

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.**

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|---|--|---|----------|-----------------------------|
| NAME THEOHARIDES, THEOHARIS C. | | POSITION TITLE Professor of Pharmacology and Internal Medicine (Allergy), and Biochemistry | | |
| eRA COMMONS USR NAME (credential, e.g. agency login) THEOHAR | | | | |
| 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 | Neuroimmunology |
| 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 Law & Diplomacy | | Certificate | 1999 | Leadership & Management |
| Harvard Univ, 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. Personal Statement

I have been studying the regulation of mast cell activation and its role in neuroinflammatory diseases for over 20 years. I was the first to report that mast cells: (a) can secrete specific mediators selectively without degranulation that allows them to participate in different tissue processes, such as inflammation and angiogenesis, (b) can regulate blood vessel permeability, (c) can be activated by corticotropin-releasing hormone (CRH) to release VEGF selectively, (d) can be activated by synergistic action of CRH and neurotensin secreted under stress, (e) can be activated by IL-33 and substance P synergistically, (f) can secrete preformed TNF, accompanied by mitochondrial translocation to the cell surface and release of mitochondrial DNA (mtDNA), which induces auto-immune responses, and (g) mtDNA and neurotensin are elevated in serum of young autistic children. I have been placed in the top 1% of authors most cited in pharmacological and top 5% of immunological journals; my review on flavonoids has been selected as a "classic" for the number of citations it has received.

B. Positions and Honors

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 Univ & Tufts Medical Center, Boston, MA
2004- Director, Molecular Immunopharmacology and Drug Discovery Laboratory, 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
 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*, Instiit of Social Welfare, Sec. of Labor & Human Res, Hellenic Republic
 1999 *Oliver Smith Award* "recognizing excellence, compassion and service", New Engl. Med. Center,
 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
 2009 *Fellow*, European Academy of Allergology and Clinical Immunology
 2011 *Honorary Doctor of Science degree*, Athens University (conferred January 25, 2011)

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 Peptides
 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 & Inflammatory Pathways
 2007 NIAID Asthma & Allergic Diseases Cooperative Research Centers
 2008 NIH ZRG1 CFS-D
 2009 DK ZDK1 GRB-6 Urology Research Centers
 2009 SEP, National Center for Minority Health & Disparities (NCMHD)
 2010 NIMSD ZRG1 MOSS-D12B SBIR: Dermatology, Rheumatology and Inflammation
 2011 NIH ZRG1 IFCN-H (80) S
 2011 NIH ZRG1 IFCN-H (90) S

C. Selected Publications (from >300 in Pubmed.gov, 9.939 citations)

Of general importance

1. 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. PMID: 49027
2. 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. PMID: 357989
3. Theoharides TC, Douglas WW. Secretion in mast cells induced by calcium entrapped within phospholipid vesicles. *Science* 201:1143-1145, 1978. PMID: 684435
4. 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. PMID: 6153130
5. Theoharides TC, Bondy PK, Tsakalos ND, Askenase PW. Differential release of serotonin and histamine from mast cells. *Nature* 297:229-231, 1982. PMID: 6176873

