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**Education**

- 1997-2001 B.S., Department of Botany, National Taiwan University, Taipei, Taiwan  
2001-2003 M.S., Graduate Institute of Pathology, National Taiwan University, Taipei, Taiwan  
2004 – 2008 Ph.D., Institute of Basic Medical Sciences, National Cheng-Kung University, Tainan, Taiwan.

**Research and Professional Positions Held in Chronological Sequence**

- 2008-2014 Postdoctoral Fellow, Immunology Research Center, National Health Research Institutes, Taiwan  
2014-2015 Assistant Research Fellow (Assistant Professor equivalent), Research and Development Center for Immunology, China Medical University, Taiwan  
2015-2022 Assistant Investigator, Immunology Research Center, National Health Research Institutes, Taiwan  
2022-present Associate Investigator, Immunology Research Center, National Health Research Institutes, Taiwan

**Research Interests**

Dr. Chuang is interested in studying the T-cell-mediated immune responses and inflammatory disease mechanisms. Dr. Chuang demonstrated that the kinase MAP4K3 (GLK) positively regulates T-cell activation and NF- $\kappa$ B signaling through phosphorylating and activating PKC- $\theta$ . Dr. Chuang's study revealed a novel subset of Th17 cells, adipose Th17 cells, and discovered a novel disease mechanism of T-cell-mediated type 2 diabetes (T2D). Dr. Chuang's current research focuses on inflammation, metabolic syndromes, and immunometabolism.

**Major Honors and Awards**

- 2010 14<sup>th</sup> International Congress of Immunology, Travel Award, Kobe, Japan  
2012 10<sup>th</sup> Yu-Ziang Hsu Scientific Paper Award for Bio-medical Technology (徐有庠科技論文獎)  
2013 National Science Council (NSC) Best Research Paper Award for Postdoctoral Fellows (國科會博士後研究人員學術著作獎)  
2013 15<sup>th</sup> International Congress of Immunology, Travel Award, Milano, Italy  
2013 Federation of Immunological Societies of Asia-Oceania (FIMSA), Travel Award for 15th ICI

- 2016 Federation of Immunological Societies of Asia-Oceania (FIMSA), Travel Award for 16<sup>th</sup> ICI
- 2017 President Rey-Shyong Tsai Outstanding Paper Award in Metabolism and Nephrology (第一屆蔡瑞熊校長優秀研究論文獎)
- 2018 Ta-You Wu Memorial Award from Ministry of Science and Technology (科技部吳大猷先生紀念獎)
- 2018 Professor Chen-Yuan Lee Medical Research Scholar Memorial Award (李鎮源教授醫學研究青年學者)
- 2018 MoST RO1 Project for Excellent Junior Research
- 2019 American Association of Immunologists (AAI) Early Career Faculty Travel Grant
- 2019 57<sup>th</sup> Ten Outstanding Young Persons (Taiwan)  
第 57 屆十大傑出青年獎-醫學研究類
- 2020 Ta-You Wu Memorial Award Grant from Ministry of Science and Technology (科技部吳大猷先生紀念獎計畫)
- 2022 American Association of Immunologists (AAI) Early Career Faculty Travel Grant
- 2022 莊淑綺女士傑出醫學研究獎 (on SLE Research)
- 2023 American Association of Immunologists (AAI) Laboratory Travel Grant

### Selected Publications

1. **Chuang HC**, Lay JD, Hsieh WC, Wang HC, Chang Y, Chuang SE, Su IJ. (2005) Epstein-Barr virus LMP1 inhibits the expression of SAP gene and upregulates Th1 cytokines in the pathogenesis of hemophagocytic syndrome. *Blood*. 10:3090-6.
2. Hsieh WC, Chang Y, Hsu MC, Lan BS, Hsiao GC, **Chuang HC**, Su IJ. (2007) Emergence of anti-red blood cell antibodies triggers red cell phagocytosis by activated macrophages in a rabbit model of Epstein-Barr virus-associated hemophagocytic syndrome. *American Journal of Pathology*. 170:1629-39.
3. **Chuang HC**, Lay JD, Chuang SE, Hsieh WC, Chang Y, Su IJ. (2007) Epstein-Barr virus (EBV) latent membrane protein-1 down-regulates tumor necrosis factor-alpha (TNF- $\alpha$ ) receptor-1 and confers resistance to TNF- $\alpha$ -induced apoptosis in T cells: implication for the progression to T-cell lymphoma in EBV-associated hemophagocytic syndrome. *American Journal of Pathology*. 170:1607-17.
4. **Chuang HC**, Lay JD, Hsieh WC, Su IJ. (2007) Pathogenesis and mechanism of disease progression from hemophagocytic lymphohistiocytosis to Epstein-Barr virus-associated T-cell lymphoma: nuclear factor- $\kappa$ B pathway as a potential therapeutic target. *Cancer Science*. 98:1281-7.
5. **Chuang HC**, Wang JM, Hsieh WC, Chang Y, Su IJ. (2008) Up-regulation of activating transcription factor-5 suppresses SAP expression to activate T cells in hemophagocytic

