

**BIOGRAPHICAL SKETCH**

NAME Scarpace, Philip	POSITION TITLE Professor		
eRA COMMONS USER NAME SCARPACE			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
California State Univesity, San Jose, CA	B.S.	1970	Physics (minor Chem)
University of Rochester, Rochester, N.Y.	Ph.D.	1974	Biophysics
University of Rochester, Rochester, N.Y.		1974-1975	NIH Fellow

**A. Positions and Honors****Positions and Employment**

1994-present	Professor of Pharmacology and Therapeutics, University of Florida
1987-2004	Research Director, Geriatric Research, Education and Clinical Center, Veterans Administration Medical Center, Gainesville, Florida.
1987-1994	Associate Professor of Pharmacology and Therapeutics, University of Florida
1988-1993	Associate Director, Center for Research on Oral Health and Aging, University of Florida
1977-1987	Chief, Molecular Biophysics Laboratory, Geriatric Research, Education and Clinical Center, Veterans Administration Medical Center, Sepulveda, California
1977-1987	Assistant Research Pharmacologist, Dept. of Medicine, UCLA
1979-1981	Assistant Professor of Mathematics, California State University at Northridge
1977-1981	Instructor of Mathematics, (Computer Sciences), Moorpark College, California.
1975-1976	Assistant Professor of Physiology, San Diego State University, San Diego, CA.

**B. Selected Peer-Reviewed Publications and Manuscripts (in chronological order).**

(Publications selected from 134 peer-reviewed publications)

- Scarpace, P.J., M. Matheny, B.H. Pollock and N. Tümer. Leptin increases uncoupling protein expression and energy expenditure. *Am J Physiol*, **273**, E226-230, 1997.
- Li, H, M. Matheny, M. Nicolson, N. Tümer and P.J.Scarpace. Leptin gene expression increases with age independent of increasing adiposity in rats. *Diabetes*, **46**, 2035-2039, 1997.
- Scarpace, P.J., and M. Matheny. Leptin induction of UCP1 is dependent on sympathetic innervation. *Am J Physiol*, **275**, E259-264, 1998.
- Li, H, M. Matheny, N. Tümer and P.J.Scarpace. Aging and fasting regulation of leptin and hypothalamic neuropeptide Y gene expression. *Am J Physiol*, **275**, E405-411, 1998.
- Scarpace, P.J., M. Nicolson and M. Matheny. UCP2, UCP3 and leptin gene expression: modulation by food restriction and leptin. *J Endocrinology*, **159**, 349-357, 1998.
- Scarpace, P.J., M. Matheny and N. Tümer. Differential down regulation of  $\beta_3$ -adrenergic receptor mRNA and signal transductin by cold exposure in brown adipose tissue of young and senescent rats. *Pflugers Arch - Eur J Physiol*, **437**, 479-483, 1999.
- Kumar, M.V, R.L. Moore and P.J. Scarpace.  $\beta_3$ -adrenergic regulation of leptin, food intake, and adiposity is impaired with age. *Pflugers Arch - Eur J Physiol*, **438**, 681-686, 1999.
- Scarpace, P.J., M. Matheny, R.L. Moore and N. Tümer. Impaired leptin responsiveness in aged rats. *Diabetes* **49**:431-435, 2000.
- Scarpace, P.J., M. Matheny and E.W. Shek. Impaired leptin signal transduction with age-related obesity. *Neuropharmacol*, **39**, 1872-1879, 2000.
- Shek, E.W, and P. J. Scarpace. Resistance to the anorexic and thermogenic effects of centrally administered leptin in obese aged rats. *Regulatory Peptides*, **92**, 65-71, 2000.
- Scarpace, P.J., M.V. Kumar, H. Li and N. Tümer. Uncoupling proteins 2 and 3 with age: regulation by fasting and  $\beta_3$ -adrenergic agonist treatment *J Gerontology*, **55A**, B588-B592, 2000.
- Scarpace, P.J. and Tümer, N. Peripheral and hypothalamic leptin resistance with age-related obesity. *Physiol Behav* **74**, 1-7, 2001.
- Dhillon, H., S.P. Kalra, V. Prima, S. Zolotukhin, P.J. Scarpace, L.L. Moldawer, N. Muzyczka, and P.S. Kalra. Centrally leptin gene therapy suppresses body weight gain, adiposity and serum insulin without effecting food consumption in normal rats: a long-term study. *Regul Pept*, **99**, 69-77, 2001.
- Scarpace, P.J., M. Matheny and N. Tümer. Hypothalamic leptin resistance is associated with impaired leptin signal transduction in aged obese rats. *Neuroscience*, **104**, 1111-1117, 2001.

