

08

INFLAMMATORY DISEASES

**Principal Investigator**

Professor Hui-yao Lan

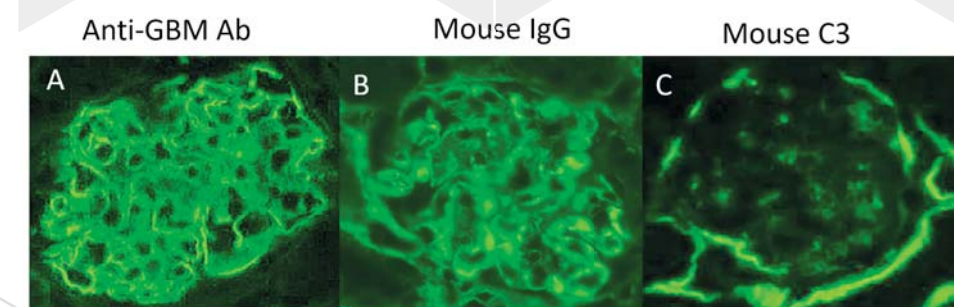
Team

Inflammatory Diseases

Research Progress Summary

The research team of Inflammatory Diseases continued to work on new mechanisms of tissue scarring by focusing on TGF- β /Smad3-dependent long non-coding RNA (lncRNAs), which have resulted in a new General Research Fund awarded. The team also identified a new role for Smad3 in type-2 diabetes and diabetic complications as mice lacking Smad3 were protected against diabetes, diabetic cardiopathy and nephropathy. The research into the Smad3-dependent cancer microenvironments has resulted in two new inventions including a modified natural killer (NK) cell immunotherapy and a traditional Chinese medicine-based therapy. An Innovation and Technology Fund was awarded as the result of the development of an engineering modified NK cell immune therapy against cancer and the research is on-going. Thus, targeting the Smad3-dependent tumour microenvironment may be the new research direction of the team in the coming years.

Based on these scientific findings, the research team won two major scientific awards including the First Prize of Chinese Medical Sciences and Technology Award 2015 and the Second Prize of The State Science & Technology Award 2015.



Mouse anti-glomerular basement membrane nephritis. Deposition of anti-glomerular basement membrane (GBM)antibody (A), Mouse IgG (B) and complement C3(C) will initiate inflammation and fibrosis in glomeruli.

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Recognitions

Awards and Fellowships

Member's Full Name	Details
Hui-yao Lan	First Prize of Chinese Medical Sciences and Technology Award 2015
Hui-yao Lan	Second Prize of The State Science & Technology Award 2015
Chunjie Li	Best oral presentation award, HK Scholar Annual Symposium 2016

Grants and Consultancy

Full Name of PI	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Hui-yao Lan	Genetic Engineering a TGF-beta Tolerant Human NK Cell Line for Effective Anticancer Immunotherapy	Innovation and Technology Commission - Innovation and Technology Fund	01/06/2016	31/12/2017	1,368,400
Hui-yao Lan	Mechanisms and Therapeutic Implication of DPP4-I, Sitagliptin, in High CRP-associated Type-2 Diabetic Nephropathy	Food and Health Bureau - Health and Medical Research Fund	01/06/2016	31/05/2018	1,200,000
Hui-yao Lan	Role of a Novel lncRNA np_5318 in Kidney Disease	Research Grants Council - General Research Fund	01/01/2016	31/12/2018	1,088,569
Hui-yao Lan (Co-PI)	An Integrated Transomics Approach to Diabetic Cardio-renal Complications: From Novel Discoveries to Personalized Medicine	Research Grants Council - Theme-based Research Scheme	01/01/2014	31/12/2018	47,000,000

