

BIOGRAPHICAL SKETCH

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NAME: WanJun Chen

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Senior Investigator

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Qingdao University Medical School (Qingdao) China)	M.D.	1984	Medicine
Shandong University Medical School and Shandong Academy of Medical Sciences (Jinan) China)	M.S.	1987	Microbiology and Immunology
Harvard Medical School (Boston)	Postdoctoral Research	1993-1996	Immunology

A. Personal Statement

I am elucidating mechanisms of TGF-beta and regulatory T cell (Treg) regulation of immunity and tolerance, and manipulating T-cell immunity versus tolerance in animal models to understand the pathogenesis of autoimmunity and inflammation, cancer and infectious diseases and to develop potential therapies for relevant human diseases.

Lab web: <https://www.nidcr.nih.gov/Research/NIDCRLaboratories/OralPharyngeal/WanJunChen.htm>
<https://irp.nih.gov/pi/wanjun-chen>

B. Positions and Honors

1987-1989 Instructor, Shandong Academy of Medical Sciences, Jinan, China
1990-1992 Visiting Scientist, The Institute of Immunology, University of Vienna, Vienna, Austria
1993-1996 Postdoctoral Fellow, Harvard Medical School, Boston, MA
1997-2003 Senior Staff Fellow, Cellular Immunology Section, OIIB, NIDCR, NIH
2004-2010 Tenure-track Investigator, Chief, Mucosal Immunology Unit, NIDCR, NIH
2011- Senior Investigator (tenured), Chief, Mucosal Immunology Section, NIDCR, NIH

- Invited Speaker, NIH Director's Seminar Series, 2009, (<http://videocast.nih.gov/summary.asp?Live=8127>)
- Primary Organizer and Co-chair, Keystone Symposium, TGF- β in Immune Responses, Snowbird, Utah, 2011, (<http://www.keystonesymposia.org/11A2>)
- The Wang Ying-Lai Memorial Lecture, and Keynote Speaker, Annual Meeting of

The Texas Chapter of Society of SCBA, Houston, 2011

(http://xray.utmb.edu/bmb/2012_WYL_Symposium.pdf)

- The Scientific Achievement Award 2013, The NIH Asian and Pacific Islander American Organization, NIH, Bethesda, 2013
(http://nihrecord.od.nih.gov/newsletters/2013/01_18_2013/milestones.htm)
- Primary Organizer and Co-chair, Keystone Symposium, TGF- β in Immunity, Inflammation and Cancer, 2017 (<http://www.keystonesymposia.org/17A3>)
- President, The Washington DC-Baltimore Chapter, Society of Chinese Bioscientists in America (SCBA), 2015

C. Contribution to Science (selected from total 100 peer-reviewed publications)

1. I was the first to discover that TGF- β induces Foxp3 gene expression in peripheral naïve CD4⁺ T cells and converts these naïve T cells into regulatory T cells. I was also the first to demonstrate that TGF β is also essential in the development of thymic regulatory T cells.

