* 项目名称：国人肺动脉高压遗传特征及发病机制研究
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1、中国医学科学院北京协和医院

2、中国医学科学院阜外医院

3、上海市肺科医院

4、首都医科大学附属北京世纪坛医院

5、河南大学

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* 提名意见

项目组近二十余年专注肺动脉高压遗传学和发病机制研究，建立了中国人最大规模肺动脉高压患者临床队列、生物样本银行及基础研究技术平台，为阐明国人肺动脉高压遗传模式、肺血管重构的关键靶点和机制从而研发新的治疗方法攻坚克难，获得主要科学发现：1）率先在国际上报道肺动脉高压新致病基因*BMP9* 和*PTGIS*及其致病机制；发现DNA甲基化转移酶3B保护肺血管重构的表观遗传调控机制；2）在国际上率先发现精胺与肺动脉高压疾病严重程度密切相关，并揭示精胺及其合成酶介导的代谢重编程是导致肺动脉高压血管重构的核心机制之一，此发现被誉为“肺血管代谢的瓦伯格效应”；3）阐明外源性雌激素逆转肺血管重构，改善肺动脉高压表型的关键机制，回答了雌激素是肺动脉高压血管重构的保护还是有害因素的长期学术争论。本项目研究长期收集和保藏了国人肺动脉高压遗传资源，在肺动脉高压遗传特征和发病机制的系列突破性发现，对国内相关研究机构和制药企业进行国人肺动脉高压新药研发提供关键支撑，为推动肺动脉高压分子诊断奠定坚实理论基础。

项目组在包括*NEJM, Lancet, Circulation, JACC, European Heart Journal, European Respiratory Journal, JAMA Cardiology, Science Advances*等国际权威期刊发表SCI论文131篇，5篇代表论著总影响因子78.832（他引126次），包括*Nature Reviews Cardiology, European Heart Journal, American Journal of Respiratory and Critical Care Medicine*等国际顶级期刊均对此进行正面评价和引用。其中BMP9 基因突变研究被*American Journal of Respiratory and Critical Care Medicine*评选为“肺血管疾病和右心功能不全”领域2019年度发现。*European Heart Journal*亦连续刊文高度评价本项目团队在肺动脉高压领域的重要贡献及引领作用。

