government
- 1997 Conference on body composition, Food and Drug Administration, Washington DC
- 1997-present Scientific Advisory Committee, GCRC, Beth Israel Deaconess Medical Center
- 1998 Junior Investigator Award, Beth Israel Deaconess Medical Center, Harvard Medical School,

Principal Investigator/Program Director (*Last, First, Middle*): Mantzoros, Christos

Boston, MA

1998 Hershey Family Award, Beth Israel Deaconess Medical Center, Harvard Medical School.

2000 Hershey Family Award, Beth Israel Deaconess Medical Center, Harvard Medical School.

Research Projects ongoing and completed during the last 3 years

NIH 5 M01 RR 01032 – 22 The role of leptin in the neuroendocrine response to fasting

National Institutes of Health / NIDDK

7/01/97 – 6/30/2005

PI Christos Mantzoros

This project studies the role of the hormone leptin in human physiology and pathophysiology, including its role in obesity and eating disorders (bulimia and anorexia nervosa).

Subcontract under Grant No. 1 U01 DK57154-01 Study of Health Outcomes of Weight Loss

National Institutes of Health / NIDDK

9/30/99 – 9/30/2009

PI David Nathan

The Study of Health Outcomes of Weight-loss is a multicenter, randomized clinical trial to study two primary research questions: 1) Do interventions designed to produce sustained weight loss in obese individuals with type 2 diabetes mellitus improve health? 2) How do the benefits and risks of interventions designed to produce weight loss compare with the benefits and risks related to treatment of obesity-related comorbid conditions in the absence of weight-loss interventions?

P 01 DK 56116 Peripheral and Central Interactions in Energy balance

National Institutes of Health / NIDDK

8/01/99 – 7/31/2004

PI on overall project: J S Flier

PI of Core grant: Christos Mantzoros

This core grant uses genetic, neuroanatomic, physiologic and biochemical techniques to better understand the peripheral and central circuits through which energy balance is regulated.

American Diabetes Association "Treatment of HIV-positive patients with protease inhibitor induced metabolic syndrome..."

Project Period: July 1, 2000 - June 30 2003

PI Christos Mantzoros

Harvard Medical School's Center of Excellence in Women's Health

"The role of leptin in the reproductive System, neuroendocrine function and bone metabolism in amenorrheic women athletes"

Project period: January 1, 2001-January 1 2003

PI Christos Mantzoros

AMGEN Pharmacokinetics of leptin administration to fasting humans and role of leptin in the neuroendocrine response to fasting

Project period: January 1, 2001-January 1 2002

PI Christos Mantzoros

The role of Insulin like Growth Factor in the pathogenesis of cancer

Relevant Publications : (selected from more than 100 publications)

1. Ahima R, Prabakaran D, Mantzoros C, Lowell B B, Qu D, Maratos-Flier E, Flier J S: Role of leptin in the neuroendocrine response to fasting. *Nature* 1996;382:250-252.
2. Houseknecht K, Mantzoros C, Kuliawat R, Hadro E, Flier J S, Khan B B: Evidence for leptin binding to proteins in serum of rodents and humans: modulation with obesity. *Diabetes* 1996;45:1638-1643.
3. Mantzoros C, Qu D, Frederich R, Maratos-Flier E, Flier J S: Activation of β_3 adrenergic receptors suppresses leptin expression and mediates a leptin independent inhibition of food intake in mice. *Diabetes* 1996;45:909-914.
4. Mantzoros C, Rosen H R, Greenspan S, Flier J S, Moses A C: Short term hyperthyroidism has no effect on leptin concentrations in man. *J Clin Endocrinol Metab* 1997;82(2):497-499.
5. Mantzoros C, Licinio J, Negrao A B, Cizza G, Bongiorno P, Karp B, Hoegland J M, Chrousos G P, Flier J S, Gold P W: Human leptin levels are pulsatile and inversely related to pituitary-adrenal function. *Nature Med* 1997;3:575-579.
6. Mantzoros C, Flier J S, Rogol A D: A longitudinal assessment of hormonal and physical alterations during puberty in boys: V. Rising leptin levels may signal the onset of puberty. *J Clin Endocrinol Metab* 1997;82:1066-1070.
7. Mantzoros C, Dunaif A, Flier: Leptin concentrations in the polycystic ovary syndrome. *J Clin Endocrinol Metab* 1997;82:1687-1691.
8. Mantzoros C, Flier J S, Lesem M D, Brewerton T D, Jimerson D C: Cerebrospinal fluid leptin in anorexia nervosa: correlation with nutritional status and potential role in resistance to weight gain. *J Clin Endocrinol Metab* 1997;82:1845-1851.
9. Mantzoros C, Varvarigou A, Kaklamani V G, Beratis G, Flier J S: Effect of birth weight and maternal smoking on cord blood leptin concentrations of full term and pre term newborns. *J Clin Endocrinol Metab* 1997;82:2856-2861.
10. Mantzoros C, Moschos S, Avramopoulos I, Kaklamani V, Liolios A, Doulgerakis D, Griveas I, Katsilambros N, Flier J S: Leptin concentrations in relation to Body Mass Index and the Tumor Necrosis Factor- α system in humans. *J Clin Endocrinol Metab* 1997;82:3408-3413.

