

Translational Genetics and Epigenetics of Immune-Related Skin Diseases

Introduction to Guest Editors

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Research interest: Epigenetic mechanism, biomarker, and treatment of autoimmune skin diseases

Dr. Qianjin Lu is currently a Professor and Director of the Institute of Dermatology at Central South University, Director of Hunan Key Laboratory of Medical Epigenomics, President of the Chinese Society of Dermatology. His researches focus on the epigenetics of autoimmune and inflammatory-related skin diseases, including lupus, psoriasis, and atopic dermatitis. He has authored over 200 peer-reviewed publications, book chapters, and review articles in high academic journals, including *Lancet*, *JAMA*, *Blood*, *J Clin Invest*, *Ann Rheum Dis*, and *J Immunol*. Dr. Lu is on the editorial board of several peer-reviewed and has been appointed as an associate editor of *Clinical Immunology* and Associate Editor of *Global Clinical and Translational Research*. He has received numerous awards, including the International League of Dermatological Societies, the Second Prize of National Scientific and Technological Progress, the First Prize of Natural Scientific Research of Hunan Province, the First Prize of Scientific and Technological Progress of Hunan Province, and Outstanding Medical Scientist of China. Dr. Lu practices clinical dermatology including outpatient and inpatient services and teach medical student, and has extensive clinical and research experience in dermatology and especially in lupus and psoriasis.

Selected publications

1. Huang C, Yi X, Long H, Zhang G, Wu H, Zhao M, **Lu Q**. Disordered cutaneous microbiota in systemic lupus erythematosus. *J Autoimmun*. 2020 Mar; 108: 102391.
2. Lu Q, Wu R, Zhao M, Garcia-Gomez A, Ballestar E. miRNAs as Therapeutic Targets in Inflammatory Disease. *Trends Pharmacol Sci*. 2019 Nov; 40(11): 853-865.
3. Liang Y, Yu B, Chen J, Wu H, Xu Y, Yang B, **Lu Q**. Thymic stromal lymphopoitin epigenetically upregulates Fc receptor γ subunit-related receptors on antigen-presenting cells and induces TH2/TH17 polarization through dectin-2. *J Allergy Clin Immunol*. 2019 Oct; 144(4): 1025-1035.
4. Wu H, Deng Y, Feng Y, Long D, Ma K, Wang X, Zhao M, Lu L, **Lu Q**. Epigenetic regulation in B-cell maturation and its dysregulation in autoimmunity. *Cell Mol Immunol*. 2018 Jul; 15(7): 676-684.
5. Wu R, Zeng J, Yuan J, Deng X, Huang Y, Chen L, Zhang P, Feng H, Liu Z, Wang Z, Gao X, Wu H, Wang H, Su Y, Zhao M, **Lu Q**. MicroRNA-210 overexpression promotes psoriasis-like inflammation by inducing Th1 and Th17 cell differentiation. *J Clin Invest*. 2018 Jun 1; 128 (6): 2551-2568.
6. Zhao M, Tan Y, Peng Q, Huang C, Guo Y, Liang G, Zhu B, Huang Y, Liu A, Wang Z, Li M, Gao X, Wu R, Wu H, Long H, **Lu Q**. IL-6/STAT3 pathway induced deficiency of RFX1 contributes to Th17-dependent autoimmune diseases via epigenetic regulation. *Nat Commun*. 2018 Feb 8; 9(1): 583.
7. Liu X, Zhang W, Zhao M, Fu L, Liu L, Wu J, Luo S, Wang L, Wang Z, Lin L, Liu Y, Wang S, Yang Y, Luo L, Jiang J, Wang X, Tan Y, Li T, Zhu B, Zhao Y, Gao X, Wan Z, Huang C, Fang M, Li Q, Peng H, Liao X, Chen

