

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 THEOHARIDES, THEOHARIS C. | POSITION TITLE Professor of Pharmacology and Internal Medicine (Allergy) | | |
| EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i> | | | |
| INSTITUTION AND LOCATION | DEGREE <i>(if applicable)</i> | 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. Sciences.; Paul Greengard, Ph.D.-2000 Nobel Laureate in Physiol & Med; Outside doctoral thesis examiner, George E. Palade, M.D.- 1974 Nobel Laureate in Physiology & Medicine**

A. 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, Allergy & Clin. Immunology, Dept. Internal Med, Yale University, CT
- 1984-86 Associate in Clinical Immunology, Tufts University School of Medicine, Boston, MA
- 1986-93 Training in Internal Medicine, Dept. of Internal Medicine, New England Medical Center, Boston, MA
- 1985-92 Director of Medical Pharmacology, Tufts University School of Medicine, Boston, MA
- 1983-88 Assistant Professor of Pharmacology, Biochemistry and Psychiatry, Tufts University, MA
- 1989- Associate Professor of Pharmacology (1989-1994), Biochemistry and Psychiatry, Tufts University
- 1995- Professor of Pharmacology, and Biochemistry (2002-), Tufts University (tenured 11/2/91)
- 1995- Professor of Internal Medicine (Allergy Section), Tufts University & New England Medical Center, Boston, MA
- 2004- Director, Laboratory of Molecular Immunopharmacology and Drug Discovery, Tufts University

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 *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
- 1986,89 *Chairman - Neuroimmunology*, 2nd & 3rd 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 *Member, Alpha Omega Alpha National Medical Honor Fraternity*, USA
- 1989-96 *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 *Chairman*, International Committee to Upgrade Medical Education in Greece, Secretary of Health
- 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
- 2002 *Dr. George Papanicolaou Gold Medal* for contributions in humanism and medicine
- 2003-08 *National Public Health Council*, Secretary of Health, Hellenic Republic
- 2006 *Hygeia Award*, New Engl. Hellenic Medical & Dental Society, Boston, MA
- 2007 *Science and Medicine Award*, Fed. HASNE, Boston, MA
- 2008 *Fellow*, American Academy of Allergy, Asthma, Immunology
- 2008 *Fellow*, European Academy of Allergology and Clinical Immunology

Public Advisory Committees

| | | | |
|---------|--|---------|---|
| 1986-10 | Massachusetts Drug Formulary Commission | 2001-02 | NSF Div. Integrative Biology and Neuroscience |
| 2000-02 | NIH Biobehavioral & Behavioral Processes-SS2 | 2002 | NIH ZDK1 GRB-B (J2) Biol Neuroendoc Peptide |
| 2002 | DK ZDK11 GRB-9 Urology Research Centers | 2002 | NIDDK Reparative Medicine Section (SSS-M) |
| 2003 | VA Neurobiology Section A | 2004 | Italian Ministry of Universities and Research |
| 2007 | ZAI1 SV-IS1 Cellular & Inflamm Pathways | 2007 | NIAID Asthma & Allergic Dis Coop Res Center |
| 2008 | NIH ZRG1 CFS-D | 2009 | DK ZDK11 GRB-9 Urology Research Centers |
| 2009 | SEP, Natl Center Minority Health & Disparities (NCMHD) | | |

B. Selected Publications (from 270 in pubmed.gov)

- 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.
- Theoharides, T.C. and Canellakis, Z.N. Antiserum monospecific to hepatic ornithine decarboxylase. *J Biol Chem* 251:1781-1784, 1976.
- Canellakis, Z.N. and Theoharides, T.C. Stimulation of ornithine decarboxylase synthesis and its control by polyamines in regenerating rat liver and cultured rat hepatoma cells. *J Biol Chem* 251:4436-4441, 1976.
- 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.
- 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, 1996.
- 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* 12:1693-1700, 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.
- 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.
- 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.
- Rozniecki JJ, Pang X, Dimitriadou V, Lambracht-Hall M, Letourneau R, Theoharides TC. Morphological and functional demonstration of rat dura mast cell-neuron interactions *in vitro* and *in vivo*. *Brain Res* 849:1-15, 1999.

