

BIOGRAPHICAL SKETCH

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NAME Jun Tan	POSITION TITLE Robert A. Silver Chair in Developmental Neurobiology, Silver Professor of Psychiatry, Molecular Medicine, Molecular Pharmacology & Physiology, and Neurosurgery		
eRA COMMONS USER NAME JUNTAN			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Third Medical University, Chongqing, China	M.D.	1978-1983	Medicine
Fudan University, Shanghai, China	MSc.	1986-1989	Human Genetics
Third Medical University/Fudan University, China	Ph.D.	1990-1992	Biomedical Science
University of Michigan Medical School	Post-Doc.	1994-1996	Genetics and Immunology
H. Lee Moffitt Cancer Center & Research Institute	Post-Doc.	1997-1998	Genetics and Immunology

A Positions and Employment

- 2007-present Robert A. Silver Chair in Developmental Neurobiology, Silver Professor (tenured), Silver Child Development Center, Department of Psychiatry & Behavioral Medicine, University of South Florida College of Medicine, Tampa, Florida, USA
- 2004-2007 Associate Professor (tenured), Department of Psychiatry & Behavioral Medicine, Director of NeuroImmunology Laboratory, Institute for Research in Psychiatry (IRP), University of South Florida College of Medicine, Tampa, Florida, USA
- 2003-2004 Assistant Professor, Department of Psychiatry & Behavioral Medicine; Department of Medical Microbiology & Immunology; Director of NeuroImmunology Laboratory, IRP, University of South Florida College of Medicine, Tampa, Florida, USA
- 1998-2003 Assistant Professor, Department of Psychiatry; Head, NeuroImmunology Division in Roskamp Institute, University of South Florida College of Medicine, Tampa, Florida, USA
- 1992-1994 Associate Professor and Head, Department of Molecular Genetics, Third Medical University/Chongqing, China
- 1985-1986 Instructor, Department of Medical Genetics, Third Medical University/Chongqing, China
- 1983-1985 Assistant Professor, Department of Anatomy & Histology, Third Medical University/Chongqing, China

B Honors

- Investigator-Initiated Award: Alzheimer Association (2003)
- Younger Investigator Award: Byrd Alzheimer's Center & Institute (2004)
- Established Investigator Award: Institute for the Study of Aging (2006)
- The 3rd Annual USF Biotechnology Achievement Award (2006)
- The Robert A. Silver Chair in Developmental Neurobiology (2007)

C Selected peer-reviewed publications (Publications selected from 80 peer-reviewed publications)

- Giunta B, Pattie Figueroa K, Town T and **Tan J***. Targets to watch - soluble CD40 ligand in dementia. Drug Future (in press 2009).
- Rrapo E, Zhu Y, Tian J, Hou H, Smith A, Fernandez F, **Tan J**, Giunta B. Green Tea-EGCG reduces GFAP associated and neuronal loss in HIV-1 Tat transgenic mice Am J Transl Res 2009; 1: 72-79.
- Antoinette B, Giunta B, Obregon D, Nikolic W, Tian J, Sanberg C, Sutton D and **Tan J***. Peripheral biomarkers in Autism: sAPP- α as a probable key player in early diagnosis. Int J Clin Exp Med 1(4):338-44 (2008).
- Giunta B, Fernandez F, Nikolic WN, Obregon D, Rrapo E, Town T and **Tan J**. Inflammation as a prodrome to Alzheimer's disease. J Neuroinflammation 5 (1):51 (2008).
- Zhu YY, Bickford P, Sanberg P, Giunta B and **Tan J***. Blueberry opposes β -amyloid peptide-induced microglial activation *via* inhibition of p44/42 Mitogen-Activation Protein Kinase. Rejuvenation Res 11(5):891-901 (2008).
- Rezai-Zadeh K, Ehrhart J, Bickford P, **Tan J** and Shytle D. Apigenin and luteolin modulate microglial activation *via* inhibition of STAT1 induced CD40 expression. J Neuroinflammation 5:41 (2008).