- J, Li F, Ling G, Zhao H, Luo H, Xiang Z, Liao J, Liu Y, Yin H, Long H, Wu H, Yang H, Wang J, **Lu Q.** T cell receptor β repertoires as novel diagnostic markers for systemic lupus erythematosus and rheumatoid arthritis. *Ann Rheum Dis.* 2019 Aug;78(8):1070-1078.
8. Zhao M, Zhou Y, Zhu B, Wan M, Jiang T, Tan Q, Liu Y, Jiang J, Luo S, Tan Y, Wu H, Renauer P, Del Mar Ayala Gutiérrez M, Castillo Palma MJ, Ortega Castro R, Fernández-Roldán C, Raya E, Faria R, Carvalho C, Alarcón-Riquelme ME, Xiang Z, Chen J, Li F, Ling G, Zhao H, Liao X, Lin Y, Sawalha AH, **Lu Q.** IFI44L promoter methylation as a blood biomarker for systemic lupus erythema-atosus. *Ann Rheum Dis.* 2016 Nov;75(11):1998-2006.
9. Zhao M, Wang J, Liao W, Li D, Li M, Wu H, Zhang Y, Gershwin ME, **Lu Q.** Increased 5-hydroxymethylcytosine in CD4(+) T cells in systemic lupus erythematosus. *J Autoimmun.* 2016 May; 69: 64-73.
10. Wu H, Zhao M, Yoshimura A, Chang C, **Lu Q.** Critical Link Between Epigenetics and Transcription Factors in the Induction of Autoimmunity: A Comprehensive Review. *Clin Rev Allergy Immunol.* 2016 Jun;50(3):333-44.

Ming Zhao, M.D, Ph.D.

Department of Dermatology, The Second Xiangya Hospital of Central South University, Changsha, Hunan, China

Research interest: Epigenetic mechanism, biomarker, and treatment of autoimmune skin diseases.

Dr. Ming Zhao is a professor in the Department of Dermatology in the Second Xiangya Hospital of Central South University and vice-director of the Hunan Key Laboratory of Medical Epigenomics. He has served as vice-director of the Experimental Chapter of the Chinese Society of Dermatology since 2016. His research focuses on the epigenetic mechanism and biomarkers of autoimmune skin diseases. Dr. Zhao is a recipient of the Excellent Youth Investigator Fund and the general grant fund of the National Natural Science Foundation. He published 30 papers as first author or corresponding author in the peer-reviewed academic journals, including *Nature Communications*, *Journal of Clinical Investigation*, and *Annals of the Rheumatic Diseases*. He is a recipient of the second prize of the National Science and Technology Progress Award in 2017 and two first prizes of Hunan Science and Technology Progress Awards.

Selected publications

1. Huang C, Yi X, Long H, Zhang G, Wu H, **Zhao M***, Lu Q. Disordered cutaneous microbiota in systemic lupus erythematosus. *J Autoimmun.* 2020 Mar; 108: 102391.
2. Feng H, Wu R, Zhang S, Kong Y, Liu Z, Wu H, Wang H, Su Y, **Zhao M***, Lu Q. Topical administration of nanocarrier miRNA-210 antisense ameliorates imiquimod-induced psoriasis-like dermatitis in mice. *J Dermatol.* 2020 Feb;47(2):147-154.
3. Jia S, Yang S, Du P, Gao K, Cao Y, Yao B, Guo R, **Zhao M***. Regulatory Factor X1 Downregulation Contributes to Monocyte Chemoattractant Protein-1 Overexpression in CD14+ Monocytes via Epigenetic Mechanisms in Coronary Heart Disease. *Front Genet.* 2019 Nov 1; 10:1098.
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7. **Zhao M***, Tan Y, Peng Q, Huang C, Guo Y, Liang G, Zhu B, Huang Y, Liu A, Wang Z, Li M, Gao X, Wu R, Wu H, Long H, Lu Q. IL-6/STAT3 pathway induced deficiency of RFX1 contributes to Th17-dependent autoimmune diseases via epigenetic regulation. *Nat Commun.* 2018 Feb 8;9(1):583.
8. Liu X, Zhang W, **Zhao M**, Fu L, Liu L, Wu J, Luo S, Wang L, Wang Z, Lin L, Liu Y, Wang S, Yang Y, Luo L, Jiang J, Wang X, Tan Y, Li T, Zhu B, Zhao Y, Gao X, Wan Z, Huang C, Fang M, Li Q, Peng H, Liao X, Chen J, Li F, Ling G, Zhao H, Luo H, Xiang Z, Liao J, Liu Y, Yin H, Long H, Wu H, Yang H, Wang J, Lu Q. T cell receptor β repertoires as novel diagnostic markers for systemic lupus erythematosus and rheumatoid arthritis. *Ann Rheum Dis.* 2019 Aug;78(8):1070-1078.
9. **Zhao M**, Zhou Y, Zhu B, Wan M, Jiang T, Tan Q, Liu Y, Jiang J, Luo S, Tan Y, Wu H, Renauer P, Del Mar Ayala Gutiérrez M, Castillo Palma MJ, Ortega Castro R, Fernández-Roldán C, Raya E, Faria R, Carvalho C, Alarcón-Riquelme ME, Xiang Z, Chen J, Li F, Ling G, Zhao H, Liao X, Lin Y, Sawalha AH, Lu Q. IFI44L promoter methylation as a blood biomarker for systemic lupus erythematosus. *Ann Rheum Dis.* 2016 Nov;75(11):1998-2006.
10. **Zhao M**, Wang J, Liao W, Li D, Li M, Wu H, Zhang Y, Gershwin ME, Lu Q. Increased 5-hydroxymethylcytosine in CD4(+) T cells in systemic lupus erythematosus. *J Autoimmun.* 2016 May; 69:64-73.