* 主要支撑材料目录
	+ 代表论著5篇
1. Wang XJ, Lian TY, Jiang X, Liu SF, Li SQ, Jiang R, Wu WH, Ye J, Cheng CY, Du Y, Xu XQ, Wu Y, Peng FH, Sun K, Mao YM, Yu H, Liang C, Shyy JY, Zhang SY, Zhang X, Jing ZC. Germline *BMP9* mutation causes idiopathic pulmonary arterial hypertension. ***Eur Respir J***. 2019;53(3):1801609. （IF 16.671）
2. Wang XJ, Xu XQ, Sun K, Liu KQ, Li SQ, Jiang X, Zhao QH, Wang L, Peng FH, Ye J, Wu Y, Jiang R, Zhang J, Huang W, Wei WB, Yan Y, Li JH, Liu QQ, Li S, Wang Y, Zhang SY, Zhang X, Jing ZC. Association of Rare PTGIS Variants With Susceptibility and Pulmonary Vascular Response in Patients With Idiopathic Pulmonary Arterial Hypertension. ***JAMA Cardiol***. 2020;5(6):677-684. （IF 14.676）
3. Yan Y, He YY, Jiang X, Wang Y, Chen JW, Zhao JH, Ye J, Lian TY, Zhang X, Zhang RJ, Lu D, Guo SS, Xu XQ, Sun K, Li SQ, Zhang LF, Zhang X, Zhang SY, Jing ZC. DNA methyltransferase 3B deficiency unveils a new pathological mechanism of pulmonary hypertension. ***Sci Adv***. 2020;6(50):eaba2470. （IF 14.143）
4. He YY, Yan Y, Jiang X, Zhao JH, Wang Z, Wu T, Wang Y, Guo SS, Ye J, Lian TY, Xu XQ, Zhang JL, Sun K, Peng FH, Zhou YP, Mao YM, Zhang X, Chen JW, Zhang SY, Jing ZC. Spermine promotes pulmonary vascular remodelling and its synthase is a therapeutic target for pulmonary arterial hypertension. ***Eur Respir J***. 2020;56(5):2000522. （IF 16.671）
5. Yuan P, Wu WH, Gao L, Zheng ZQ, Liu D, Mei HY, Zhang ZL, Jing ZC. Oestradiol ameliorates monocrotaline pulmonary hypertension via NO, prostacyclin and endothelin-1 pathways. ***Eur Respir J***. 2013;41(5):1116-25. （IF 16.671）
	* 代表引文5篇
6. Goncharova EA, Chan SY, Ventetuolo CE, Weissmann N, Schermuly RT, Mullin CJ, Gladwin MT. Update in Pulmonary Vascular Diseases and Right Ventricular Dysfunction 2019. ***Am J Respir Crit Care Med***. 2020;202(1):22-28.
7. Southgate L, Machado RD, Gräf S, Morrell NW. Molecular genetic framework underlying pulmonary arterial hypertension. ***Nat Rev Cardiol***. 2020;17(2):85-95.
8. Wang Q, Tian J, Li X, Liu X, Zheng T, Zhao Y, Li X, Zhong H, Liu D, Zhang W, Zhang M, Li M, Zhang M. Upregulation of Endothelial DKK1 (Dickkopf 1) Promotes the Development of Pulmonary Hypertension Through the Sp1 (Specificity Protein 1)/SHMT2 (Serine Hydroxymethyltransferase 2) Pathway. ***Hypertension***. 2022;79(5):960-973.
9. Tamosiuniene R, Manouvakhova O, Mesange P, Saito T, Qian J, Sanyal M, Lin YC, Nguyen LP, Luria A, Tu AB, Sante JM, Rabinovitch M, Fitzgerald DJ, Graham BB, Habtezion A, Voelkel NF, Aurelian L, Nicolls MR. Dominant Role for Regulatory T Cells in Protecting Females Against Pulmonary Hypertension. ***Circ Res***. 2018;122(12):1689-1702.
10. Al-Naamani N, Ventetuolo CE. Another Piece in the Estrogen Puzzle of Pulmonary Hypertension. ***Am J Respir Crit Care Med***. 2020;201(3):274-275.
	* 第三方评价
11. Morrell NW. Finding the needle in the haystack: BMP9 and 10 emerge from the genome in pulmonary arterial hypertension. ***Eur Respir J***. 2019;53(3):1900078.
12. <https://pvrinstitute.org/en/professionals/news/2020/4/27/novel-ipah-mutations-found-in-chinese-patients-study-reports/>
13. Rhodes CJ. The cancer hypothesis of pulmonary arterial hypertension: are polyamines the new Warburg? ***Eur Respir J***. 2020;56(5):2002350.
14. Paulus JK, Roberts KE. Oestrogen and the sexual dimorphism of pulmonary arterial hypertension: a translational challenge. ***Eur Respir J***. 2013;41(5):1014-6.
15. Jiang X, Xu XQ, Jing ZC. The Key Laboratory of Pulmonary Vascular Medicine, Chinese Academy of Medical Sciences (KLPVM-CAMS). ***Eur Heart J***. 2019;40(48):3881-3885.
16. Nicholls M. Pioneering pulmonary vascular medicine in China. ***Eur Heart J***. 2022;43(17):1605-1608.
17. Hoeper MM, Humbert M, Souza R, Idrees M, Kawut SM, Sliwa-Hahnle K, Jing ZC, Gibbs JS. A global view of pulmonary hypertension. ***Lancet Respir Med***. 2016;4(4):306-22.
18. Newman JH, Rich S, Abman SH, Alexander JH, Barnard J, Beck GJ, Benza RL, Bull TM, Chan SY, Chun HJ, Doogan D, Dupuis J, Erzurum SC, Frantz RP, Geraci M, Gillies H, Gladwin M, Gray MP, Hemnes AR, Herbst RS, Hernandez AF, Hill NS, Horn EM, Hunter K, Jing ZC, Johns R, Kaul S, Kawut SM, Lahm T, Leopold JA, Lewis GD, Mathai SC, McLaughlin VV, Michelakis ED, Nathan SD, Nichols W, Page G, Rabinovitch M, Rich J, Rischard F, Rounds S, Shah SJ, Tapson VF, Lowy N, Stockbridge N, Weinmann G, Xiao L. Enhancing Insights into Pulmonary Vascular Disease through a Precision Medicine Approach. A Joint NHLBI-Cardiovascular Medical Research and Education Fund Workshop Report. ***Am J Respir Crit Care Med***. 2017;195(12):1661-1670.