- Chen W*, Jin WJ, Lei K-j, Hardegen N, Li L, Marinos N, and Wahl SM. Conversion of peripheral CD4⁺CD25⁻ regulatory T cells by TGF- β induction of transcription factor Foxp3. **J Exp Med.** 2003; 198: 1875-1886.
- Chen W, and Wahl SM. TGF- β : the missing link in CD4⁺ CD25⁺ regulatory T cell-mediated immunosuppression. **Cytokine Growth Factor Rev.** 2003; 14:85-89.
- Wahl SM, Vazquez N, and Chen W. Regulatory T cells and transcription factors: gatekeepers in allergic inflammation. **Curr Opin Immunol.** 2004; 16: 768-774
- Wahl SM, and Chen W. TGF- β -induced T regulatory cells referee inflammatory and autoimmune diseases. **Arthritis Res Ther.** 2005; 7:62-68.
- Liu Y, Amarnath S, and Chen W. Requirement of CD28 signaling in homeostasis/survival of TGF- β converted CD4⁺CD25⁺ Tregs from thymic CD4⁺CD25⁻ single positive T cells. **Transplantation.** 2006; 82:953-64.
- Amarnath S, Dong L, Li J, Wu, Y, and Chen W. Endogenous TGF- β activation by reactive oxygen species is key to Foxp3 induction in TCR-stimulated and HIV-1-infected human CD4⁺CD25⁻ T cell. **Retrovirology.** 2007; 4:57.
- Liu Y, Zhang P, Perruche S, Li J, Kurlkani A, and Chen W. A critical function for TGF- β signaling in the development of natural CD4⁺CD25⁺Foxp3⁺ regulatory T cells. **Nat Immunol.** 2008; 9:632-640.
- Chen W and Konkel JE. TGF- β and adaptive regulatory T cells, **J Mol Cell Bol.** 2010; 2:30-6
- Chen W.IDO: more than an enzyme. **Nat Immunol.** 2011; 18;12(9):809-11.
- Belkaid Y, Chen W. Regulatory ripples. **Nat Immunol.** 2010;11(12):1077-8.
- Maruyama T, Konkel JE, Zamarron BF, Chen W. The molecular mechanisms of Foxp3 gene regulation. **Semin Immunol.** 2011;23(6):418-23.
- Zhang P, Nakatsukasa H, Tu E, Kasagi S, Cui K, Ishikawa M, Konkel JE, Maruyama T, Wei G, Abbatiello B, Wang ZQ, Zhao K, Chen W. PARP-1 regulates expression of TGF- β receptors in T cells. **Blood.** 2013;122(13):2224-32.
- Zhang P, Maruyama T, Konkel JE, Abbatiello B, Zamarron B, Wang ZQ, Chen W. Immunosuppressive function of regulatory T cells by destabilizing Foxp3. **PLoS One.** 2013;8(8):e71590.
- Konkel JE, Jin W, Abbatiello B, Grainger JR, Chen W. Thymocyte apoptosis drives the intrathymic generation of regulatory T cells. **Proc Natl Acad Sci U S A.** 2014;111(4):E465-73.
- Yang R, Qu C, Zhou Y, Konkel J, Shi S, Liu Y, Chen C, Liu S, Liu D, Chen Y, Zandi E, Chen W, Zhou Y, Shi S Hydrogen Sulfide Controls Regulatory T Cell Development *via* Regulation of Tet1/2-mediated Foxp3 Demethylation. **Immunity**, 2015, 43(2):251-63.
- Chen W & Konkel JE, Development of thymic Foxp3⁺ regulatory T cells: TGF- β matters (*Review*). **Eur J Immunol.** 2015 Apr;45(4):958-65.
- Tu E, Chia PZ, Chen W. TGF β in T cell biology and tumor immunity: Angel or devil? **Cytokine Growth Factor Rev.** 2014 Aug;25(4):423-35.
- Luo X, Nie J, Wang S, Chen Z, Chen W, Li D, Hu H, Li B. Poly(ADP-ribose)ylation of FOXP3 Mediated by PARP-1 Regulates the Function of Regulatory T Cells. **J Biol Chem.** 2015 Oct 1. pii: jbc.M115.661611.

- Chen W & Peter ten Dike, Immunoregulation by members of TGF β superfamily. **Nat Rev Immunol**. 2016
- Katarzyna Placek, Gangqing Hu, Kairong Cui, Dunfang Zhang, Yi Ding, Ji-Eun Lee, Chaochen Wang^{1,4}, Joanne E. Konkel, Jiuzhou Song, Chengyu Liu, Kai Ge, Wanjun Chen, Keji Zhao* MLL4 regulates Treg cell differentiation by remotely shaping enhancer landscape via chromatin looping. **Nat Immunol**, 2017, *in press* (* co-corresponding authors)

2. Demonstrated that TGF- β regulates T cell differentiation, activation and apoptosis; TGF- β plays a critical role in apoptosis-mediated immune tolerance; Discovered a pathway to induce autoantigen-specific Tregs to treat autoimmune diseases in vivo.