6. 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. PMID: 7588332
7. 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 Ther* 287(1):307-14, 1998. PMID: 9765351
8. Singh LK, Pang X, Alexacos N, Letourneau R, Theoharides TC. Acute immobilization stress triggers skin mast cell degranulation via corticotropin releasing hormone, neurotensin, and substance P: A link to neurogenic skin disorders. *Brain Behav Immun* 13(3):225-39, 1999. PMID:10469524
9. Kandere-Grzybowska, K., Letourneau, R., Kempuraj, D., Donelan, J., Paplawski, S., Boucher, W., Athanassiou, A. and Theoharides, TC. Interleukin-1 induces vesicular secretion of interleukin-6 without degranulation from human mast cells. *J Immunol* 171:4830-4836, 2003. PMID: 14568962
10. Donelan J, Papadopoulou N, Marchand J, Kempuraj D, Lytinas M, Boucher W, Papaliadis 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. PMID: 16682628
11. 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. PMID: 17498052
12. Theoharides TC, Papaliadis D, Tagen M, Konstantinidou A, Kempuraj D, Clemons A. Chronic fatigue syndrome, mast cells, and tricyclic antidepressants. *J Clin Psychopharmacol* 25(6):515-20, 2005. PMID: 16282830
13. 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(7):1076-84, 2008. PMID:18806808
14. Theoharides TC. Mast cells and pancreatic cancer. *N Engl J Med* 358(17):1860-1, 2008. PMID: 18434656
15. Tagen M, Elorza A, Kempuraj D, Boucher W, Kepley CL, Shirihai OS, Theoharides TC. Mitochondrial uncoupling protein 2 inhibits mast cell activation and reduces histamine content. *J Immunol* 183:6313-6319, 2009. PMID: 19846869
16. Theoharides TC, Kempuraj D, Redwood L. Autism-an emerging “neuroimmune disorder” in search of therapy. *Exp Opin Pharmacotherapy* 10(13):2127-2143, 2009. PMID: 19640207
17. Theoharides TC, Zhang B, Kempuraj D, Tagen M, Vasiadi M, Angelidou A, Alysandratos KD, Kalogeromitros D, Asadi S, Stavrianeas N, Peterson E, Leeman S, Conti P. IL-33 augments substance P-induced VEGF secretion from human mast cells and is increased in psoriatic skin. *Proc Natl Acad Sci USA* 107(9):4448-53, 2010. PMID: 20160089
18. Zhang B, Alysandratos KD, Angelidou A, Asadi S, Sismanopoulos N, Delivanis D-A, Weng Z, Miniati A, Vasiadi M, Katsarou-Katsari A, Miao B, Leeman S, Kalogeromitros D, Theoharides TC. Human mast cell degranulation and granule-stored TNF secretion requires mitochondrial translocation to sites of exocytosis. *J Allergy Clin Immunol* 127(6):1522-1531.e8. 2011. PMID: 21453958
19. Angelidou A, Francis K, Vasiadi M, Alysandratos KD, Zhang B, Theoharides A, Lykouras L, Sideri K, Kalogeromitros D, Theoharides TC. Neurotensin is increased in serum of young children with autistic disorder. *J Neuroinflammation* 7:48, 2010. PMID: 20731814
20. Theoharides TC, Zhang B, Kempuraj D, Tagen M, Vasiadi M, Angelidou A, Alysandratos KD, Kalogeromitros D, Asadi S, Stavrianeas N, Peterson E, Leeman S, Conti P. IL-33 augments substance P-induced VEGF secretion from human mast cells and is increased in psoriatic skin. *Proc Natl Acad Sci USA* 107(9):4448-53, 2010. PMID: 20160089
21. Zhang B, Alysandratos KD, Angelidou A, Asadi S, Sismanopoulos N, Delivanis D-A, Weng Z, Miniati A, Vasiadi M, Katsarou-Katsari A, Miao B, Leeman S, Kalogeromitros D, Theoharides TC. Human mast cell degranulation and granule-stored TNF secretion requires mitochondrial translocation to sites of exocytosis. *J Allergy Clin Immunol* 127(6):1522-1531.e8. 2011. PMID: 21453958
22. Zhang B, Angelidou A, Alysandratos KD, Vasiadi M, Francis K, Asadi S, Theoharides A, Sideri K, Lykouras L, Kalogeromitros D, Theoharides TC. Mitochondrial DNA and anti-mitochondrial antibodies in serum of autistic children. *J Neuroinflammation* 7:80, 2010. PMID:21083929
23. Clemons A, Vasiadi M, Kempuraj D, Kourelis T, Vandoros G, Theoharides TC. Amitriptyline and prochlorperazine inhibit proinflammatory mediator release from human mast cells: possible relevance to chronic fatigue syndrome. *J Clin Psychopharmacol* 31(3):385-7, 2011. PMID: 21532369