syndrome associated with Epstein-Barr virus infection and immune disorders. *American Journal of Pathology*. 173:1397-405.

6. Yang JC, Teng CF, Wu HC, Tsai HW, **Chuang HC**, Tsai TF, Hsu YH, Huang W, Wu LW, Su IJ. (2009) Enhanced expression of vascular endothelial growth factor-A in ground glass hepatocytes and its implication in hepatitis B virus hepatocarcinogenesis. *Hepatology*. 49:1962-71.
7. **Chuang HC**, Lan JL, Chen DY, Yang CY, Chen YM, Li JP, Huang CY, Liu PE, Wang X, and Tan TH. (2011). The kinase GLK controls autoimmunity and NF- $\kappa$ B signaling by activating the kinase PKC- $\theta$  in T cells. *Nature Immunology*. 12:1113-18.
8. Chen DY, **Chuang HC**, Lan JL, Chen YM, Hung WT, Lai KL, Tan TH. (2012) Germinal center kinase (GCK)-Like kinase (GLK/MAP4K3) expression is increased in adult-onset Still's disease and may act as an activity marker. *BMC Medicine*. 10:84.
9. Wang X, **Chuang HC**, Li JP, and Tan TH. (2012) PKC- $\theta$ -mediated signal delivery from the T-cell receptor. *Frontiers in Immunology*. 3: 197. (Invited review article)
10. Chen YM\*, **Chuang HC\***, Lan JL, Hung WT, Lin YT, Gong NR, Lin WC, Lan TH, Tan TH, Chen DY. (2013) Germinal center kinase-like kinase overexpression in T cells as a novel biomarker of rheumatoid arthritis. *Arthritis & Rheumatism* (Renamed as *Arthritis & Rheumatology*). 65: 2573-2582. \*, **co-first authors with equal contribution**.
11. Yang CY, Li JP, Lan JL, Chiu LL, **Chuang HC**, Huang CY, Chen DY, Tan TH. (2014) Dual-specificity phosphatase 14 (DUSP14/MKP6) negatively regulates T-cell receptor signaling by inhibiting TAK1 activation. *Journal of Immunology*. 192:1547-1557.
12. Li JP, Yang CY, **Chuang HC**, Huang PY, Chen YR, Wang X, Belmont J, and Tan TH. (2014) The phosphatase JKAP/DUSP22 inhibits T-cell receptor signaling and autoimmunity by inactivating Lck. *Nature Communications*. 5:3618.
13. **Chuang HC**, Sheu W, Lin YT, Tsai CY, Yang CY, Cheng YJ, Huang PY, Li JP, Chiu LL, Wang X, Xie M, Schneider M, and Tan TH. (2014) HGK/MAP4K4 deficiency induces TRAF2 stabilization and Th17 differentiation leading to insulin resistance. *Nature Communications*. 5: 4602.
14. **Chuang HC**, Wang X, and Tan TH. (2016) MAP4K family kinases in immunity and inflammation. *Advances in Immunology*. 129:277-314. (Invited review article)
15. Hsu CP, **Chuang HC**, Lee MC, Tsou HH, Lee LW, Li JP, and Tan TH. (2016) GLK/MAP4K3 overexpression associates with recurrence risk for non-small cell lung cancer. *Oncotarget*. 7:41748-41757.
16. Ho CH\*, **Chuang HC\***, Wu IC, Tsai HW, Lin YJ, Sun HY, Young KC, Chiu YC, Cheng PN, Liu WC, Tan TH, and Chang TT. (2016) Prediction of early hepatocellular carcinoma recurrence using germinal center kinase-like kinase. *Oncotarget*. 7:49765-49776. \*, **co-first authors with equal contribution**.
17. **Chuang HC\***, Chen YM\*, Hung WT, Li JP, Chen DY, Lan JL, and Tan TH. (2016) Downregulation of the phosphatase JKAP/DUSP22 in T cells may as a potential new

