Publication List

- Liu M, Ren D, Wu D, Zheng J, <u>Tu W*</u>. Stem cell and Idiopathic pulmonary fibrosis: mechanisms and treatment. *Current Stem Cell Research & Therapy*. 2015 May 18. [Epub ahead of print]. [IF: 2.861]
- 2. Liu DW, Zhang ZY, Zhao Q, Jiang LP, Liu W, <u>Tu W</u>, Song WX, and Zhao XD. Wiskott-Aldrich Syndrome/X-Linked Thrombocytopenia in China: Clinical Characteristic and Genotype-Phenotype Correlation. *Pediatr Blood Cancer*. 2015 Apr 30. doi: 10.1002/pbc.25559. [Epub ahead of print] [**IF: 2.562**]
- 3. Wu Y, <u>Tu W*</u>, Lam KT, Chow KH, Ho PL, Guan Y, Peiris JS, Lau YL. Lethal co-infection of influenza virus and Streptococcus pneumoniae lowers antibody response to influenza virus in lung, and reduces germinal center B cells, T follicular helper cells and plasma cells in mediastinal lymph node. *Journal of Virology*. 2015 Feb;89(4):2013-23. doi: 10.1128/JVI.02455-14. [IF:5.402]
- 4. Lu Q, Yu M, Shen C, Chen X, Feng T, Yao Y, Li J, Li H and <u>Tu W</u>*. Negligible immunogenicity of induced pluripotent stem cells derived from human skin fibroblasts. *Plos One* 2014 Dec 11;9(12):e114949. doi: 10.1371/journal.pone.0114949. [**IF:4.092**]
- <u>Tu WW*</u>, Lau YL, Peiris JS. Use of humanised mice to study antiviral activity of human γδ-T cells against influenza A viruses. Hong Kong Med J. 2014 Dec;20 Suppl 6:4-6.
- 6. Qi X, Ng KTP, Liu XB, Li CX, Geng W, Ling CC, Ma YY, Yeung WH, <u>Tu W</u>, Fan ST, Lo CM, Man K. Clinical significance and therapeutic value of Glutathione peroxidase 3 (GPx3) in hepatocellular carcinoma. *Oncotarget* 2014 Nov 30;5(22):11103-20. [IF: 6.627]
- Xiang Z, Liu Y, Zheng J, Liu M, Lv A, Gao Y, Hu H, Lam KT, Chan GC, Yang Y, Chen H, Tsao GS, Bonneville M, Lau YL, <u>Tu W*</u>. Targeted activation of human Vγ9Vδ2-T cells controls Epstein-Barr virus-induced B cell lymphoproliferative disease. *Cancer Cell* 2014 Oct 13;26(4):565-576. doi: 10.1016/j.ccr.2014.07.026. *M* [IF: 24.755].{CI: 5}

Current treatment strategies for EBV-LPD include restoring EBV-specific cytotoxic T lymphocytes (CTL) and depleting the B cells with monoclonal antibodies or chemotherapy. However, Restoration of EBV-specific CTL is limited by the difficulties in generating enough numbers of EBV-specific CTL in vitro and the lack of in vivo expansion of infused CTL. Antibody-mediated targeting EBV-infected B cells and chemotherapy have unwanted side-effects and lead to general immunosuppression. This study has demonstrated that targeted activation of human $V\gamma 9V\delta 2$ -T cells can control EBV-LPD. It provides a strong preclinical proof of principle for a novel therapeutic approach using pamidronate to boost human $V\gamma 9V\delta 2$ -T-cell immunity against EBV-LPD. As pamidronate has been already used for decades in osteoporosis treatment, this 'new application of an old drug' potentially offers a safe and readily available option for the treatment of EBV-LPD. The clinical implication of this new approach has been intensively discussed and highlighted in a commentary published in New England Journal of Medicine (N Engl J Med. 2015;372:569) recently. On patent