11. Mantzoros C, Tzonou A, Signorello L, Stampfer M, Trichopoulos D, Adami O: Insulin like Growth Factor - 1 in relation to prostate cancer and benign prostatic hyperplasia. *Br J Cancer* 1997;76:1115-1118.
12. Mantzoros C, Prasad A S, Beck F W J, Grabowski S, Kaplan J, Adair C, Brewer G J: Zinc may regulate serum leptin concentrations in humans. *J Am Coll Nutrition* 1998;17:270-275.
13. Lagiou P, Signorello L, Trichopoulos D, Tzonou A, Trichopoulou A, Mantzoros C: Leptin in relation to prostate cancer and benign prostatic hyperplasia. *Int J Cancer* 1998;76:25-28.
14. C-c Hsieh, Signorello L, Lipworth L, Lagiou P, Mantzoros C, Trichopoulos D: Predictors of sex hormone levels among the elderly. A study in Greece. *J Clin Epidem* 1998;51:837-841.
15. Wolk A, Mantzoros C, Andersson S-O, Signorello L, Lagiou P, Bergstrom R, Trichopoulos D, Adami H-O: Insulin Like Growth Factor I and prostate cancer risk: A population based case-control study. *J Natl Cancer Inst* 1998;90:911-915.
16. Bohlke K, Cramer D, Trichopoulos D, Mantzoros C: Insulin Like Growth Factor I (IGF-1) and IGF Binding protein 3 (IGF BP3) in relation to Ductal Carcinoma In Situ. *Epidemiology* 1998; 9: 57-573.
17. Mantzoros C, Frederich R C, Qu D, Maratos-Flier E, Lowell B B, Flier J S: Severe leptin resistance in brown fat deficient UCP-DTA mice despite suppression of hypothalamic NPY and serum corticosterone. *Diabetes* 1998;47:230-238.
18. Licinio J, Negrao A, Mantzoros C, Kaklamani V, Wong M-L, Bongiorno P B, Mulla A, Cearnal L, Veldhuis J D, Flier J S, McCann S M, Gold P W: Synchronicity of frequently sampled, 24-h concentrations of circulating leptin, luteinizing hormone, and estradiol in healthy women. *P Natl Acad Sci* 1998; 95:2541-2546.
19. Roemmich J N, Clark P, Berr S S, Mai V, Mantzoros C, Flier J S, Weltman A, Rogol A D: Alterations in growth and body composition during puberty. II: Relation of plasma leptin concentration to gender, maturation, body composition, fat distribution and energy expenditure. *Am J Physiol* 1998;275:543-551.
20. Audi L, Mantzoros C, Vidal-Puig A, Deisi V, Gussinye M, Carrascossa A: Leptin in relation to recovery of menstruation in women with anorexia nervosa. *Mol Psych* 1998;3:544-7.
21. Licinio J, Negrao A B, Mantzoros C, Kaklamani V, Wong M-L, Bongiorno P B, Mulla A, Veldhuis J, Cearnal L, Flier J S, Gold P W: Sex differences in circulating human leptin pulse amplitude: clinical implications. *J Clin Endocrinol Metab* 1998;83:4140-7.
22. Lagiou P, Signorello IB, Mantzoros C, Trichopoulos D, Hsieh C-C, Trichopoulou A: Hormonal, lifestyle and dietary factors in relation to leptin among elderly men. *Ann Nutr Metab* 1999 ;43:23-29.
23. Mantzoros C, Bohlke K, Moschos S, Cramer D: Leptin in relation to carcinoma in situ of the breast: a study of premenopausal cases and controls. *Int J Cancer* 1999;80:523-526.
24. Cittadini A, Mantzoros C, Hampton TG, Katz SH, Travers KE, Flier JS, Morgan JP, Douglas PS: Cardiovascular phenotype of obese transgenic mice with reduced brown fat. *Circulation* 1999;100:2177-2183.
25. Mantzoros C, Bohlke K, Moschos S, Cramer D: Leptin in relation to carcinoma in situ of the breast: a study of premenopausal cases and controls. *Int J Cancer* 1999;80:523-526.
