

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format on preceding page for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Theoharis C. Theoharides		POSITION TITLE Professor of Pharmacology and Internal Medicine	
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
Yale University, New Haven, CT	B.A.	1972	Biology & Hist. of Medicine
Yale University, New Haven, CT	M.S.	1975	Neuropharmacology
Yale University, New Haven, CT	M.Phil.	1975	Immunopharmacology
Yale University, New Haven, CT	Ph.D.*	1978	Pharmacology
Yale University, New Haven, CT	M.D.	1983	Medicine
Tufts University, Fletcher School of Law and Diplomacy	Certificate	1999	Leadership & Management
Harvard University, J.F. Kennedy School of Government	M.P.A.	Deferred	Biomedical Research Policy

*Thesis advisors: W.W. Douglas, M.D.-Royal Acad. Sci.; Paul Greengard, Ph.D.-2000 Nobel Laureate in Physiology & Medicine

Academic Appointments

- 1968-71 Assistant in Research, Department of Biology, Yale University, New Haven, CT
 1971-78 Assistant in Research, Department of Pharmacology, Yale University, New Haven, CT
 1978-83 Research Associate, Clin. Immunology, Dept. Internal Med, Yale Uni & Bioch. Res. Lab. UAMC, CT
 1983-88 Assistant Professor of Pharmacology, Biochemistry and Psychiatry, Tufts University, MA
 1985-92 Director of Medical Pharmacology, Tufts University School of Medicine, Boston, MA
 1989-93 House Staff, Dept. of Internal Medicine, New England Medical Center, Boston, MA
 1989- Associate Professor of Pharmacology (1989-1994), Biochemistry and Psychiatry, Tufts University
 1995- Professor of Pharmacology & Internal Medicine, and Biochemistry (2002-), Tufts University (tenured 11/2/91)

Honors

- 1971 *Connecticut Commission for Undergraduate Research Award*
 1971 *Yale College Dean's Award* for senior research thesis
 1972 *Cum Laude & Divisional Honors* for joint Bachelor of Arts, Yale College
 1972 *Theodore Cuyler Award* "for outstanding Yale College graduates", Yale University
 1975-77 *Advisory Committee to the Dean*, Yale University Graduate School
 1977 *G. Papanicolaou Graduate Research Award*, Hellenic University Club of New York
 1979,83 *Medical Award*, Hellenic Medical Society of New York
 1980 *Travel Award*, American Society for Cell Biology
 1980 *Winternitz Prize* "for the best work in Pathology", Yale Univ. School of Medicine
 1981,82 *Research Fellowship*, International Inst. of Cellular & Molecular Pathology, Brussels
 1984 *Chairman - Immunopharmacology*, 9th Int'l Congress of Pharmacology, London
 1984 *Travel Award*, American Society for Pharmacology and Experimental Therapeutics
 1986 *Chairman - Neuroimmunology*, 2nd World Conference on Inflammation, Monte Carlo
 1986 *Distinguished Service Citation* for faculty excellence, Tufts University
 1987,88 *Special Faculty Recognition Award*, Tufts University School of Medicine
 1987 *Honorary Member, Alpha Omega Alpha* National Medical Honor Fraternity, USA
 1989 *Chairman - Neuroimmunomodulation*, 3rd World Conference on Inflammation, Monte Carlo
 1989,90 *Citation for Excellence in Teaching*, Tufts University School of Medicine
 1991,93 *Advisory Committee*, 4th & 5th World Conferences on Inflammation, Geneva
 1991-94 *Citation for Excellence in Teaching*, Tufts University School of Medicine
 1993 *Medical Awareness and Patient Support Award*, Interstitial Cystitis Association, NY
 1994 *Diocean Award for Humanitarian Health Care*, Greek Orthodox Diocese of Boston
 1995,97 *Advisory Committee*, 6th & 7th World Conference on Inflammation, Geneva
 1995 *Chairman*, International Committee to Upgrade Medical Education in Greece, Secretary of Health
 1996 *Citation for Excellence in Teaching*, Tufts University School of Medicine
 1997-01 *Supreme Scientific Advisory Health Council*, Secretary of Health, Hellenic Republic
 1998 *Community Service Award*, Mayor Thomas Menino of Boston, MA
 1999-02 *Supreme Health Board*, Institute of Social Welfare, Sec. of Labor & Human Resources, Hellenic Republic
 1999 *Oliver Smith Award* "recognizing excellence, compassion and service", New Engl. Med. Center, Boston
 2000 *Archon of the Ecumenical Patriarchate of Constantinople*, Greek Orthodox Church, Instambul, Turkey
 2001 *Plenary Speaker*, National Minority Research Symposium (USA), Cancun, Mexico
 2002 *Dr. George Papanicolaou Gold Medal* for contributions in humanism and medicine
 2003-05 *National Public Health Council*, Secretary of Health, Hellenic Republic

Selected Publications (from over 200)

Theoharides TC and Canellakis ZN. Spermine inhibits induction of ornithine decarboxylase by cAMP but not by dexamethasone in rat hepatoma cells. *Nature* 255:733-734, 1975.