- 8. Wu JF, Liu DW, <u>Tu W</u>, Song W, and Zhao X. <u>T-cell receptor diversity is selectively skewed in T-cell populations of patients with Wiskott-Aldrich syndrome. *Journal of Allergy & Clinical Immunology* 2015 Jan;135(1):209-16. doi: 10.1016/j.jaci.2014.06.025. *h* [IF:12.04] {CI: 1}</u>
- 9. Tang WJ, An YF, Dai RX, Wang QH, Jiang LP, Tang XM, Yang XQ, Yu J, <u>Tu W</u>, Zhao XD. Clinical, molecular, and T cell subset analyses in a small cohort of Chinese patients with hyper-IgM syndrome type 1. *Human Immunology*. 2014 Jul; 75(7): 633-40. doi: 10.1016/j.humimm.2014.04.014.. *h* [IF:2.298] {CI: 1}
- 10. Mao H, Yen HL, Lau YL, Peiris JS, <u>Tu W*</u>, Conservation of T cell epitopes of seasonal influenza virus in novel H7N9 virus. *Virologica Sinica*. 2014. Jun; 29(3):170-5. doi: 10.1007/s12250-014-3473-3. *M*. {CI:1}
- 11. Xia Q, Zhou L, Peng C, Hao R, Ni K, Zang N, Ren L, Deng Y, Xie X, He L, Tian D, Wang L, Huang A, Zhao Y, Zhao X, Fu Z, <u>Tu W</u>, Liu E. Detection of respiratory syncytial virus fusion protein variants between 2009 and 2012 in China. *Arch Virol*. 2014 May;159(5):1089-98. h [IF:2.03] {CI: 2}
- 12. Liu T, Zang N, Zhou N, Li W, Xie X, Deng Y, Li S, Luo R¹, Long X, Zhou L, Zhao X, <u>Tu W</u>, Wang L, Tan B, Liu E. Resveratrol inhibits the TRIF dependent pathway by up-regulating SARM, contributing to anti-inflammatory effects after respiratory syncytial virus infection. *Journal of Virology* 2014 Apr;88(8):4229-36. doi: 10.1128/JVI.03637-13. *m* [IF:5.402] {CI:2}
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- 14. Lee PPW, Mao H, Yang W, Chan KW, Ho MHK, Lee TL, Chan J, Woo PCY, <u>Tu W</u> and Lau YL. Penicillium marneffei infection and Impaired Interferon-gamma Immunity in humans with Autosomal Dominant Gain-of-phosphorylation STAT1 mutations. *Journal of Allergy & Clinical Immunology* 2014 Mar;133(3):894-6.e5. doi: 10.1016/j.jaci.2013.08.051. Epub 2013 Nov 1.h [IF:12.04] {4}
- 15. Zheng J, Chan PL, Liu Y, Qin G, Xiang Z, Lam KT, Lewis DB, Lau YL, <u>Tu W*</u>. ICOS regulates the generation and function of human CD4⁺ Treg in a CTLA-4 dependent manner. *PLoS ONE* 2013 Dec 2; 8(12): e82203. doi:10.1371/journal.pone.0082203. *M* [IF:4.092] {1}
- 16. Lau YL, **Tu W.** Case-control study of Sichuan and Hong Kong children with melamine-associated renal stones: renal ultrasonography and urinary IL-8 and MCP-1 levels. Hong Kong Med J. 2013 Dec;19 Suppl 8:26-30. *M*
- 17. Dou Y, Zhao Y, Zhang ZY, Mao H, <u>Tu W</u>, Zhao X. Respiratory syncytial virus infection induces higher Toll-like receptor-3 expression and TNF-α production than human metapneumovirus infection. *Plos One* 2013 Sep 9;8(9):e73488. doi: 10.1371/journal.pone. 0073488. *h* [**IF:4.092**] {CI: 4}.
- 18. Chan PL, Zheng J, Liu Y, Lam KT, Xiang Z, Mao H, Liu Y, Qin G, Lau YL, and <u>Tu W*.</u> TLR5 signaling enhances the proliferation of human allogeneic CD40-activated B cell induced CD4hiCD25+ regulatory T cells. *Plos One* 2013 Jul 3; 8(7): e67969. doi:10.1371/journal.pone.0067969. *M* [IF:4.092] {CI: 2}
- 19. Li J, Li H, Mo H, Yu M, Feng T, Yang F, Fan Y, Lu Q, Shen C, Yin Z, Mao M, <u>Tu W*</u>. Impaired NK cell antiviral cytokine response against influenza virus in