26. Petridou E, Trichopoulos D, Dessypris N, Spanos E, Mantzoros C, Skalkidou A, Kosmidis H, Panagiotou JP, Tzortzatou F: Insulin-like growth factor-1 and binding protein-3 in relation to childhood leukemia. *Int J Cancer* 1999;80:494-496.
27. Kaklamani V, Linos A, Kaklamani E, Markaki I, Mantzoros C: Age, gender and smoking predict circulating insulin like growth factor 1 (IGF I) and insulin like growth factor binding protein 3 (IGF BP-3). *J Clin Oncology* 1999;17:813-7.
28. Kaklamani V, Linos A, Kaklamani E, Markaki I, Mantzoros C: Dietary Fat and Carbohydrates Are Independently Associated With Circulating Insulin-Like Growth Factor 1 and Insulin-Like Growth Factor-Binding Protein 3 Concentrations in Healthy Adults. *J Clin Oncol J Clin Oncol*. 1999;17(10):3291-3298.
29. Manousos O, Souglakos I, Bosetti C, Tzonou A, Chatzidakis V, Trichopoulos D, Adami H-O, Mantzoros C: IGF-I and IGF-II in relation to colorectal cancer. *Int J Cancer*. 1999;83(1):15-7.
30. Shaneyfelt T, Husein R, Bublely G, Mantzoros C: Hormonal predictors of prostate cancer: a meta-analysis of case control and cohort studies. *J Clin Oncol* 2000;18:847-853.
31. Stuver SO, Kuper HE, Tzonou A, Lagiou P, Spanos E, Hsieh CC, Mantzoros C, Trichopoulos D: Insulin like growth factor I in hepatocellular carcinoma and metastatic liver cancer in men. *Int J Cancer* 2000;87(1):118-21.
32. Mantzoros C, Cramer D, Lieberman R, Barbieri R: Predictive value of serum and follicular fluid leptin concentrations during assisted reproductive cycles in normal women and women with the polycystic ovarian syndrome. *Human Reproduction* 2000;15:539-544.
33. Ziotopoulou M, Erani D, Hileman S, Bjorbaek C, Mantzoros C: Unlike leptin, Ciliary Neurotrophic Factor does not reverse the starvation induced changes of serum corticosterone and hypothalamic neuropeptide levels, but induces expression of hypothalamic inhibitors of leptin signaling. *Diabetes* 2000; 49(11):1890-6.
34. Ziotopoulou M, Mantzoros C, Hileman S, Flier JS: Differential expression of hypothalamic neuropeptides in the early phase of diet induced obesity in mice. *Am J Physiology* 2000;279:E838-845.
35. Papanthanasoglou ED, Moynihan JA, Ackerman MH, Mantzoros CS: Serum leptin levels are higher but are not independently associated with severity or mortality of the multiple organ dysfunction / systemic inflammatory response syndrome: a matched case control and a longitudinal study. *Clinical Endocrinology* 2001 (in press)
36. Jimerson JC, Mantzoros CS, Wolfe BE, Metzger ED: Decreased serum leptin in bulimia nervosa. *JCEM* 2000;85(12):4511-4514.

37. Christou H, Connors JM, Ziotopoulou M, Hatzidakis V, Papathanassoglou E, Ringer SA, Mantzoros CS. Cord Blood Leptin and Insulin-Like Growth Factor Levels are Independent Predictors of Fetal Growth. *J Clin Endocrinol Metab.* 2001 ;86(2):935-938.
38. Mantzoros C, Licinio J, Cogswell R, Prolo P, Negrao A, Wong M-L, Cearnal L, Veldhuis J D, Gold P W, Flier J S: Synchronicity of frequently sampled, 24-h concentrations of circulating leptin and TSH in healthy men *J Clin Endocrinol Metab* 2001 (in press).
39. Wolk A, Andersson S-O, Mantzoros C, Trichopoulos D, Adami H-O: The association between Insulin Like Growth Factor I, its binding protein -3 and prostate cancer depends critically on prostate specific antigen level. *Lancet* 2000 (in press).