15. Scarpace, P.J., M. Matheny, Y. Zhang, N. Tümer, C.D. Frase, E.W. Shek, B. Hong, V. Prima, and S. Zolotukhin. Central leptin gene delivery evokes persistent leptin signal transduction in young and aged-obese rats but physiological responses become attenuated over time in aged-obese rats. *Neuropharmacol*, 42, 549-562, 2002.
16. Zhang, Y., J.T. Wilsey, C.D. Frase, M.M. Matheny, B.S. Bender, and S. Zolotukhin, and P.J. Scarpace. Peripheral but not central leptin prevents the immunosuppression associated with hypoleptinemia in rats. *J Endocrinology*, 174,455-461, 2002.
17. Wilsey, J., S. Zolotukhin, V. Prima, E.W. Shek, M. Matheny, and P.J. Scarpace. Hypothalamic delivery of doxycycline-inducible leptin gene allows for reversible transgene expression and physiological responses. *Gene Therapy*, 9, 1492-1499, 2002.
18. Zhang, Y., M. Matheny, S. Zolotukhin, N. Tümer and P.J. Scarpace. Regulation of adiponectin and leptin gene expression in white and brown adipose tissues: Influence of  $\beta$ 3-adrenergic agonists, leptin, retinoic acid, and fasting. *Biochim Biophys Acta*, 1584, 115-122, 2002.
19. Li, G, R.L. Klein, M. Matheny, M.A. King, E.M. Meyer and P.J. Scarpace. Induction of uncoupling protein 1 by central IL-6 gene delivery is dependent on sympathetic innervation of brown adipose tissue and underlies one mechanism of body weight reduction in rats. *Neuroscience* 115, 879-889, 2002.
20. Scarpace, P.J., M. Matheny, Y. Zhang, E.W. Shek, V. Prima, S. Zolotukhin and N. Tümer. Leptin-induced leptin resistance reveals separate roles for the anorexic and thermogenic responses in weight maintenance. *Endocrinology* 143,143, 3026-3035, 2002.
21. Scarpace, P.J., M. Matheny, S. Zolotukhin, N. Tümer and Y. Zhang. Leptin-induced leptin resistance rats exhibit enhanced responses to the melanocortin agonist MTII. *Neuropharmacol*, 45, 211-219, 2003.
22. Li, G, C.V. Mobbs and P.J. Scarpace. Central Pro-melanocortin gene delivery results in hypophagia, reduced visceral adiposity and improved insulin sensitivity in genetically obese Zucker rats. *Diabetes*, 52, 1951-1957, 2003.
23. Wilsey, J.T., S. Zolotukhin, V. Prima, and P. J. Scarpace. Central leptin gene therapy fails to overcome leptin resistance associated with diet-induced obesity. *Am J Physiol*, 285, R1011-R1020, 2003.
24. Shklyayev, S., G. Aslanidi, M. Tennant , V. Prima , E. Kohlbrenner, V. Kroutov, M. Campbell-Thompson, J. Crawford,, E.W. Shek, P. J. Scarpace, and S. Zolotukhin. Sustained rAAV-mediated peripheral expression of transgene adiponectin offsets the development of diet-induced obesity in rats. *PNAS*, 100, 14217-14222, 2003.
25. Prima V., M. Tennant, O.S. Gorbatyuk, N. Muzyczka, P.J. Scarpace, and S. Zolotukhin. Differential Modulation of Energy Balance by Leptin, CNTF, and LIF Gene Delivery: Microarray DNA-chip Analysis of Gene Expression. *Endocrinology*, 145, 2035-2045, 2004.
26. Wilsey, J.T. and P.J. Scarpace. Caloric restriction reverses the deficits in leptin receptor protein and leptin signaling capacity associated with diet-induced obesity: role of leptin in the regulation of hypothalamic ObRb expression. *J Endocrinology*, 181, 297-306, 2004.
26. Zhang, Y., M. Matheny, N. Tümer, and P.J. Scarpace. The melanocortin agonist MTII circumvents aged related leptin resistance. *Neurobiol Aging*, 25, 1349-1360, 2004.
27. Li, G., Y. Zhang, J.T. Wilsey, and P.J. Scarpace. Unabated Anorexic and Enhanced Thermogenic Responses to MTII in Diet-Induced Obese Rats Despite Reduced Melanocortin 3/4 Receptor Expression. *J Endocrinology*, 182,123-132, 2004.
28. Zhang, Y. and P.J. Scarpace. Circumventing Central Leptin Resistance: Lessons from Central Leptin and POMC Gene Delivery. *Peptides*, Nov 3, 2005, [Epub ahead of print].
29. Li, G., Y. Zhang, and P.J. Scarpace. Hypothalamic pro-opiomelanocortin gene delivery ameliorates obesity and glucose intolerance in aged rats. *Diabetologia*, Oct 5, 2005; [Epub ahead of print].
30. Tümer, N., P.J. Scarpace, M.D. Dogan, C.S. Broxon, M. Matheny, D.M. Yurek, O. Gorbatyuk, C.S. Peden, C. Burger, N. Muzyczka, and R.J. Mandel. Hypothalamic rAAV-mediated GDNF gene delivery ameliorates age-related obesity. *Neurobiol Aging*, June 15, 2005, [Epub ahead of print].
31. Scarpace P.J., M. Matheny, Y. Zhang, K.Y. Cheng, and N. Tümer. Leptin-induced leptin resistance exacerbates diet-induced obesity and is associated with impaired maximal leptin signaling capacity. *Diabetologia*, 48, 1075-1083, 2005.
32. Wilsey, J.T. and P.J. Scarpace. Oral Vanadium Enhances the Catabolic Effects of Central Leptin in Lean Rats. *Endocrinology*, 147, 493-501, 2006.