- small-for-gestational-age neonates. *Cellular and Molecular Immunology* **2013** Sep;10(5):437-43. doi: 10.1038/cmi.2013.31. *M* [**IF: 4.185**] {CI: 3} (This paper was highlighted in <u>Human Immunology News 1.19</u>).
- Chong WP, Ling MT, Liu Y, Caspi RR, Wong WM, Wu W, <u>Tu W</u> and Lau YL. Essential Role of NK Cells in IgG Therapy for Experimental Autoimmune Encephalomyelitis. *Plos One*. 2013 April 5. 8(4): e60862. doi:10.1371/journal.pone.0060862. *h* [IF:4.092].{CI: 5}
- 21. Li J, Li H, Mo H, Yu M, Feng T, Yang F, Fan Y, Lu Q, Shen C, Yin Z, <u>Tu W*</u>, Mao M. <u>Vγ9Vδ2-T lymphocytes have impaired antiviral function in small-for-gestational-age</u> and preterm neonates. Cellular and Molecular Immunology 2013 May;10(3):253-60. *M* [IF: 4.185]. {CI: 2}
- 22. Li H, Xiang Z, Feng T, Li J, Liu Y, Fan Y, Lu Q, Yin Z, Yu M, Shen C, <u>Tu W*</u>. Human Vγ9Vδ2-T cells efficiently kill influenza virus-infected lung alveolar epithelial cells. Cellular and Molecular Immunology 2013;10(2): 159-64. doi: 10.1038/cmi.2012.70. *M* [IF:4.185] {CI: 6}.
- 23. Zheng J, Liu Y, Liu M, Xiang Z, Lam KT, Lewis DB, Lau YL*, <u>Tu W*</u>. Human CD8 regulatory T cells inhibit graft-versus-host disease and preserve general immunity in humanized mice. Science Translational Medicine 2013 Jan 16;5(168):168ra9. M [IF:15.843] {CI: 19} [We established a novel human allogeneic GVHD model in humanized mice and provide a more relevant approach for studies of human immunopathogenesis and therapeutics for GVHD after bone marrow transplantation (BMT). Using this model, we demonstrated that human CD8hi Treg induced ex vivo by allogeneic hCD40-B cells can control acute GVHD in an allo-specific manner via reduction of alloreactive T cell proliferation and inflammatory cytokines secretion within target organs through a CTLA-4 dependent mechanism. Importantly, these CD8^{hi} Treg can induce long-term tolerance effectively without compromising general immunity and GVT activity. Therefore, our study provided proof-of-concept of using ex vivo-induced human CD8hi Treg to control GVHD after BMT. This novel strategy could readily be extended to human clinical trials using human CD8^{hi} Treg alone or in combination with minimal conventional immunosuppression to control GVHD. The GVHD model established here may also provide a more relevant platform for further studies of human immunopathogenesis and therapeutics for GVHD after BMT. One paten based on this study has been filed].
- 24. Zheng J, Liu Y, Lau YL and <u>Tu W*</u>. Gammadelta-T Cells: unpolished sword in human antiviral Immunity. *Cellular and Molecular Immunology*, 2013 Jan;10(1):50-7. *M* [IF: 4.185] {CI: 22}.
- 25. Xiong F, Tong Y, You Y, Li P, Huo T, <u>Tu W</u>, Mao M. Prospective cohort study about the lymphocyte subpopulations'change and impact on the pregnancy outcome in fetal growth restriction. *Journal of Maternal-Fetal & Neonatal Medicine* 2012 Aug 6. [Epub ahead of print] *h* [IF:1.518] {1}.