- Principal Investigator/Program Director (Last, first, middle): Theoharides, Theoharis, C.
Sieghart W, Theoharides TC, Alper LS, Douglas WW, Greengard P. Calcium dependent protein phosphorylation during exocytotic release of mast cell secretory granules. **Nature** 275:329-331, 1978.
- Theoharides TC, Douglas WW. Secretion in mast cells induced by calcium entrapped within phospholipid vesicles. **Science** 201:1143-1145, 1978.
- Theoharides TC, Sieghart W, Greengard P, Douglas, WW. Anti-allergic drug cromolyn may inhibit histamine secretion by regulating phosphorylation of a mast cell protein. **Science** 207:80-82, 1980.
- Theoharides TC, Bondy PK, Tsakalos ND, Askenase PW. Differential release of serotonin and histamine from mast cells. **Nature** 297:229-231, 1982.
- Theoharides TC. Mast cells: the immune gate to the brain. **Life Sciences** 46:607-617, 1990.
- Lambracht-Hall M, Dimitriadou V, Theoharides TC. Migration of mast cells in the rat brain. **Brain Res** 56:151-9, 1990.
- Dimitriadou V, Lambracht-Hall M, Reichler J, Theoharides TC. Histochemical and ultrastructural characteristics of rat brain perivascular mast cells stimulated with compound 48/80 and carbachol. **Neuroscience** 39:209-224, 1990.
- Dimitriadou V, Buzzi MG, Moskowitz MA, Theoharides TC. Trigeminal sensory fiber stimulation induces morphologic changes reflecting secretion in rat dura mater mast cells. **Neuroscience** 44:97-112, 1991.
- Theoharides TC, Dimitriadou V, Letourneau R, Rozniecki JJ, Vliagoftis H, Boucher W. Synergistic action of estradiol and myelin basic protein on mast cell secretion and brain demyelination. **Neuroscience** 57:861-871, 1993.
- Rozniecki JJ, Hauser SL, Stein M, Lincoln R, Theoharides TC. Elevated mast cell tryptase in cerebrospinal fluid of multiple sclerosis patients. **Ann Neurol** 37:63-66, 1995.
- Theoharides TC, Sant GR, El-Mansoury M, Letourneau RJ, Ucci A, Meares E. Activation of bladder mast cells in interstitial cystitis - a light and electron microscopic study. **J Urol** 153:629-636, 1995.
- Pang X, Marchand J, Sant GR, Kream RM, Theoharides TC. Increased number of substance P positive nerve fibers in interstitial cystitis. **Br J Urol** 75:744-750, 1995.
- Theoharides TC, Spanos C, Pang X, Alferes L, Ligris K, Letourneau R, Rozniecki JJ, Webster E, Chrousos GP. Stress-induced intracranial mast cell degranulation: A CRH-mediated effect. **Endocrinology** 136:5745-5750, 1995.
- Pang X, Letourneau R, Rozniecki JJ, Wang L, Theoharides TC. Definitive characterization of brain mast cells. **Neuroscience** 73:889-902, 1995.
- Theoharides TC, Singh L, Boucher W, Pang X, Letourneau R, Webster E, Chrousos G. Corticotropin-releasing hormone induces skin mast cell degranulation and increased vascular permeability: a possible explanation for its pro-inflammatory effects. **Endocrinology** 139:403-413, 1998.
- Pang X, Alexacos N, Letourneau R, Seretakis D, Gao W, Boucher W, Cochrane DE, Theoharides TC. A neurotensin receptor antagonist inhibits acute immobilization stress-induced cardiac mast cell degranulation, a corticotropin-releasing hormone-dependent process. **J Pharmacol Exp Therap** 287:307-314, 1998.
- Conti P, Reale M, Barbacane RC, Letourneau R, Theoharides TC. Intramuscular injection of hrRANTES causes mast cell recruitment and increased transcription of histidine decarboxylase in mice. Lack of effects in genetically mast cell-deficient W/W^v mice. **FASEB J** 12:169-1700, 1998.
- Singh L, Boucher W, Pang X, Letourneau R, Seretakis D, Green M, Theoharides TC. Potent mast cell degranulation and vascular permeability triggered by urocortin through CRH receptors. **J Pharmacol Exp Therap** 288:1349-1356, 1999.
- Theoharides TC, Wang L, Pang X, Letourneau R, Culm KE, Basu S, Wang Y, Correia I. Cloning and cellular localization of the rat mast cell 78kD protein phosphorylated in response to the mast cell "stabilizer" cromolyn. **J Pharmacol Exp Therap** 294:810-821, 2000.
- Deliargyris EN, Raymond RJ, Theoharides TC, Boucher W, Tate D, Dehmer GJ. Sites of interleukin-6 release in patients with acute coronary syndromes and in patients with congestive heart failure. **Am J Cardiol** 86:913-918, 2000.
- Theoharides T.C., Patra P, Boucher W, Letourneau R., Kempuraj D, Chiang G., Jeudy S, Hesse L, Athanasiou A. Chondroitin sulfate inhibits connective tissue mast cells. **Br J Pharmacol** 131:1039-1049, 2000.
- Chiang G, Patra P, Letourneau R, Jeudy S, Boucher W, Green M, Sant GR, Theoharides TC. Pentosanpolysulfate inhibits mast cell histamine secretion and intracellular calcium ion levels: an alternative explanation of its beneficial effect in interstitial cystitis. **J Urology** 164: 2119-2125, 2000.
- Middleton E, Kandaswami C, Theoharides TC. The effect of plant flavonoids on mammalian cells: implications for inflammation, heart disease and cancer. **Pharmacol Rev** 52:673-751, 2000.