## C. Research Support

### Ongoing Research Support

R01 AG20985 Scarpace (PI)

08/03-07/07

NIH

"Age-related Obesity: Interventions with Gene Delivery"

The major goals of this project are: Does leptin-induced or age-induced leptin resistance result from diminished melanocortin tone? Will silencing of the rAAV-delivered leptin transgene restore melanocortin tone? Will treatment with rAAV-POMC circumvent leptin resistance and reduce adiposity in leptin resistant rats.

Role: P.I.

R01 AG026159 Scarpace (PI) 09/04-08/09

NIH

"Leptin Resistance: One Mechanism Underlying Age-related Obesity"

The major goals of this project are: Is the leptin activated IRS-PI3K pathway impaired with leptin resistance or age-related obesity? Does the leptin mediated IRS-PI3K pathway differentially regulate the anorexic and energy expenditure responses to leptin? Is elevated leptin, independent of obesity, the primary factor in leptin resistance.

Role: P.I.

**Completed Research Support**

VA Merit Review Scarpace (PI) 04/01/00-03/31/05

Veterans Administration

"Leptin, TNF $\alpha$  and IL-6: Role in the Increase in Body Weight with Age"

The major goals of this project are: 1) Does the adiposity set point increase with age and can replacement leptin prevent the regain of fat following lipectomy? 2) Does TNF and IL-6 complement or enhance leptin function and is this coordinated response diminished with age? 3) What are the mechanisms of leptin signal transduction as assessed in an *in vitro* hypothalamic signal transduction assay?

Role: P.I.

R01 AG17047 Scarpace (PI) 09/99-08/03

NIH

"Impaired Leptin Responsiveness with Age"

The major goals of this project are: 1) Is there impaired responsiveness to short-term pharmacologically administered leptin in aged rats? 2) Is leptin receptor density and/or leptin receptor signal transduction impaired in the hypothalamus of aged rats. 3) Is the regulation of leptin gene expression impaired with age? 4) Can dietary vitamin A supplementation decrease serum leptin and partially reverse the leptin resistance in aged rats?

Role: P.I.