- 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.
- 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.
- 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. *Cardiovasc 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.
- 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. *Cardiovasc 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.
- 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.
- Theoharides TC, Conti P. Mast cells: the Jekyll and Hyde of tumor growth. *Trends Immunol* 25:235-241, 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.
- 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 Sci* 25:563-568, 2004.
- Cao J, Papadopoulou N, Kempuraj D, Boucher WS, Sugimoto K, Cetrulo CL, Theoharides TC. Human mast cells express corticotropin-releasing hormone (CRH) receptors and CRH leads to selective secretion of vascular endothelial growth factor (VEGF). *J Immunol* 174:7665-7675, 2005.
- Theoharides TC, Donelan JM, Kandere-Grzybowska K, Konstantinidou A. The role of mast cells in migraine pathophysiology. *Brain Res Rev* 49:65-76, 2005.
- Kempuraj D, Madhappan B, Christodoulou S, Boucher W, Papadopoulou N, Cetrulo CL, Theoharides TC. Flavonols Inhibit pro-inflammatory mediator release, intracellular calcium ion levels and protein kinase C theta phosphorylation in human mast cells. *Br J Pharmacol* 145:934-944, 2005.
- Papadopoulou N, Kalogeromitros D, Staurianeas NG, Tiblalex D, Theoharides TC. CRH receptor and histidine decarboxylase expression in chronic urticaria. *J Invest Dermatol* 125:952-955, 2005.
- Papadopoulou N, Oleson L, Kempuraj D, Donelan J, Cetrulo CL, Theoharides TC. Regulation of corticotropin-releasing hormone receptor-2 in human umbilical cord blood derived cultured mast cells. *J Mol Endocrinol* 35:R1-R8, 2005.
- Theoharides TC, Papaliadis D, Tagen M, Konstantinidou A, Kempuraj D, Clemons A. Chronic fatigue syndrome, mast cells and tricyclic antidepressants. *J Clin Psychopharmacol* 25:515-520, 2005.
- Paus R, Theoharides TC, Arck PC. Neuroimmunoendocrine circuitry of the "brain-skin connection." *Trends Immunol* 27:32-39, 2006.
- Cao J, Curtis CL, Theoharides TC. Corticotropin-releasing hormone (CRH) induces vascular endothelial growth factor (VEGF) release from human mast cells via the cAMP/protein kinase A/p38 MAPK pathway. *Mol Pharmacol* 69:998-1006, 2006.
- Donelan J, Marchand J, Kempuraj D, Papadopoulou N, Papaliadis D, Theoharides TC. Perifollicular and perivascular mouse skin mast cells express corticotropin-releasing hormone receptor. *J Inv Dermatol* 126:932-935, 2006.
- Kandere-Grzybowska K, Kempouraj S, Cao J, Theoharides TC. Regulation of IL-1-induced selective IL-6 release from human mast cells and inhibition by quercetin. *Br J Pharmacol* 148:208-215, 2006.

Donelan J, Papadopoulou N, Marchand J, Kempuraj D, Lytinas M, Boucher W, Papaliodis D, Theoharides TC. Corticotropin-releasing hormone (CRH) induces skin vascular permeability through a neurotensin (NT)-dependent process. **Proc Natl Acad Sci USA** 103:7759-7764, 2006.

Lucas HJ, Brauch CM, Settas L, Theoharides TC. Fibromyalgia-New concepts of pathogenesis and treatment. **Intl J Immunopathol Pharmacol** 19:5-10, 2006.

Cao J, Boucher W, Donelan J, Theoharides TC. Intravesical corticotropin-releasing hormone (CRH) induces mast cell-dependent vascular endothelial growth factor (VEGF) release from bladder explants. **J Urol** 176:1208-1213, 2006.

Theoharides TC, Konstantinidou A. Corticotropin-releasing hormone and the blood-brain-barrier. **Front Biosci** 12:1615-1628, 2007.

Boucher W, Cao J, Kempuraj D, Donelan J, Theoharides TC. Intravesical IPD inhibits experimental bladder inflammation. **J Urol** 177:1186-1190, 2007.

Theoharides TC, Kalogeromitros D. Mast cells in allergy and inflammation. **Ann New York Acad Sci** 1088:78-99, 2006.

Theoharides TC. Current approaches to the pharmacological management of painful bladder syndrome/interstitial cystitis. **Drugs** 67:215-235, 2007.

Theoharides TC, Kempuraj D, Tagen M, Conti P, Kalogeromitros D. Differential release of mast cell mediators and the pathogenesis of inflammation. **Immunol Rev** 217:65-78, 2007.

Tagen M, Stiles L, Kalogeromitros D, Gregoriou S, Kempuraj D, Makris M, Donelan J, Vasiadi M, Staurianeas G, Theoharides TC. Skin CRH receptor expression in psoriasis. **J Inv Dermatol** 127:1789-91, 2007.