Publications

A. Journal Papers

1. Lv LL, Tang PM, Li CJ, You YK, Li J, Huang XR, Ni J, Feng M, Liu BC, Lan HY. The pattern recognition receptor, Mincle, is essential for maintaining the M1 macrophage phenotype in acute renal inflammation. *Kidney International*. 2017; 91(3):587-602.
2. Meng XM, Wang S, Huang XR, Yang C, Xiao J, Zhang Y, To KF, Nikolic-Paterson DJ, Lan HY. Inflammatory macrophages can transdifferentiate into myofibroblasts during renal fibrosis. *Cell Death and Disease*. 2016; 7(12):e2495.
3. Shen X, Jiang H, Ying M, Xie Z, Li X, Wang H, Zhao J, Lin C, Wang Y, Feng S, Shen J, Weng C, Lin W, Wang H, Zhou Q, Bi Y, Li M, Wang L, Zhu T, Huang X, Lan HY, Zhou J, Chen J. Calcineurin inhibitors cyclosporin A and tacrolimus protect against podocyte injury induced by puromycin aminonucleoside in rodent models. *Scientific Reports*. 2016; 6:32087.
4. Lai W, Tang Y, Huang XR, Tang PM, Xu A, Szalai AJ, Lou TQ, Lan HY. C-reactive protein promotes acute kidney injury via Smad3-dependent inhibition of CDK2/cyclin E. *Kidney International*. 2016; 90(3):610-26.
5. You YK, Huang XR, Chen HY, Lyu XF, Liu HF, Lan HY. C-reactive protein promotes diabetic kidney disease in db/db mice via the CD32b-Smad3-mTOR signaling pathway. *Scientific Reports*. 2016; 6:26740.
6. Lee WY, Li N, Lin S, Wang B, Lan HY, Li G. miRNA-29b improves bone healing in mouse fracture model. *Molecular and Cellular Endocrinology*. 2016; 430:97-107.
7. Meng XM, Nikolic-Paterson DJ, Lan HY. TGF-beta: the master regulator of fibrosis. *Nature Reviews Nephrology*. 2016; 12(6):325-38. (Review)
8. Wang H, Zhang H, Chen X, Zhao T, Kong Q, Yan M, Zhang B, Sun S, Lan HY, Li N, Li P. The decreased expression of electron transfer flavoprotein beta is associated with tubular cell apoptosis in diabetic nephropathy. *International Journal of Molecular Medicine*. 2016; 37(5):1290-8.
9. Dai XY, Huang XR, Zhou L, Zhang L, Fu P, Manthey C, Nikolic-Paterson DJ, Lan HY. Targeting c-fms kinase attenuates chronic aristolochic acid nephropathy in mice. *Oncotarget*. 2016; 7(10):10841-56.
10. Zhao T, Sun S, Zhang H, Huang X, Yan M, Dong X, Wen Y, Wang H, Lan HY, Li P. Therapeutic effects of Tangshen Formula on diabetic nephropathy in rats. *PLOS ONE*. 2016; 11(1):e0147693.
11. Wang S, Meng XM, Ng YY, Ma FY, Zhou S, Zhang Y, Yang C, Huang XR, Xiao J, Wang YY, Ka SM, Tang YJ, Chung AC, To KF, Nikolic-Paterson DJ, Lan HY. TGF-beta/Smad3 signalling regulates the transition of bone marrow-derived macrophages into myofibroblasts during tissue fibrosis. *Oncotarget*. 2016; 7(8):8809-22.
12. Yiu WH, Wong DW, Wu HJ, Li RX, Yam I, Chan LY, Leung JC, Lan HY, Lai KN, Tang SC. Kallistatin protects against diabetic nephropathy in db/db mice by suppressing AGE-RAGE-induced oxidative stress. *Kidney International*. 2016; 89(2):386-98.

B. Invited Lectures / Seminars by International Scientific Meetings

1. Lan HY. Macrophage-myofibroblast transition in tissue scarring: role of Smad3. In: *Stem Cells: Fundamental Biology And Clinical Translation- Joint 6th Margaret River Region Forum And 9th ASSCR Annual Scientific Meeting*; The University of Western Australia; 2016 December 4-8.
2. Lan HY. Treatment of diabetic nephropathy by targeting TGF-beta/Smad signaling. In: *PCS 2nd Annual World Pathology Conference*; Prague, Czech Public; 2016 June 18-19.
3. Lan HY. Disrupted the Angiotensin II degradation pathway Promotes Hypertensive Nephropathy. In: *The International Symposium of Cardiovascular Basic & Translational Medicine*; Guangzhou, China; 2016 April 8-10.
4. Lan HY. Mechanisms of TGF beta regulate renal inflammation and fibrosis: Role of lncRNAs. In: *5th Nephrology Update West Lake Forum*; Hangzhou, China; 2016 May 12-14.