- Esposito P, Georghe D, Pang X, Kandere K, Connolly R, Jacobson S, Theoharides TC. Acute stress increases permeability of the blood-brain barrier through activation of brain mast cells. *Brain Res* 888:117-127, 2001.
- Katsarou-Katsari A, Singh LK, Theoharides TC. Alopecia areata and affected skin CRH receptor upregulation induced by acute emotional stress. *Dermatology* 203:157-161, 2001.
- Boucher WS, Letourneau R, Huang M, Kempuraj D, Green M, Sant GR, Theoharides TC. Intravesical sodium hyaluronate inhibits the rat urinary mast cell mediator increase triggered by acute immobilization stress. *J Urol* 167:380-384, 2002.
- Theoharides TC. Mast cells and stress - A psychoneuroimmunological perspective. *J Clin Psychopharm* 22:103-108, 2002.
- Chandler N, Jacobson S, Esposito P, Connolly R, Theoharides TC. Acute stress shortens the time of onset of experimental allergic encephalomyelitis (EAE) in SJL/J mice. *Brain, Behavior, Immunity* 13:225-239, 2002.
- Esposito P, Chandler N, Kandere K, Basu S, Jacobson S, Connolly R, Tutor D, Theoharides TC. Corticotropin-releasing hormone (CRH) and brain mast cells regulate blood-brain-barrier permeability induced by acute stress, *J Pharmacol Exp Therap* 303:1061-1066, 2002.
- Huang M, Pang X, Letourneau R, Boucher W, Theoharides TC. Acute stress induces cardiac mast cell activation and histamine release that are increased in apolipoprotein E knockout mice. *Cardiovascular Res* 55:150-160, 2002.
- Esposito P, Basu S, Letourneau R, Jacobson S, Theoharides, TC. Corticotropin-releasing factor (CRF) can directly affect brain microvessel endothelial cells. *Brain Res* 968:192-198, 2003.
- Lytinas M, Kempuraj D, Huang M, Boucher W, Esposito P, Theoharides TC. Acute stress results in skin CRH secretion, mast cell activation and vascular permeability, an effect mimicked by intradermal corticotropin-releasing hormone and inhibited by histamine -1 receptor antagonists. *Intl Arch Allergy Immunol* 130: 224-231, 2003.
- Madhappan B, Kempuraj D, Christodoulou S, Boucher W, Tsapikidis S, Karagiannis V, Athanassiou A, Theoharides TC. High levels of intrauterine corticotropin-releasing hormone, urocortin, tryptase and interleukin-8 in spontaneous abortions. *Endocrinology* 144:2285-2290, 2003.
- Huang M, Pang X, Karalis K, Theoharides TC. Stress-induced interleukin-6 release in mice is mast cell-dependent and more pronounced in Apolipoprotein E knockout mice. *Cardiovascular Res* 59:241-249, 2003.
- Kandere-Grzybowska K, Georghe D, Esposito P, Huang M, Gerard NP and Theoharides TC. Stress-induced dura vascular permeability does not develop in mast cell-deficient and neurokinin-1 receptor knockout mice. *Brain Res* 980:213-220, 2003.
- Kandere-Grzybowska K, Letourneau R, Kempuraj D, Donelan J, Paplawski S, Boucher W, Athanassiou A, Theoharides, TC. IL-1 induces vesicular secretion of IL-6 without degranulation from human mast cells. *J Immunol* 171:4830-4836, 2003.
- Letourneau R, Rozniecki JJ, Dimitriadou V, Theoharides TC. Ultrastructural evidence of brain mast cell activation without degranulation in monkey experimental allergic encephalomyelitis (EAE). *J Neuroimmunol* 145:18-26, 2003.
- Alexandrakis M, Letourneau R, Kempuraj D, Kandere-Grzybowska K, Huang M, Christodoulou S, Boucher W, Seretakis D, Theoharides TC. Flavones inhibit proliferation and increase mediator content in human leukemic mast cells (HMC-1). *Eur J Hematol* 71:1-7, 2003.
- Maurer M, Theoharides TC, Granstein RD, Bischoff SC, Bienenstock J, Henz B.M., Kovanen, P.T., Piliponsky, A.M., Kambe, N., Vliagoftis, H., Levi-Schaffer, F., Metz, M., Miyachi, H., Befus, D., Forsythe, P., Kitamura, Y., Galli, S. What is the physiological function of mast cells? *Exp. Dermatol* 12:1-24, 2003.
- Kempuraj D, Basu S, Huang M, Kandere-Grzybowska K, Boucher W, Letourneau R, Athanassiou A, Theoharides TC. Azelastine inhibits secretion of IL-6, TNF- α and IL-8 as well as NF- κ B activation and intracellular calcium ion levels in normal human mast cells. *Intl Arch Allergy Immunol* 132:231-239, 2003.
- Letourneau R, Rozniecki JJ, Dimitriadou V, Theoharides TC. Ultrastructural evidence of brain mast cell activation without degranulation in monkey experimental allergic encephalomyelitis (EAE). *J Neuroimmunol* 145:18-26, 2003.
- Theoharides TC, Cochrane D. Critical role of mast cells in inflammatory diseases and the effect of acute stress. *J Neuroimmunol* 146:1-12, 2004.
- Kempuraj D, Papadopoulou N, Lytinas M, Huang M, Kandere-Grzybowska K, Madhappan B, Boucher W, Christodoulou S, Athanassiou A, Theoharides TC. Corticotropin-releasing hormone (CRH) and its structurally related urocortin (Ucn) are synthesized and secreted by human mast cells. *Endocrinology* 145:43-48, 2004.
- Green M., Filippou A, Sant GR, Theoharides TC. Expression of intercellular adhesion molecules in the bladder of interstitial cystitis patients. *Urology* 63:688-693, 2004.