Juan Tao, MD, PhD

Department of Dermatology, The Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China.

Research interest: Immunologic mechanism and translational medicine of severe cutaneous diseases (malignant melanoma, psoriasis and lupus erythematosus) and skin repair

Dr. Juan Tao is a Professor and Chairman of the department of dermatology of Wuhan Union Hospital, and the director of Hubei Engineering Research Center for Skin Repair and Theranostics. She has led six research programs of the National Natural Science Foundation of China and one New Century Talent Project from the Ministry of Education in China. She has published 64 peer-reviewed papers as the first or corresponding author, including five papers in academic journals such as *Angew Chem Int Ed*, *J Invest Dermatol*, *JAAD*, *BJD*, *Biomaterials*, and *Small*. She is a recipient of the first prize of the Hubei Provincial Science and Technology Progress Award (Ranked the first) and filed 21 invention patents in China, one of which one has been granted, and clinical transformation has been realized. She organized and participated in establishing eight experts' consensus/guidelines. Dr. Juan Tao has been invited as an editorial consultant of *Br J Dermatol*, deputy editor of the Chinese edition of *J Am Acad Dermatol*, and served as a reviewer for many domestic and international journals.

Selected publications

1. Lan J#, Song Z#, Miao X, Li H, Li Y, Dong L, Yang J, An X, Zhang Y, Yang L, Zhou N, Yang L, Li J, Cao J, Wang J, **Tao J***. Skin damage and the risk of infection among healthcare workers managing coronavirus disease-2019. *J Am Acad Dermatol.* 2020 Mar 11; DOI: 10.1016/j.jaad.2020.03.014
2. **Tao J***, Song Z, Yang L, Huang C, Feng A, Man X. Emergency Management for Preventing and Controlling Nosocomial Infection of 2019 Novel Coronavirus: Implications for the Dermatology Department. *Br J Dermatol.* 2020 Mar 5; DOI: 10.1111/bjd.19011
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5. Xu N#, Li J#, Gao Y#, Zhou N, Ma Q, Wu M, Zhang Y, Sun X, Xie J, Shen G, Yang M, Tu Q, Xu X, Zhu J*, **Tao J***. Apoptotic cell-mimicking gold nanocages loaded with LXR agonist for attenuating the progression of murine systemic lupus erythematosus. *Biomaterials*. 2019 Mar; 197:380-392
6. Liu Q#, Zhou Y#, Li M, Zhao L, Ren J, Li D, Tan Z, Wang K, Li H, Hussain M, Zhang L, Shen G, Zhu J*, **Tao J***. Polyethylenimine Hybrid Thin-Shell Hollow Mesoporous Silica Nanoparticles as Vaccine Self-Adjuvants for Cancer Immunotherapy. *ACS Appl Mater Interfaces*. 2019 Dec 26;11(51): 47798-47809.
7. Dong L#, Li Y, Li Z, Xu N, Liu P, Du H, Zhang Y, Huang Y, Zhu J, Ren G, Xie J, Wang K, Zhou Y, Shen C, Zhu J*, **Tao J***. Au Nanocage-Strengthened Dissolving Microneedles for Chemo Photothermal Combined Therapy of Superficial Skin Tumors. *ACS Appl Mater Interfaces*. 2018 Mar 21; 10(11): 9247-56.
8. Zhang Y#, Li J#, Zhou N#, Zhang Y, Wu M, Xu J, Shen C, An X, Shen G, Yang M, Zhang C, **Tao J***. The Unknown Aspect of BAFF: Inducing IL-35 Production by a Novel CD5+CD1dhiFcγRIIbhi Regulatory B Cell Subset in Lupus. *J Invest Dermatol*. 2017 Dec;137(12):2532-2543.
9. Xie J #, Yang C, Liu Q, Li J, Liang R, Shen C, Zhang Y, Wang K, Liu L, Shezad K, Sullivan M, Xu Y, Shen G, **Tao J***, Zhu J *, Zhang Z *. Encapsulation of Hydrophilic and Hydrophobic Peptides into Hollow Mesoporous Silica Nanoparticles for Enhancement of Antitumor Immune Response. *Small*. 2017 Oct;13(40).
10. Xu J#, Li J#, Yang Y, Wang K, Xu N, Li J, Liang R, Shen L, Xie X, **Tao J***, Zhu J*. Block Copolymer Capsules with Structure-Dependent Release Behavior. *Angew Chem Int Ed Engl*. 2016 Nov 14;55(47):14633-14637.