Theoharides TC, Kempuraj D, Iliopoulou BP. Mast cells, T Cells and inhibition by luteolin: Implications for the pathogenesis and treatment of multiple sclerosis. **Adv Exp Med Biol** 601:423-30, 2007.

Sant GR, Kempuraj D, Marchand JE, Theoharides TC. The mast cell in interstitial cystitis-role in pathophysiology and pathogenesis. **Urology** 69 (suppl 4A):34-40, 2007.

Theoharides TC. Treatment approaches for painful bladder syndrome/interstitial cystitis. **Drugs** 67:215-235, 2007.

Boucher W, Stern J, Kempuraj D, Papaliodis D, Kotsinyan, V, Cohen MS, Theoharides TC. Intravesical nanocrystalline silver inhibits experimental bladder inflammation. **J Urol** 179:1598-602, 2008.

Papaliodis D, Boucher W, Kempuraj D, Theoharides TC. The flavonoid luteolin inhibits niacin-induced flush. **Br J Pharmacol** 153:1382-1387, 2008.

Kalogeromitros D, Makris M, Cliva C, Aggelides X, Kempuraj D, Theoharides TC. A quercetin containing supplement reduces niacin-induced flush in humans. **Intl J Immunopathol Pharmacol** 21:467-472, 2008.

Theoharides TC. Mast cells and pancreatic cancer. **New Engl J Med** 358:1860-1861, 2008.

Theoharides TC, Doyle R, Francis K, Conti P, Kalogeromitros D. Novel therapeutic targets for autism. **Trends Pharmacol Sci** 29:375-382, 2008.

Theoharides TC, Doyle R. Autism, gut-blood-brain barrier and mast cells. **J Clin Psychopharm** 28:479-483, 2008.

Papaliodis D, Boucher W, Kempuraj D, Michaelian M, Wolfberg A, House M, Theoharides TC. Niacin-induced "flush" involves release of PGD₂ from mast cells and serotonin from platelets: evidence from human cells *in vitro* and an animal model. **J Pharmacol Exp Therap** 327:665-672, 2008.

Theoharides TC, Whitmore K, Stanford E, Moldwin R, O'Leary MP. Interstitial cystitis: bladder pain and beyond. **Expert Opin Pharmacother** 9:2979-2994, 2008.

Kempuraj D, Tagen M, Iliopoulou BP, Clemons A, Vasiadi M, Boucher W, House M, Wolfberg A, Theoharides TC. Luteolin inhibits myelin basic protein-induced human mast cell activation and mast cell-dependent stimulation of Jurkat T cells. **Br J Pharmacol** 155:1076-1084, 2008.

Theoharides TC, Rozniecki JJ, Sahagian G, Jacobson S, Kempuraj D, Conti P, Kalogeromitros D. Impact of stress and mast cells on brain metastases. **J Neuroimmunol** 205:1-7, 2008.

Theoharides TC, Vakali S, Kempuraj D, Sant GR. Treatment of refractory interstitial cystitis/painful bladder syndrome with CystoProtek-an oral multiagent natural supplement. **Canadian J Urol** 15:4410-4414, 2008.

Theoharides TC, Kempuraj D, Redwood L. Autism-an emerging "neuroimmune disorder" in search of therapy. **Exp. Opinion Pharmacotherapy**, in press, 2009.

C. Research Support

Recently Completed Research Support

1 R01 NS38326 NINDS (PI: Theoharides)

CRH-induced dura mast cell activation

Duration: 7/1/99-6/30/0340%

Direct Cost/yr: \$153,573

BC024430 DOD- Concept Award (PI: Theoharides)

Duration: 7/1/03- 6/30/04 10%

1 R21 NS055681-01 (PI: Theoharides)

Mast cells, tricyclic antidepressants and chronic fatigue syndrome

Duration: 9/1/06-9/29/0820%

Direct cost: \$175,000

1 R01 DK062861-04 NIDDK (PI: Theoharides)-no cost extension

Acute restraint stress-induced neurogenic bladder inflammation

Duration: 5/1/03-4/30/0930%

Direct Cost/yr: \$175,000

Active Research Support

2 R01 AR47652-08 NIAMS (PI: Theoharides)

Stress induces skin mast cell activation and vasodilation

Duration: 9/1/07-3831/12 30%

Direct Cost/yr: \$215,000

National Autism Association (PI: Theoharides)

Mast cell-related biomarkers in autism

Duration: 5/1/09-12/31/09

Direct cost: \$35,000