24. Alysandratos KD, Angelidou A, Vasiadi M, Zhang B, Kalogeromitros D, Katsarou-Katsari A, Theoharides TC. Increased affected skin gene expression and serum levels of thymic stromal lymphopoietin in atopic dermatitis. *Ann Allergy Asthma Immunol* 105(5):403-4, 2010. PMID: 21055671
25. Kempuraj D, Conti P, Vasiadi M, Alysandratos KD, Tagen M, Kalogeromitros D, Kourelis T, Gregoriou S, Makris M, Stavrianeas NG, Theoharides TC. IL-32 is increased along with tryptase in lesional psoriatic skin and is up-regulated by substance P in human mast cells. *Eur J Dermatol* 20(6):865-7, 2010. PMID: 21047723
26. Rozniecki JJ, Sahagian GG, Kempuraj D, Tao K, Jacobson S, Zhang B, Theoharides TC. Brain metastases of mouse mammary adenocarcinoma is increased by acute stress. *Brain Res* 1366:204-10, 2010. .PMID: 20887716
27. Theoharides TC, Sismanopoulos N, Delivanis DA, Zhang B, Hatziagelaki EE, Kalogeromitros D. Mast cells squeeze the heart and stretch the gird: Their role in atherosclerosis and obesity. *Trends Pharmacol Sci* 32(9):534-542., 2010. PMID: 21741097
28. Theoharides TC, Asadi S, Weng Z, Zhang B. Serotonin-selective reuptake inhibitors and nonsteroidal anti-inflammatory drugs-Important considerations of adverse interactions especially for the treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *J Clin Psychopharmacol* 31(4):403-5, 2011. PMID:21694612
29. Angelidou A, Alysandratos KD, Asadi S, Zhang B, Francis K, Vasiadi M, Kalogeromitros D, Theoharides TC. Brief Report: "Allergic Symptoms" in children with Autism Spectrum Disorders. More than meets the Eye? *J Autism Dev Disord*. 2011 Jan 6. [Epub ahead of print] PMID:21210299
30. Theoharides TC, Alysandratos KD, Angelidou A, Delivanis DA, Sismanopoulos N, Zhang BD, Asadi S, Vasiadi M, Weng Z, Miniati A, Kalogeromitros D. Mast cells and Inflammation. *Biochim Biophys Acta*. 2010 Dec 23. [Epub ahead of print] PMID: 21185371
31. Asadi S, Alysandratos K-D, Angelidou A, Miniati A, Sismanopoulos N, Vasiadi M, Zhang B, Kalogeromitros D, Theoharides TC. Substance P (SP) induces expression of functional corticotropin-releasing hormone receptor-1 (CRHR-1) in human mast cells. *J Investig Dermatol*, in press, 2011

D. Research Support

Active

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|---|----------------------------|
| 2 R01 AR047652-10 (PI: Theoharides) Stress induces skin mast cell activation and vasodilation | Duration: 9/1/07-8/31/12 |
| Autism Research Collaborative (PI: Theoharides) Mast cell-related biomarkers in autism | Duration: 5/1/10-4/30/12 |
| 1 R01 NS066205-02 (MPI: Veves and LoGerfo; TCT role:Consultant) Role of neuropeptides in diabetic foot problems | Duration: 7/1/10-6/30/15 |
| 1 R01 DK091949-01-01 (PI:Veves; TCT role: Subcontract) Mechanisms of neuropeptide action in diabetes | Duration: 10/1/11-6/30/15 |
| 1 R01 NS071361-02 (PI: Theoharides) Brain mast cells and chronic fatigue syndrome | Duration: 7/1/10-6/30/15 |
| Safe Minds/Autism Research Collaborative (PI: Theoharides) Mast cell stimulation leads to secretion of mitochondrial components that contribute to autism | Duration: 1/1/11-12/31/12 |
| Autism Research Collaborative (PI: Theoharides) Investigation of IL-9, IL-33 and TSLP in serum of autistic children | Duration: 4/19/11-12/31/11 |

Recently Completed Research Support

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| BC024430 DOD-Concept Award (PI: Theoharides) Role of mast cells in mammary gland carcinogenesis | Duration: 7/1/03– 6/30/04 |
| 1 R01 DK062861-04 (PI: Theoharides) Acute restraint stress-induced neurogenic bladder inflammation | Duration: 5/1/2003-4/30/07 |
| 1 R21 NS055681-02 (PI: Theoharides) Mast cells, tricyclic antidepressants and chronic fatigue syndrome | Duration: 9/1/2006-9/29/08 |
| Mastocytosis Society (PI: Theoharides) Skin mast cell expression of CRH receptors | Duration: 5/1/09-12/31/09 |
| National Autism Association (PI: Theoharides) Mast cell-related biomarkers in autism | Duration: 5/1/09-12/31/09 |
| Safe Minds (PI: Theoharides) Effect of mercury on human mast cells | Duration: 5/1/09-12/31/09 |