A large-scale genome-wide association analysis of lung function in the Chinese population identifies novel loci and highlights shared genetic aetiology with obesity

Zhaozhong Zhu[1,2,14], Jiachen Li[3,14], Jiahui Si[1,3,14], Baoshan Ma[4,14], Huwenbo Shi[1], Jun Lv[3,5,6], Weihua Cao[3], Yu Guo[7], Iona Y. Millwood[8,9], Robin G. Walters[8,9], Kuang Lin[8,9], Ling Yang[8,9], Yiping Chen[8,9], Huaidong Du[8,9], Bo Yu[10], Kohei Hasegawa[2], Carlos A. Camargo Jr[1,2], Miriam F. Moffatt[11], William O.C. Cookson[11], Junshi Chen[12], Zhengming Chen[9], Liming Li[3], Canqing Yu[3,15] and Liming Liang[1,13,15]

[1]Program in Genetic Epidemiology and Statistical Genetics, Dept of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA. [2]Dept of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA. [3]Dept of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing, China. [4]College of Information Science and Technology, Dalian Maritime University, Dalian, China. [5]Key Laboratory of Molecular Cardiovascular Sciences (Peking University), Ministry of Education, Beijing, China. [6]Peking University Institute of Environmental Medicine, Beijing, China. [7]Chinese Academy of Medical Sciences, Beijing, China. [8]Medical Research Council Population Health Research Unit at the University of Oxford, Oxford, UK. [9]Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), Nuffield Dept of Population Health, University of Oxford, Oxford, UK. [10]NCDs Prevention and Control Dept, Nangang CDC, Harbin, China. [11]Section of Genomic Medicine, National Heart and Lung Institute, Imperial College London, London, UK. [12]China National Center for Food Safety Risk Assessment, Beijing, China. [13]Dept of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA. [14]These four authors contributed equally to this article. [15]These two authors contributed equally to this article as lead authors and supervised the work.

Corresponding author: Canqing Yu (yucanqing@pku.edu.cn)

Shareable abstract (@ERSpublications)
Novel loci provide additional insights into the genetic basis of lung function. Understanding the shared genetic aetiology of lung function and obesity may open new avenues for molecular-targeted therapies for obesity and lung function improvement. http://bit.ly/38oCnez

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Abstract

Background Lung function is a heritable complex phenotype with obesity being one of its important risk factors. However, knowledge of their shared genetic basis is limited. Most genome-wide association studies (GWASs) for lung function have been based on European populations, limiting the generalisability across populations. Large-scale lung function GWASs in other populations are lacking.

Methods We included 100 285 subjects from the China Kadoorie Biobank (CKB). To identify novel loci for lung function, single-trait GWAS analyses were performed on forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC in the CKB. We then performed genome-wide cross-trait analysis between lung function and obesity traits (body mass index (BMI), BMI-adjusted waist-to-hip ratio and BMI-adjusted waist circumference) to investigate the shared genetic effects in the CKB. Finally, polygenic risk scores (PRSs) of lung function were developed in the CKB and their interaction with BMI's association on lung function were examined. We also conducted cross-trait analysis in parallel with the CKB using up to 457 756 subjects from the UK Biobank (UKB) for replication and investigation of ancestry-specific effects.

Results We identified nine genome-wide significant novel loci for FEV_1, six for FVC and three for FEV_1/FVC in the CKB. FEV_1 and FVC showed significant negative genetic correlation with obesity traits in both the CKB and UKB. Genetic loci shared between lung function and obesity traits highlighted important biological pathways, including cell proliferation, embryo, skeletal and tissue development, and regulation of gene expression. Mendelian randomisation analysis suggested significant negative causal

effects of BMI on FEV_1 and on FVC in both the CKB and UKB. Lung function PRSs significantly modified the effect of change in BMI on change in lung function during an average follow-up of 8 years.

Conclusion This large-scale GWAS of lung function identified novel loci and shared genetic aetiology between lung function and obesity. Change in BMI might affect change in lung function differently according to a subject's polygenic background. These findings may open new avenues for the development of molecular-targeted therapies for obesity and lung function improvement.