7. Town T, Laouar Y, Pittenger C, Mori T, Szekely C, **Tan J**, Duman R and Flavell R. Blocking TGF- β -Smad2/3 innate immune signaling mitigates Alzheimer's-like pathology. Nat Med 14(6):681-7 (2008).
8. Wang Y, Li M, Song M, Xu X, **Tan J** and Bai Y. Expression of OX40 ligand in microglia activated by IFN- γ sustains a protective CD4(+) T-cell response in vitro. Cell Immunol 251(2):86-92 (2008).
9. Zhu YY, Hou HY, Nikolic W, Bickford P, Giunta B and **Tan J***. CD45RB is a novel molecular therapeutic target to inhibit A β peptide-induced microglial MAPK activation. PLoS ONE 3(5):e2135 (2008).
10. Rezai-Zadeh K, Arendash G, Fernandez F, Shytle D and **Tan J***. Green tea EGCG reduces β -amyloid mediated cognitive impairment and modulates tau pathology in Alzheimer transgenic mice. Brain Res 1214:177-187 (2008).
11. Mori T, **Tan J**, Arendash G, Koyama N, Nojima Y and Town T. Overexpression of Human S100B Exacerbates Brain Damage and Peri-infarct Gliosis after Permanent Focal Ischemia. Stroke 39(7):2114-21 (2008).
12. Rezai-Zadeh K, Shytle D, Tian J, Hou HY, Zeng J, Obregon D, Mori T, Town T, and **Tan J***. Flavonoid-mediated presenilin-1 phosphorylation reduces Alzheimer's disease β -amyloid production. J Cell Mol Med 2008 Apr 9 [Epub ahead of print]
13. Hou HY, Obregon D, Luo D, Ehrhart J, Fernandez F, Silver A and **Tan J***. Modulation of neuronal differentiation by CD40 isoforms. Biochem Biophys Res Commun 369 (2) 641-647 (2008).
14. Nikolic W, Town T, Mori T, Zeng J, Luo, D, Sanberg C, Sanberg P and **Tan J***. Peripherally administered HUCBC reduce parenchymal and vascular A β deposits in Alzheimer mice. Stem Cells Dev 17:1-17 (2008).
15. Giunta B, Zhou YY, Hou HY, Rrapo E, Fernandez F and **Tan, J**. HIV-1 Tat inhibits microglial phagocytosis of A β peptide. Int J Clin Exp Pathol 1 (3):260-275 (2008).
16. Obregon D, Nikolic W, Mori T, Zeng, J, Luo D, Ehrhart J, Fernandez F, Morgan D, Town T and **Tan J***. CD40L disruption enhances A β vaccine-mediated reduction of cerebral amyloidosis while minimizing cerebral amyloid angiopathy and inflammation. Neurobiol Dis 29 (2) 336-353 (2008).
17. Shytle D, Ehrhart J, **Tan J**, Vila J, Cole M, Sanberg C, Sanberg P and Bickford P. Oxidative stress of neural, hematopoietic, and stem cells: protection by natural compounds. Rejuvenation Res 10(2):173-178 (2007).
18. Nikolic WV, Obregon D, Hou H, Mori T, Zeng J, Ehrhart J, Shytle D, Giunta B, Morgan D, Town T and **Tan J***. Transcutaneous β -amyloid immunization of transgenic Alzheimer's mice reduces cerebral β -amyloid deposits without T-cell infiltration and microhemorrhage. Proc Natl Acad Sci U S A 104:2507-2512 (2007).
19. Cracchiolo JR, Mori T, Nazian SJ, **Tan J**, Potter H, Arendash GW. Enhanced cognitive activity--over and above social or physical activity--is required to protect Alzheimer's mice against cognitive impairment, reduce Abeta deposition, and increase synaptic immunoreactivity. Neurobiol Learn Mem 88(3):277-94 (2007).
20. Giunta B, Obregon D, Hou H, Zeng J, Nikolic V, Ehrhart J, Shytle D, Fernandez F and **Tan J***. EGCG mitigates neurotoxicity mediated by HIV-1 proteins gp120 and Tat in the presence of IFN- γ : role of JAK/STAT1 signaling and implications for HIV-associated dementia. Brain Res 11 (23):216-225 (2006).
21. Arendash GW, Schleif W, Rezai-Zadeh K, Jackson EK, Zacharia LC, Cracchiolo JR, Shippy D and **Tan J**. Caffeine protects Alzheimer's mice against cognitive impairment and reduces brain β -amyloid production Neuroscience 142 (4):941-952 (2006).
22. Mori T, Town T, **Tan J**, Shimoda T, Kamanaka Y, Tateishi N and Asano T. Arundic Acid Ameliorates Cerebral Amyloidosis and Gliosis in Alzheimer Transgenic Mice. J Pharmacol Exp Ther 318 (2):571-578 (2006).
23. Obregon D, Rezai-Zadeh K, Zeng J, Shytle D, Town T and **Tan J***. ADAM10 activation is required for green tea EGCG-induced α -secretase cleavage of amyloid precursor protein. J Biol Chem 281 (24):16419-16427 (2006).
24. Bickford PC, **Tan J**, Shytle D, Sanberg CD, El-Badri N and Sanberg PR. Nutraceuticals synergistically promote proliferation of human stem cells. Stem Cells Dev 15 (1):118-23 (2006).
25. Town T, Jeng D, Alexopoulou L, **Tan J** and Flavell R. Microglia recognize double-stranded RNA *via* Toll-like receptor 3. J Immunol 176:3804-3812 (2006).
26. Ehrhart J, Obregon D, Mori T, Hou H, Zeng J, Bai Y, Klein T, Fernandez F, **Tan J*** and Shytle RD. Stimulation of cannabinoid receptor 2 (CB₂) suppresses microglial activation. J Neuroinflammation 2:29 (2005).
27. Town T, Nikolic V and **Tan J***. The microglial "activation" continuum: from innate to adaptive responses (review). J Neuroinflammation 2:24 (2005).
28. Rezai-Zadeh K, Shytle D, Mori T, Hou H, Ehrhart J, Zeng J, Hardy J, Morgan D, Town T and **Tan J***. Green tea epigallocatechin-3-gallate (EGCG) modulates amyloid precursor protein cleavage and reduces cerebral amyloidosis in Alzheimer's transgenic mice. J Neurosci 25 (38):8807-8814 (2005).