Liangdan Sun, MD, PhD

Department of Dermatology, the First Affiliated Hospital, Anhui Medical University; Institute of Dermatology, Anhui Medical University; The Key Laboratory of Dermatology of the Ministry of Education, Hefei, Anhui, China

Research interest: Genetics and genomics of common diseases

Dr. Liangdan Sun is Professor and Director of the Key Laboratory of Dermatology in Hefei, the Ministry of Education, Director of Department of Research and Development (R&D) of the First Affiliated Hospital, Anhui Medical University, Visiting Scholar of the University of Colorado and the Royal Swedish Academy of Engineering Sciences. His researches focus on the genetic and genomic studies of diseases. Dr. Sun has identified more than 200 susceptibility genes and diagnostic biomarkers for 40 diseases and has constructed the unique precision variation database of the whole Human Leukocyte Antigens (HLA) based on 10,000 samples in the Chinese population. Through the genome-wide association and sequencing study, he has constructed the genome-wide variation maps for different diseases, demonstrated the mechanisms of genetic susceptibilities and etiologies, which will provide the necessary evidence for the precision medicine of these diseases. Dr. Sun has published over 170 papers, including those in *Nat Genet*, *New Engl J Med*, and *Nat Commun*, and has been cited more than 6,300 times, including by publications in *Nature*, *Cell*, *New Engl J Med*.

Selected publications

1. **Sun LD**, Cheng H, Wang ZX, Zhang AP, Wang PG, Xu JH, Zhu QX, Zhou HS, Ellinghaus E, Zhang FR, Pu XM, Yang XQ, Zhang JZ, Xu AE, Wu RN, Xu LM, Peng L, Helms CA, Ren YQ, Zhang C, Zhang SM,