- biomarker of systemic lupus erythematosus nephritis. *Oncotarget*. 7:57593-57605. \*, **co-first authors with equal contribution.**
18. **Chuang HC**, Wang JS, Lee IT, Sheu W and Tan TH. (2016) Epigenetic regulation of HGK/MAP4K4 in T cells of type 2 diabetes patients. *Oncotarget*. 7:10976-10989.
  19. **Chuang HC** and Tan TH. (2017). MAP4K4 and IL-6<sup>+</sup> Th17 cells play important roles in non-obese type 2 diabetes. *Journal of Biomedical Science*. 24:4. (Invited review article)
  20. **Chuang HC** and Tan TH. (2017) MAP4K3, GLK, *Encyclopedia of Signaling Molecules*. ISBN: 978-1-4614-6438-9 (Print) 978-1-4614-6438-9 (Online).
  21. Chen YR, Chou HC, Yang CH, Chen HY, Liu YW, Lin TY, Yeh CL, Chao WT, Tsou HH, **Chuang HC**, and Tan TH. (2017) Deficiency in VHR/DUSP3, a suppressor of focal adhesion kinase, reveals its role in regulating cell adhesion and migration. *Oncogene*. 23:6509-6517.
  22. Yang CY, Chiu LL, Chang CC, **Chuang HC\***, and Tan TH\*. (2018) Induction of DUSP14 ubiquitination by PRMT5-mediated arginine methylation in T-cell signaling. *FASEB Journal*. 32:6760-6770. \*, **co-corresponding authors.**
  23. **Chuang HC**, Tsai CY, Hsueh CH, and Tan TH. (2018) GLK-IKK $\beta$  signaling induces dimerization and translocation of AhR-ROR $\gamma$ t complex in IL-17A induction and autoimmune disease. *Science Advances*. 4:eaat5401.
  24. Chen HF, **Chuang HC\***, Tan TH\*. (2019) Regulation of dual-specificity phosphatase (DUSP) ubiquitination and protein stability. *International Journal of Molecular Sciences*. 20: 2668. \*, co-corresponding authors.
  25. **Chuang HC**, Chen YM, Chen MH, Hung WT, Yang HY, Tseng TH, and Tan TH. (2019) AhR-ROR $\gamma$ t complex is a therapeutic target for MAP4K3/GLK high IL-17A high subpopulation of systemic lupus erythematosus. *FASEB Journal*. 33:11469-11480.
  26. **Chuang HC**, Chang CC, Teng CF, Hsueh CH, Chiu LL, Hsu PM, Lee MC, Hsu CP, Chen YR, Liu YC, Lyu PC, and Tan TH. (2019) MAP4K3/GLK promotes lung cancer metastasis by phosphorylating and activating IQGAP1. *Cancer Research*. 79:4978-4993. (Cover Story in 2019 October issue of *Cancer Research*)
  27. **Chuang HC** and Tan TH. (2019) MAP4K3/GLK is a therapeutic target for autoimmune disease and cancer recurrence. *Journal of Biomedical Science*. 26:82.
  28. **Chuang HC** and Tan TH. (2019) MAP4K family kinases and DUSP family phosphatases in systemic lupus erythematosus. *Cells*. 8:1433.
  29. Yang CY\*, **Chuang HC\***, Tsai CY, Xiao YZ, Yang JY, Huang RH, Shih YJ, and Tan TH. (2020) DUSP11 attenuates lipopolysaccharide-induced macrophage activation by targeting TAK1. *Journal of Immunology*. (Published Online on Aug 12) \*, **co-first authors with equal contribution.**
  30. Lai CH, Chang CC, **Chuang HC**, Tan TH, Lyu PC. (2020) Structural insights into the active site formation of DUSP22 in N-loop-containing protein tyrosine phosphatases. *International*

*Journal of Molecular Sciences*. 21:7515.