29. Morgan D, Gordan M, **Tan J**, Wilcock D and Rojiani A. Dynamic Complexity of the Microglial activation response in transgenic models of amyloid deposition. Implications for Alzheimer's therapeutics (review). J Neuropathol Exp Neurol 64(9):743-753 (2005).
30. Townsend K, Town T, Zeng J, Shytle D, Morgan D and **Tan J***. Regulation of the A β -induced innate and adaptive immune responses by CD40 signaling in microglial cells. Eur J Immunol 35 (3):901-910 (2005).
31. Mori T, Town T, **Tan J**, Tateishi N, Asano T. Modulation of astrocytic activation by arundic acid (ONO-2506) mitigates detrimental effects of the apolipoprotein E4 isoform after permanent focal ischemia in apolipoprotein E knock-in mice. J Cereb Blood Flow Metab 25(6):748-62 (2005).
32. Mori T, Town T, Kobayashi M, **Tan J**, Fujita SC, Asano T. Augmented delayed infarct expansion and reactive astrocytosis after permanent focal ischemia in apolipoprotein E4 knock-in mice. J Cereb Blood Flow Metab 24(6):646-56 (2004).
33. Townsend K, Shytle D, Zeng J, Fernandez F, Morgan D, Sanberg, P and **Tan J***. Lovastatin modulation of microglial activation *via* suppression of functional CD40 expression. J Neurosci Res 78:167-176 (2004).
34. Giunta B, Ehrhart J, Zeng J, Shytle D and **Tan J*** and Fernandez F. Galantamine and nicotine have a synergistic effect on inhibition of microglial activation induced by HIV-1 gp120. Brain Res Bull 64 (2):165-170 (2004).
35. Todd Roach J, Volmar CH, Dwivedi S, Town T, Crescentini R, Crawford F, **Tan J** and Mullan M. Behavioral effects of CD40-CD40L pathway disruption in aged PSAPP mice. Brain Res 1015(1-2):161-168 (2004).
36. Townsend K, Vendrame M, Ehrhart J, Faza B, Zeng J, Town T and **Tan J***. CD45 isoform RB as a molecular target to oppose LPS-induced microglial activation. Neurosci Lett 362 (1):26-30 (2004).
37. Shytle D, Mori T, Vendrame M, Sun N, Zeng J, Ehrhart J, Silver A, Sanberg P and **Tan J***. Cholinergic modulation of microglial activation by $\alpha 7$ nicotinic receptors. J Neurochem 89:337-343 (2004).
38. Mott R, Town T, Mori T, Vendrame M, Zeng J, Ehrhart J, Mullan M and **Tan J***. Neuronal expression of CD22: a novel mechanism for inhibiting microglial proinflammatory cytokine production. GLIA 46:369-379 (2004).
39. **Tan J**, Town T, Crawford F, Mori T, DelleDonne A, Crescentini R, Obregon D, Flavell RA and Mullan MJ. Role of CD40 ligand in amyloidosis in transgenic Alzheimer's mice. Nat Neurosci 5(12):1288-1293 (2002).
40. Town T, Vendrame M, Patel A, Poetter D, DelleDonne A, Mori T, Smeed R, Crawford F, Klein T, **Tan J*** and Mullan M. Reduced Th1 and enhanced Th2 immunity after immunization with Alzheimer's beta-amyloid (1-42). J Neuroimmunol 132(1-2):49-59 (2002).
41. **Tan J***, Town T, Abdullah L, Placzek A, J Kroeger, Crawford F, Dan R, Mullan M. CD45 isoform alteration in CD4+ T cells as a potential diagnostic marker of Alzheimer's disease. J Neuroimmunol 132 (1-2):164-172 (2002).
42. **Tan J***, Town T, Mori T, Wu Y, DelleDonne A, Obregon D, Rojiani A, Flavell R, Mullan M. CD40 is expressed and functional on neuronal cells. EMBO J 21 (4):37224-37231 (2002).
43. **Tan J***, Town T, Mullan M. CD45 inhibits CD40L-induced Microglial Activation via negative regulation of the Src/p44/42 MAPK Pathway. J Biol Chem 275 (47):37224-37231 (2000).
44. **Tan J***, Town T, Mori T, Wu Y, Saxe M, Crawford F, Mullan M. CD45 opposes β -amyloid peptide-induced microglial activation via inhibition of p44/42 MAPK. J Neurosci 20 (20):7587-7594 (2000).
45. Town T, Schinka J, **Tan J**, Mullan M. The opioid receptor system and alcoholism: a genetic perspective (review). Eur J Pharmacol 410(2-3):243-248 (2000).
46. **Tan J**, Town T, Paris D, Mori T, Crawford F, Mattson M, Flavell R, Mullan M. The CD40-CD40L interaction leads to microglial activation after β -amyloid stimulation. SCIENCE 286 (17):2352-2355 (1999).
47. **Tan J***, Town T, Saxe M, Paris D, Wu J, Mullan M. Ligation of microglial CD40 results in p44/42 MAP kinase-dependent TNF- α production that is opposed by TGF- β 1 and IL-10. J Immunol 163 (12):6614-6621 (1999).