- Chen W, Jin WW, Tian HS, Frank M, and Wahl SM. Requirement for TGF- β 1 in controlling T cell apoptosis. 2001; **J Exp Med**. 194:439-53.
- Chen W, Frank ME, Jin WW, and Wahl SM. Release of TGF- β by apoptotic T cells contributes to an immunosuppressive milieu. **Immunity** 2001; 14:715-25.
- Perruche S, Zhang P, Liu Y, Saas P, Bluestone JA, and Chen W. CD3-specific antibody-induced immune tolerance involves TGF- β from phagocytes digesting apoptotic T cells. **Nat Med**. 2008; 14:528-535.
- Perruche S, Zhang P, Maruyama T, Bluestone JA, Saas P, and Chen WJ. Lethal effect of CD3-specific antibody in mice deficient in TGF-beta1 by uncontrolled "flu-like" syndrome. **J. Immunol**. 2009; 183:953-61.
- Perruche S, Saas P, Chen W. Apoptotic cell-mediated suppression of Streptococcal Cell Wall-induced arthritis is associated with alteration of macrophage function and local regulatory T cell increase: a potential cell-based therapy? **Arthritis Res Ther**, 2009;11(4):R104. Epub 2009; Jul 2
- Liu Y, Wang L, Kikuri T, Akiyama K, Chen C, Chen W, Wang S, Shi S. Bone marrow mesenchymal stem cell-based tissue regeneration is governed by recipient T lymphocyte response. **Nat Med**. 2011, 17:1594-601
- Ghoreschi K, Laurence A, Yang XP, Tato CM, McGeachy MJ, Konkel JE, Ramos HL, Wei L, Davidson TS, Bouladoux N, Grainger JR, Chen Q, Kanno Y, Watford WT, Sun HW, Eberl G, Shevach EM, Belkaid Y, Cua DJ, Chen W, O'Shea JJ. Generation of pathogenic T(H)17 cells in the absence of TGF- β signalling. **Nature**. 2010; 467:967-71.
- Zhang D, Tu E, Kasagi S, Zanvit P, Chen Q, Chen W. Manipulating regulatory T cells: a promising strategy to treat autoimmunity. **Immunotherapy**. 2015 Nov;7(11):1201-11
- Kasagi S, Zhang P, Che L, Abbatiello B, Maruyama T, Nakatsukasa H, Zanvit P, Jin W, Konkel JE, Chen W. In Vivo-Generated Antigen-Specific Regulatory T Cells Treat Autoimmunity Without Compromising Antibacterial Immune Response. **Sci Transl Med**. 2014, 6, 241ra78
- Kuang R, Perruche S, Chen W. Apoptotic cell-linked immunoregulation: implications for promoting immune tolerance in transplantation. **Cell Biosci**. 2015 Jun 7;5:27. doi: 10.1186/s13578-015-0019-9.
- Joanne E. Konkel, Dunfang Zhang, Peter Zanvit, Wenwen Jin, Songlin Wang and WanJun Chen TGF β signaling in regulatory T cells controls Th17 cells and tissue-specific immune responses, **Immunity**, 2017, 46: 660-674

3. Discovered that Inhibitor of DNA-binding 3 (Id3) played an important role in the differentiation of Tregs, Th17, Th9 and Tfh cells; discovered that Id3 controls the development of $\gamma\delta$ T cell lymphoma.

- Maruyama T, Li J, Vague JP, Konkel JE, Wang W, Zhang B, Zhang P, Zamarron BF, Yu D, Wu Y, Zhuang Y, Gutkind JS, and Chen W. Control of regulatory T cell and Th17 cell differentiation by inhibitor of DNA binding 3. **Nat Immunol**. 2011; 12:86-95.
- Li J, Maruyama T, Zhang P, Konkel J, Hoffman V, Zamarron B, and Chen W*. Mutation of inhibitory helix-loop-helix protein Id3 causes $\gamma\delta$ T cell lymphoma in mice. **Blood**. 2010, 116:5615-21.
- Liu X, Chen X, Zhong B, Wang A, Wang X, Chu F, Nurieva RI, Yan X, Chen P, van der Flier LG, Nakatsukasa H, Neelapu SS, Chen W, Clevers H, Tian Q, Qi H, Wei L, Dong C. Transcription factor achaete-scute homologue 2 initiates follicular T-helper-cell development. **Nature**. 2014. 507:513-8.
- Nakatsukasa H, Zhang D, Maruyama T, Chen H, Cui K, Ishikawa M, Deng L, Zanvit P, Tu E, Jin W, Abbatiello B, Goldberg N, Chen Q, Sun L, Zhao K, Chen W. The DNA-binding inhibitor Id3 regulates IL-9 production in CD4⁺ T cells. **Nat Immunol**, 2015, 16(10):1077-84