Theoharides TC, Conti P. Mast cells: the Jekyll and Hyde of tumor growth. *Trends Immunol* 25:235-241, 2004.

Theoharides TC, Bielory L. Mast cells and mast cell mediators as targets of dietary supplements. *Ann Allergy Asthma Immunol* 93 (2 Suppl 1):S24-34, 2004.

Theoharides TC. Panic disorder, interstitial cystitis and mast cells. *J Clin Psychopharmacol* 24:361-364, 2004.

Kempuraj D., Papadopoulou N, Stanford J, Christodoulou S, Madhappan B, Sant GR, Theoharides, T.C. Increased numbers of activated mast cells in endometriosis sites positive for corticotropin-releasing hormone. *Am J Reprod Immunol* 52:267-275, 2004.

Theoharides TC, Donelan JM, Papadopoulou N, Cao J, Duraisamy K, Conti P. Mast cells as targets of corticotropin-releasing factor and related peptides. *Trends Pharmacol Sciences*, 25:563-568, 2004.

Theoharides TC, Sant GR. Immunomodulators for the treatment of interstitial cystitis. *Urology*, in press.

Papadopoulou N, Oleson L, Cao J, Kempuraj D. Kandere-Grzybowska K., Boucher W, Theoharides TC. Human umbilical cord-derived cultured mast cells (hCBMC) express corticotropin-releasing hormone (CRH) receptors and upregulate CRH-R2 in response to interleukin-4 (IL-4) and lipopolysaccharide (LPS). *Endocrinology*, in press.