D Research Support (Ongoing Research Support)R01 NINDS NS048335

Tan (PI)

06/01/04-05/31/09

CD40 Modulation of A β -Vaccine Immune Responses - The specific aims of this proposal are 1) investigate the effects of CD40 signaling on microglial phagocytic and antigen presentation phenotypes *in vitro*; 2) test whether the depletion of CD40L could synergistically affect microglial phagocytosis and its association AD-like pathology and cognitive impairment in A β -immunized PSAPP mice; 3) evaluate the effects of CD40 signaling on modulation of microglial phagocytosis of anti-A β antibody-opsonization A β peptides *in vitro* and *in vivo*.

NIH Training Grant in Neurogenerative Disorders (Demian Obregon, Ph.D./M.D. student, supplement to my RO1 funding)

P01 NIH/NIA 04418 Project 2

Tan (PI)

10/01/06-09/30/11

CD45 Modulation of Microglial Activation and Neuroprotective Property - In this proposal, we hypothesize that CD45 deficient mice will increase activated microglia at an early age, and therefore will show increased neurodegeneration. To test this hypothesis, we plan to fully characterize the role of CD45 in modulation of microglial activation *in vitro* and *in vivo* by examining its signaling pathways and resultant effects on microglial phagocytic capability, cytokine profiles and degeneration of cholinergic/dopaminergic neurons, and specifically its impact on aging in Alzheimer transgenic mice, as its effects on AD-like pathology and behavioral changes.