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- 27. Qin G, Liu Y, Zheng J, Ng IH, Peiris JSM, Lau YL* and <u>Tu W*.</u> Phenotypic and functional characterization of human γδ T cell subsets in response to influenza A viruses. *Journal of Infectious Diseases*. 2012 Jun;205(11):1646-53. *M* [IF:6.410].{CI: 16}
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- 29. Mao H, Yang W, Lee PPW, Ho MHK, Yang J, Zeng S, Chong CY, Lee TL, <u>Tu W*</u>, Lau YL*. Exome Sequencing Identifies Novel Compound Heterozygous Mutations in *Interleukin-10 Receptor A* in a Neonatal-Onset Crohn's Disease Patient. *Genes and Immunity* 2012 Jul;13(5):437-42. [IF:4.367] {CI: 27}
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- 36. Hui KP, Lee SM, Cheung CY, Mao H, Lai AK, Chan RW, Chan MC, Tu W, Guan Y, Lau YL, Peiris JS*. H5N1 Influenza Virus-Induced Mediators Upregulate RIG-I in Uninfected Cells by Paracrine Effects Contributing to Amplified Cytokine Cascades. *Journal of Infectious Diseases*. 2011; 204(12):1866-78. m [IF:6.410] {CI: 23}
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- 38. Qin G, Liu Y, Zheng J, Ng IH, Xiang Z, Lam KT, Mao H, Li H, Peiris JSM, Lau YL* and <u>Tu W*.</u> Type-1 responses of human Vγ9Vδ2 T cells to influenza A viruses. *Journal of Virology*. 2011 oct; 85(19):10109-16. *M* [**IF:5.402**] {CI: 23}
- 39. Mok CK, Yen HL, Yu MY, Yuen KM, Sia SF, Chan MC, Qin G, <u>Tu W</u>, and Peiris JSM*. Amino acid residues 253 and 591 of the PB2 protein of avian influenza virus A H9N2 contributes to mammalian pathogenesis. *Journal of Virology*. 2011 Sept, 85(18):9641-5. *h* [IF:5.402] {CI: 21}
- 40. <u>Tu W*</u>, Zheng J, Liu Y, Sia SF, Liu M, Qin G, Ng IHY, Lam KT, Peiris JSM, and Lau YL*. The aminobisphosphonate pamidronate controls influenza pathogenesis by expanding a gammadelta T cell population in humanized mice. *Journal of Experimental Medicine*. 2011 Jul 4; 208(7):1511-22. *M* [IF:14.8] {CI: 42} (Recommended by Faculty 1000 F factor 8.0)

 (We had established the humanized mouse model with a complete human immune system. My laboratory is one of the very few laboratories worldwide to have

we had established the humanized mouse model with a complete human immune system. My laboratory is one of the very few laboratories worldwide to have successfully established this humanized mouse model. Using this model, we have demonstrated for the first time that pamidronate can control influenza infection through boosting the human Vγ9Vδ2-T cell immunity and that this beneficial effect is active against viruses of varying subtypes and virulence. Our finding provided proof-of-concept of a novel therapeutic strategy for treating influenza by targeting the host rather than the virus, thereby reducing the opportunity for the emergence of drug resistant viruses. As pamidronate is commonly used clinically for the treatment of osteoporosis and Paget's disease, this 'new application of an old drug' potentially offers a safe and readily available option either alone or in combination with conventional antiviral drugs for the treatment of influenza, especially for combating pandemic or drug resistant viruses. Now we are planning to do the human clinical trials).

This work was selected as one of 20 Medical Breakthroughs during 1990s to 2010s listed in the publication "Impact 100" in HKU 2012.

- 41. Zheng J, Liu Y, Qin G, Chan PL, Mao H, Lewis DB, Lau YL* and <u>Tu W*</u>. Generation of human Th1-like regulatory CD4⁺ T Cells by an intrinsic IFN-γ- and T-bet-dependent pathway. *European Journal of Immunology*. 2011;41(1):128-39. *M* [IF:5.179] {CI: 27}
- 42. Wang Z#, Luo H#, <u>Tu W#</u>, Yang H, Wong WHS, Wong WT, Yung KF, Zhou N, Zhang J, Li X,, Wang Z, Guo W, Mu D, Li F, Mao M* and Lau YL*. Melamine-tainted milk products associated urinary stones in children. *Pediatrics International*. 2011;53(4):489-96. (# equal contribution). *M* [IF:0.875] {CI: 12}
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- 44. <u>Tu W*</u>, Mao H, Zheng J, Liu Y, Chiu SS, Qin G, Chan PL, Lam KT, Guan J, Zhang L, Guan Y, Yuen KY, Peiris JSM and Lau YL*. Cytotoxic T Lymphocytes Established by Seasonal Human Influenza Cross-react against 2009 Pandemic H1N1 Influenza Virus. *Journal of Virology*. 2010 Jul;84(13):6527-35. *M* [IF:5.402] {CI: 102} (This is the first study to demonstrate that memory CTLs established by seasonal