4. Discovered that TGF β controls the development of intraepithelial TCR $\alpha\beta$ ⁺CD8 $\alpha\alpha$ ⁺ lymphocytes; discovered that TGF- β induces CD8 α expression from peripheral CD4⁺ T cells
- Konkel J, Maruyama T, Carpenter AC, Xiong Y, Zamarron B, Hall BE, Kulkarni A, Zhang P, Bosselut R and Chen W. Control of CD8 $\alpha\alpha$ intestinal intraepithelial lymphocyte development by TGF- β . **Nat Immunol.** 2011;12:312-9
 - Konkel JE, Chen W. Balancing acts: the role of TGF- β in the mucosal immune system. **Trends Mol Med.** 2011;17(11):668-76.
 - Wu RQ, Zhang DF, Tu E, Chen QM, Chen W. The mucosal immune system in the oral cavity-an orchestra of T cell diversity. **Int J Oral Sci.** 2014 Sep;6(3):125-132.
5. Discovered a critical role of gut microbiota at neonatal age in regulation of immune responses and autoimmunity at adult age; demonstrated that antibiotics in neonatal life increase murine susceptibility to experimental psoriasis
- Zanvit P, Konkel JE, Kasagi S, Zhang D, Wu R, Chia C, Ajami NJ, Smith DP, Petrosino JF, Jiao X, Abbatiello B, Nakatsukasa H, Chen Q, Belkaid Y, Chen Z, Chen W, Antibiotics in neonatal life increase murine susceptibility to experimental psoriasis. **Nat Communications**, 2015, Sep 29;6:8424.
6. Discovered that D-mannose induces regulatory T cells and prevents and suppresses experimental type I diabetes and lung inflammation
- Dunfang Zhang, Cheryl Chia, Xue Jiao, Wenwen Jin, Shimpei, Kasagi, Ruiqing Wu, Joanne E. Konkel, Hiroko Nakatsukasa, Peter Zanvit, Nathan Goldberg, Zi-Jiang Chen and WanJun Chen D-Mannose induces regulatory T cells and suppresses immunopathology. 2017, **Nat Med.** *In press*

D. Editorial Responsibilities and Journal Reviewing Activities:

Ad hoc Reviewer for New England Journal of Medicine, Nature Medicine, Nature Immunology, Immunity, Cancer Cell, Journal of Experimental Medicine, Journal of Clinical Investigation, Blood, Journal of Immunology, Trends in Immunology, Transplantation, Circulation, European Journal of Immunology, European Journal of Cell Biology, Rheumatology, FASEB Journal, International Immunology, Molecular Therapy, Frontiers in Bioscience, Expert Review of Clinical Immunology, Cellular Immunology, Journal of Leukocyte Biology

- *Associate Editor*, **Frontiers in Immunology**
- *Member*, Editorial Board, **Bone Research**
- *Member*, Editorial Board, **International Journal of Oral Science**
- *Member*, Editorial Board, **Bioscience**

E. Invited Presentations:

More than 100 invited lectures and talks have been delivered at international conferences and meetings, and in prestigious universities and institutions over the world.

F. Extramural Activities:

Reviewer for grants for NIH and The National Science Foundation, China and also science foundations from US, and Europe

Co-organizer and chair for many international, national and NIH scientific meetings and symposia

G. Membership and Activity in Professional Societies:

American Association of Immunologists

Society for Mucosal Immunology

International Society for Interferon and Cytokine Research

H. List of Invention Reports and Patents

Inventors: Wanjun Chen (NIDCR).

Title: Development of Immune System Tolerance for the Treatment of Autoimmune Disease

Intellectual Property: HHS Reference No. E-186-2009/0—US Provisional Application No. 61/844,564 filed July 10, 2013.

I. Research Support

My research is supported by the Intramural Research Program of NIH, NIDCR.

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