- Nair RP, Wang HY, Lin GS, Stuart PE, Fan X, Chen G, Tejasvi T, Li P, Zhu J, Li ZM, Ge HM, Weichenthal M, Ye WZ, Zhang C, Shen SK, Yang BQ, Sun YY, Li SS, Lin Y, Jiang JH, Li CT, Chen RX, Cheng J, Jiang X, Zhang P, Song WM, Tang J, Zhang HQ, Sun L, Cui J, Zhang LJ, Tang B, Huang F, Qin Q, Pei XP, Zhou AM, Shao LM, Liu JL, Zhang FY, Du WD, Franke A, Bowcock AM, Elder JT, Liu JJ, Yang S, and Zhang XJ. Association analyses identify six new psoriasis susceptibility loci in the Chinese population. *Nat Genet*. 2010; 42(11): 1005-9.
2. Sun LD, Xiao FL, Li Y, Zhou WM, Tang HY, Tang XF, Zhang H, Schaarschmidt H, Zuo XB, Foelster-Holst R, He SM, Shi M, Liu Q, Lv YM, Chen XL, Zhu KJ, Guo YF, Hu DY, Li M, Li M, Zhang YH, Zhang X, Tang JP, Guo BR, Wang H, Liu Y, Zou XY, Zhou FS, Liu XY, Chen G, Ma L, Zhang SM, Jiang AP, Zheng XD, Gao XH, Li P, Tu CX, Yin XY, Han XP, Ren YQ, Song SP, Lu ZY, Zhang XL, Cui Y, Chang J, Gao M, Luo XY, Wang PG, Dai X, Su W, Li H, Shen CP, Liu SX, Feng XB, Yang CJ, Lin GS, Wang ZX, Huang JQ, Fan X, Wang Y, Bao YX, Yang S, Liu JJ, Franke A, Weidinger S, Yao ZR, Zhang XJ. Genome-wide association study identifies two new susceptibility loci for atopic dermatitis in the Chinese Han population. *Nat Genet*. 2011 Jun; 43(7):690-4.
3. Zhou F, Cao H, Zuo X, Zhang T, Zhang X, Liu X, Xu R, Chen G, Zhang Y, Zheng X, Jin X, Gao J, Mei J, Sheng Y, Li Q, Liang B, Shen J, Shen C, Jiang H, Zhu C, Fan X, Xu F, Yue M, Yin X, Ye C, Zhang C, Liu X, Yu L, Wu J, Chen M, Zhuang X, Tang L, Shao H, Wu L, Li J, Xu Y, Zhang Y, Zhao S, Wang Y, Li G, Xu H, Zeng L, Wang J, Bai M, Chen Y, Chen W, Kang T, Wu Y, Xu X, Zhu Z, Cui Y, Wang Z, Yang C, Wang P, Xiang L, Chen X, Zhang A, Gao X, Zhang F, Xu J, Zheng M, Zheng J, Zhang J, Yu X, Li Y, Yang S, Yang H, Wang J, Liu J, Hammarström L, Sun L, Wang J, Zhang X. Deep sequencing of the MHC region in the Chinese population contributes to studies of complex disease. *Nat Genet*. 2017 Jul; 48(7):740-6.
4. Wang C, Zheng X, Jiang P, Tang R, Gong Y, Dai Y, Wang L, Xu P, Sun W, Wang L, Han C, Jiang Y, Wei Y, Zhang K, Wu J, Shao Y, Gao Y, Yu J, Hu Z, Zang Z, Zhao Y, Wu X, Dai N, Liu L, Nie J, Jiang B, Lin M, Li L, Li Y, Chen S, Shu L, Qiu F, Wu Q, Zhang M, Chen R, Jawed R, Zhang Y, Shi X, Zhu Z, Pei H, Huang L, Zhao W, Tian Y, Zhu X, Qiu H, Gershwin ME, Chen W, Seldin MF, Liu X, Sun L, Ma X. Genome-wide Association Studies of Specific Antinuclear Autoantibody Subphenotypes in Primary Biliary Cholangitis. *Hepatology*. 2019 Jul; 70(1):294-307.
5. Sheng Y, Jin X, Xu J, Gao J, Du X, Duan D, Li B, Zhao J, Zhan W, Tang H, Tang X, Li Y, Cheng H, Zuo X, Mei J, Zhou F, Liang B, Chen G, Shen C, Cui H, Zhang X, Zhang C, Wang W, Zheng X, Fan X, Wang Z, Xiao F, Cui Y, Li Y, Wang J, Yang S, Xu L, Sun L, Zhang X. Sequencing-based approach identified three new susceptibility loci for psoriasis. *Nat Commun*. 2014 Jul 9; 5:4331.
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9. Zhen Q, Yang Z, Wang W, Li B, Bai M, Wu J, Ge H, Dong Z, Shen J, Tang H, Sun S, Qiu Y, Xu J, Qu X, Wang Y, Yi M, Hu H, Xu Y, Cheng H, Liang B, Gao J, Shao H, Jiang Z, Gao Q, Sun L. Genetic Study on Small Insertions and Deletions in Psoriasis Reveals a Role in Complex Human Diseases. *J Invest Dermatol*. 2019 Nov; 139(11):2302-2312.e14.
10. Gao J, Zhu C, Zhang Y, Sheng Y, Yang F, Wang W, Qian W, Chen S, Zhu Q, Zuo X, Tang H, Tang X, Li Y, Cheng H, Zhou F, Liu S, Chen G, Zheng X, Zhu Z, Wang Z, Yang S, Luo X, Ye D, Zhang X, Sun L. Association Study and Fine-Mapping Major Histocompatibility Complex Analysis of Pemphigus Vulgaris in a Han Chinese Population. *J Invest Dermatol*. 2018 Nov; 138(11):2307-2314.