- influenza A viruses or vaccines had cross-reactivity against pandemic H1N1 influenza virus. Our data suggest that individuals who were infected with seasonal human influenza A viruses previously or who received seasonal human influenza vaccines may derive benefit, at least in part, from the preexisting cross-reactive memory CTLs to reduce the severity of pdmH1N1 infection even without protective antibodies. This study also provided some valuable insights for the future design of broadly protective vaccines to prevent influenza, especially pandemic influenza.)
- 45. Chong WP, Zhou J, Law HKW, <u>Tu W</u>, Lau YL*. Natural killer cells become tolerogenic after interaction with apoptotic cells. *European Journal of Immunology*. 2010 Apr 9;40(6):1718-1727. *h* [IF:5.179] {CI: 9}
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- 47. Mao H, <u>Tu W*</u>, Qin G, Sia SF, Chan PL, Liu Y, Lam KT, Zheng J, Peiris JSM and Lau YL*. Inhibition of human natural killer cell activity by influenza virion and hemagglutinin. *Journal of Virology*, 2010; 84(9):4148-57. *M* [IF:5.402] {CI: 50}
- 48. Zheng J, Liu Y, Lau YL* and <u>Tu W*</u>. CD40-activated B cells are more potent than immature dendritic cells to induce regulatory T cells. *Cellular and Molecular Immunology*. 2010, 7(1):44-50. *M* [IF: 4.185] {CI: 44}
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- 50. <u>Tu W*</u>, Zheng J, Liu Y and Lau YL*. Stimulatory or tolerogenic role of CD40-activated B cells depends on the strength of the activation to T cells. *Blood.* 2009, July 16, 114(3): 747-8. *M* [10.896] {2}
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- 52. Zheng J, Liu Y, Qin G, Chan PL, Mao H, Lewis DB, Lau YL* and <u>Tu W*.</u> Efficient induction and expansion of human alloantigen-specific CD8 regulatory T cells from naive precursors by CD40-activated B cells. *Journal of Immunology* 2009 Sep 15;183(6):3742-50. *M* [IF:6.068] {CI: 45}

 (This is the first paper describing how to generate human alloantigen-specific CD8 regulatory T cells in large-scale by using a simple and low-cost method. This may facilitate the clinical applications of Treg-based immunotherapy for the treatment of allograft rejection, autoimmune diseases, and leukemia in the future).
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- 56. <u>Tu W*</u>, Lau YL*, Zheng J, Liu Y, Chan PL, Mao H, Dionis K, Schneider P, and Lewis DB. Efficient generation of human alloantigen-specific CD4+ regulatory T cells from naïve precursors by CD40-activated B cells. *Blood*. 2008:112(6):2554-62. *M* [IF:10.896] {CI: 81}

 (This is the first paper describing a novel low-cost method to generate human alloantigen-specific CD4 regulatory T cells in large-scale. 4 patents based on this study for preventing GVHD during bone marrow transplantation and inhibiting allograft rejection have been filed and now are pending.)
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- 61. Tu W, Potena L, Stepick-Biek P, Liu L, Dionis KY, Luikart H, Fearon WF, Holmes TH, Chin C, Cooke JP, Valantine HA, Mocarski ES, Lewis DB*. T-Cell Immunity to Subclinical Cytomegalovirus Infection Reduces Cardiac Allograft Disease. *Circulation*. 2006 Oct; 114(15): 1608-15. *M* [IF:15.202]. {CI: 71}

 (This paper demonstrated for the first time that an early CMV-specific Th1 immunity is beneficial rather than deleterious in terms of cardiac allograft rejection and early transplant arteriopathy. Our findings indicate potentially important benefits for allograft function of limiting CMV replication by enhancing T-cell immunity in the posttransplantation setting, eg, by vaccination or the adoptive transfer of autologous CMV-specific T cells or, alternatively, by more prolonged antiviral prophylaxis. The importance of this study was also discussed intensively in the *Editorial* (Circulation. 2006;114(15):1561-4) and *Clinical Perspective* (Circulation. 2006;114(15):1615) of the same issue).
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 (This novel study demonstrated that there is a persistent and selective deficiency of CD4 T-cell immunity to cytomegalovirus (CMV) in immunocompetent young children, and this selective deficiency contributes to their viral shedding. In contrast, the CMV-specific CD8 T-cell responses are normal during the primary infection of CMV in these young children, compared to that in adults. These novel findings were given the prominence to be included in the section of "*In This Issue*" of the Journal of Immunology (172(5):2725).
- 64. Chen S, <u>Tu W</u>, He X, Sharp M, Dekker C, Manganello AM, Maecker HT, Holmes TH, Wang Z, Kemble G, Adler S, Lewis DB and Arvin A. Antiviral CD8 T cells in the control of primary human cytomegalovirus infection in early childhood. *Journal of Infectious Diseases*. 2004; 189(9):1619-27. *M* [IF:6.035] {CI: 47}
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