Theoharides TC, Weinkauff C, Conti P. Brain cytokines and neuropsychiatric disorders. *J Clin Psychopharmacol*, in press.

Theoharides TC, Donelan JM, Kandere-Grzybowska K. Brain mast cells and migraines. *Brain Res.*, in press.

Cao J, Papadopoulou N, Theoharides TC. Human mast cells express multiple corticotropin-releasing hormone (CRH) receptor isoforms activation of which leads to selective VEGF release. *Submitted*.

Public Advisory Committees:

1986-05	Massachusetts Drug Formulary Commission	2002	NIH ZDK1 GRB-B (J2) Biol Neuroendoc Peptides
2000-02	NIH Biobehavioral & Behavioral Processes -SS2	2002	NIDDK Reparative Medicine Section (SSS-M)
2001-02	NSF Div. Integrative Biology and Neuroscience	2002	DK ZDK11 GRB-9 Urology Research Centers
2003	VA Neurobiology Section A		

Research Support

Active

1 R01 AR47652 NIAMSD (PI: Theoharides) Stress induces skin mast cell activation and vasodilation	Duration: 4/1/01-3/31/06 Direct Cost/yr: \$175,000	30%
1 R01 DK062861 NIDDK (PI: Theoharides) Acute restraint stress-induced neurogenic bladder inflammation	Duration: 5/1/03-4/30/07 Direct Cost/yr: \$175,000	30%
BC024430 DOD-Concept Award (PI: Theoharides) Role of mast cells in mammary gland carcinogenesis	Duration: 9/1/03-8/31/04 Direct Cost/yr: \$75,000	5%

Pending

1 R01 HL080379-01 (PI: Theoharides) Asthma worsening by stress, role of CRH and mast cells	Duration 4/1/05-3/31/10 Direct Cost/yr: \$250,000	20%
1 R01 HD044917- 01?2 NICHD (PI: Theoharides) Stress, uterine CRH, tryptase, cytokines and abortions	Duration: 1/1/05 – 12/31/09 Direct Cost/yr: \$200,000	20%
BC021977-A1 DOD Idea Award (PI: Theoharides) Stromal cellular elements in mammary carcinogenesis	Duration: 9/1/04– 8/31/07 Direct Cost/yr: \$155,054	20%
NSF 0447340 (PI: Theoharides) Regulation of selective mast cell secretion by distinct CRH receptors	Duration: 1/1/05– 12/31/08 Direct Cost/yr: \$128,162	20%

U.S. Patents:**Method claims**

#5,250,529 (10/05/93)	Method of alleviating migraine headache with mast cell degranulation blocking agents.
#5,648,350 (07/15/97)	Method of treatment of endogenous, painful gastrointestinal conditions of non-ulcerative origin.
#5,821,259 (10/13/98)	Histamine-3 receptor agonists as therapeutic agents.
#5,855,884 (01/05/99)	Treatment of stress-induced migraine headache with a corticotropin releasing hormone blocker.
#5,994,357 (11/30/99)	Method of treatment of interstitial cystitis.
#6,020,305 (02/01/00)	Treatment of stress-induced skin diseases by CRH antagonists and mast cell inhibitors.
#6,689,748 (02/10/04)	Method of treating mast cell activation-induced diseases with a proteoglycan
#10/166,088 (filed 06/11/02)	Method of treating IL-6-mediated inflammatory diseases.
#08/67,310 (filed 07/09/96)	Method of treating myocardial ischemia by inhibitors of cardiac mast cell activation.

Composition claims

#6,624,148 (09/23/03)	Proteoglycan compositions for treatment of cardiovascular inflammatory diseases
#6,635,625 (10/21/03)	Proteoglycan compositions for treating prostate and bladder inflammatory conditions
#6,641,806 (11/04/03)	Proteoglycan compositions for treating arthritic inflammation conditions
#6,645,482 (11/11/03)	Proteoglycan compositions for the treatment of arthritic inflammatory diseases
#09/711,669 (allowed 08/10/04)	Synergistic proteoglycan compositions for treatment of inflammatory diseases
#10/329367 (filed 05/20/03)	Proteoglycan compositions for the treatment of skin inflammatory diseases
#09/773, 576 (filed 02/02/01)	Proteoglycans/antihistamines divisional (DIV of 09/056.707)
#10/439,139 (filed 05/16/03)	Proteoglycans/flavonoids for inflammation (CIP of 09/056.707) allowed 12/16/2003
#PCT/US02/00476 (filed 01/03/02)	Proteoglycans/flavonoids for inflammation (CIP of 09/771,669) EPO entered National Phases