Hong Liu, MD, PhD

Shandong Provincial Hospital for Skin Diseases, The First Medical University of Shandong; Shandong Provincial Institute of Dermatology and Venereology, Shandong Academy of Medical Sciences, Jinan, Shandong, China

Research interest: Clinical and experimental studies of infectious diseases, such as leprosy, fungal infectious diseases, auto-immune blistering diseases, and severe cutaneous adverse drug reactions

Dr. Hong Liu is the vice director of Shandong Provincial Dermatovenereology Key Laboratory. She has presided five national research programs, including one National Science Fund for Excellent Youth Investigator and one National "863" Yong Investigator Program. As the first/corresponding author, she has published over 30 papers, including those in high profile journals such as *Nature Genetics*, *Nature Comm*, *JAMA Dermatology*, *American Journal of Human Genetics*, and *Journal of Investigative Dermatology*. As a major participant, she has received awards for the first prize of Shandong Provincial Science and Technology Progress (2011), the first prize of Shandong Provincial Nature and Science (2015), and the first prize of Shandong Provincial Technology and Invention (2018). She obtained three National Invention Patents and four International Invention Patents, and was selected for the "National Hundred-Thousand-Ten Thousand Project" and honored with National Outstanding Young and Middle-aged Expert, Shandong Provincial Outstanding Young and Middle-aged Expert and Young experts For Taishan Scholars with excellent achievements.

Selected publications

1. **Liu H**, Irwanto A, Fu X'A, et al. Discovery of six new susceptibility loci and analysis of pleiotropic effects in leprosy. *Nat Genet*. 2015;47(3):267-71. doi: 10.1038/ng.3212.
2. **Liu H**, Irwanto A, Tian H, et al. Identification of IL18RAP/IL18R1 and IL12B as Leprosy Risk Genes Demonstrates Shared Pathogenesis between Inflammation and Infectious Diseases. *Am J Human Genet*. 2012 91(5):935-41.
3. **Liu H**, Wang ZZ, Li Y, et al. Genome-Wide Analysis of Protein-Coding Variants in Leprosy. *J Invest Dermatol*. 2017 Dec;137(12):2544-2551
4. **Liu H**, Wang ZZ, Bao FF, et al. Evaluation of Prospective HLA-B*13:01 screening to prevent dapsonic hypersensitivity syndrome. *JAMA Dermatol*. 2019 Jun 1;155(6): 666-672.
5. **Liu H**, Bao F, Irwanto A, et al. Association study of TOLL and CARD with leprosy susceptibility in the Chinese population. *Hum Mol Genet*. 2013 Jun 19.
6. Wang ZZ, **Liu H***, Zhang FR*. A Large-scale Genome-wide Association and Meta-analysis Identified Four Novel Susceptibility Loci for leprosy. *Nat Commun*. 2016 Dec 15; 7:13760
7. Sun Y, **Liu H***, Zhang FR*. The HLA-DQB1*03:01 is associated with Bullous Pemphigoid in the Han Chinese population. *J Invest Dermatol*. 2018 Aug;138(8): 1874-1877.
8. Li LL, You JB, **Liu H***. Variants of CARD14 are predisposing factors for generalized pustular psoriasis (GPP) with psoriasis Vulgaris but not for GPP alone in a Chinese population. *Br J Dermatol*. 2019 Feb;180(2):425-426. doi: 10.1111/bjd.17392.
9. **Liu H**, Chuan W, et al. Case report of two cases with fever, rash, and organ involvement during the treatment of leprosy. *PLoS Neglected Tropical Diseases*. 2014 Aug 28;8(8): e3130. doi: 10.1371/journal.pntd.0003130.
10. Zhang FR*, **Liu H**, Irwanto A, et al. HLA-B*13:01 and Dapsone-induced Hyper-sensitivity Syndrome. *N Engl J Med* 2013 Oct 24;369(17):1620-8. doi: 10.1056/NEJMoa1213096