R21 NIH/NIMH Tan (PI) 07/01/07-06/30/09

Green tea derived EGCG opposes AIDS dementia-like neuronal damage - The specific aims of this proposal are 1) EGCG inhibits JAK/STAT1 signaling pathway. The mechanism whereby EGCG modulates JAK/STAT1 signaling pathway in primary neuronal cells will be fully explored; 2) EGCG prevents HIV dementia-like neuronal cell death *in vivo* and *in vitro*.

R21 NIH/NIA Tan (Co-PI; Shytle, PI) 03/01/07-02/28/09

Nicotine/Cannabinoid Therapy for Alzheimer's disease - The goal of this proposal is to test whether cholinergic modulation would impact AD-like pathology in AD animal model. Furthermore, these studies will gain an insight into the mechanisms of action of nicotine and/or galantamine to mitigate AD-like pathology.

ARG-2007-01 (Byrd AD Center & Institute) Tan (PI) 11/01/07-10/30/08

Activation of α -secretase as a potential therapeutic strategy for Alzheimer's disease - This work will be completed by investigation of the following aims: (1) *In vivo* evaluation of the effects of atranorin and octyl gallate for the promotion of non-amyloidogenic APP alpha-secretase proteolysis; (2) Investigation of therapeutic/preventive effects of atranorin and octyl gallate on A β /beta-amyloid pathology and cognitive impairment.

STTR NIH/NIA Tan (PI) 10/01/07-09/30/08

HUCBC Modulation of Alzheimer-like Pathology and Behavioral Changes - This work will be carried out by the following aims: (1) Determine AD-like pathological changes associated with multiple HUCBC injections in PSAPP mice; (2) Determine cognitive and behavioral changes in HUCBC-infused PSAPP mice.

SBIR NIH/NCAAM Tan (PI) 07/01/08-06/30/09

Oral administration of TeaMemTM inhibits Alzheimer's disease pathogenesis - This work could lay the foundation for AD clinical trials with pure TeaMemTM or/and piperine in the near future.

FADRC NIH/HIA (Pilot Project) Tan (PI) 04/01/08-03/31/09

Characterization of AlzFlu vaccine in APP transgenic mice - This work will be carried out by the following aims: (1) Characterize immune responses in Tg2576 and control mice following AlzFlu vaccination; (2) Examine AD-like pathology and behavioral changes in Tg2576 mice following AlzFlu vaccination.

K08 NIH/NIMH Tan (Primary Mentor; Giunta, PI) 03/01/08-02/28/12

The Role of HIV-1 Tat in Alzheimer's disease - This work will be carried out by the following: (1) Research aims, (2) Other specialized training experiences, (3) Coursework and (4) Presentations will provide the best possible training experience for progression toward an independent research career.

E Research Projects Concluded

Alzheimer Association IIRG-02-4064 Tan (PI) 08/01/02-07/31/06

Role of CD40L in Gliosis and Amyloidosis in Alzheimer Transgenic Mice - The major goals of this project are (1) the examination of age-dependent A β / β -amyloid pathology in Tg2576/CD40L deficient mice compared to Tg2576 mice; (2) characterization of markers of the activated microglia (CD40, CD11b, MHC II) and the reactive microglial product complement C1q component Tg2576/CD40L deficient versus Tg2576 mice as they age; (3) investigation of the activated astrocytes and their production apolipoprotein E in aging Tg2576/CD40L deficient mice compared to Tg2576 mice.

RSCH 04053 (Byrd Center & Institute) Tan (PI) 07/01/04-06/30/06

Th1/Th2 Cytokine Modulation in AD-like Pathology - The goal of this proposal is to test whether modulation of Th1/Th2 associated cytokines peripherally and in the CNS could impact AD-like pathology, particularly, glia-associated chronic inflammation and A β plaque formation. Further, these studies will gain an insight into the mechanism(s) of action of A β ₁₋₄₂ immunization to mitigate AD-like pathology, and will additionally highlight therapeutic strategies to boost or enhance the effect of A β ₁₋₄₂ immunization and allow the development of novel therapeutic strategies for treatment of AD.

Institute for the Study of Aging (ISOA) Tan (PI) 03/01/06-02/28/08

Green tea EGCG modulates amyloid precursor protein cleavage and reduces amyloidosis in Alzheimer's transgenic mice - The goal of this proposal is to test if oral administration of EGCG could oppose AD-like pathology and improve cognitive impairment. This study could lay the foundation for AD clinical trials with pure EGCG in the nearest future.