31. **Chuang HC<sup>§\*</sup>**, Chen MH<sup>§</sup>, Chen YM<sup>§</sup>, Yang HY, YR Ciou, CH Hsueh, CY Tsai, Tan TH\*. (2021) BPI overexpression suppresses Treg differentiation and induces exosome-mediated inflammation in systemic lupus erythematosus. *Theranostics*. 11:9953-9966. **§, co-first authors with equal contribution; \*, co-corresponding authors.**
32. **Chuang HC**, Chen MH, Chen YM, Ciou YR, Hsueh CH, Tsai CY, Tan TH. (2022) ECP overexpression in T cells and exosomes induces IFN- $\gamma$  production and tissue inflammation. *Arthritis & Rheumatology*. 74:92-104.
33. **Chuang HC<sup>§\*</sup>**, Hung WT<sup>§</sup>, Chen YM, Hsu PM, Yen JH\*, Lan JL\*, Tan TH\*. (2022) Genomic sequencing and functional analyses identify MAP4K3/GLK germline and somatic variants associated with systemic lupus erythematosus. *Annals of the Rheumatic Diseases*. 81: 243-254. **§, co-first authors; \*, co-corresponding authors.**
34. Chi JN, Yang JY, Hsueh CH, Tsai CY, **Chuang HC\***, Tan TH\*. (2022) MAP4K3/GLK inhibits Treg differentiation by direct phosphorylating IKK $\beta$  and inducing IKK $\beta$ -mediated FoxO1 nuclear export and Foxp3 downregulation. *Theranostics*. 12:5744-5760. **\*co-corresponding authors.**
35. **Chuang HC\***, Hsueh CH, Hsu PM, Huang RH, Tsai CY, Chung NH, Chow YH\*, Tan TH\*. (2022) SARS-CoV-2 spike protein enhances MAP4K3/GLK-induced ACE2 stability in COVID-19. *EMBO Molecular Medicine*. e15904:1-18. **\*, co-corresponding authors.**
36. Chen MH\*, **Chuang HC\***, Yeh YC, Chou CT, and Tan TH. (2023) Dual-specificity phosphatases 22-deficient T cells contribute to the pathogenesis of ankylosing spondylitis. *BMC Medicine*. 21:46. **\*, co-first authors with equal contribution.**
37. Wang CW\*, **Chuang HC\***, Tan TH. (2023) ACE2 in chronic disease and COVID-19: gene regulation and post-translational modification. *Journal of Biomedical Science*. 30:71. **\*, co-first authors with equal contribution.**
38. **Chuang HC\***, CH Hsueh, PM Hsu, CY Tsai, YC Shih, HY Chiu, YM Chen, WK Yu, MH Chen, TH Tan\*. (2023) DUSP8 induces TGF $\beta$ -stimulated IL-9 transcription and Th9-mediated allergic inflammation by promoting nuclear export of Pur- $\alpha$ . *Journal of Clinical Investigation*. 133: e166269. **\*, co-corresponding authors.**
39. Shin YC, Chen SF, Wu CY, Ciou YR, Wang CW, **Chuang HC\***, and Tan TH\*. (2023) The phosphatase DUSP22/JKAP inhibits UBR2-mediated K63-ubiquitination and activation of Lck in TCR signaling. *Nature Communications*. (Provisionally acceptable pending formatting checks) **\*, co-corresponding authors.**

## Patent Held

Tan TH and **Chuang HC**. MAP kinase kinase kinase kinase 3 (MAP4K3) as a biomarker and therapeutic target for autoimmune disease, cancer, inflammation and IL-17-associated disease.

*U.S. Patent No. 8,846,311 B2 (2014)*

*R.O.C. Patent No. 101125449 (2015)*

*Korea Patent No. 10-1640326 (2016)*

*China Patent No. 201280034960.9 (2017)*

*Europe Patent No. 7232045 (2017)*

*Japan Patent No. JP1010021 (2018)*

Tan TH and **Chuang HC**. The AhR-ROR $\gamma$ t complex as a biomarker and therapeutic target for autoimmune disease and IL-17-associated disease.

*U.S. Patent No. 11,360,080 B2 (2022)*

*R.O.C. Patent No. I804669 (2023)*