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Title: Clinical significance and functional roles of FoxM1 in non-small cell lung cancer

Dr. Nuo 29465 Xu a_meng99@yahoo.com.cn MD ¹, Mr. Deshui 29521 Jia waterprice2008@yahoo.com.cn ², Mr. Wenfeng 29522 Chen 09111020003@fudan.edu.cn ³, Dr. Di 29594 Ge ge.di@zs-hospital.sh.cn ⁴ and Dr. Chunxue 29601 Bai bai.chunxue@zs-hospital.sh.cn ¹. ¹ Department of Pulmonary Medicine, Fudan University, Shanghai, China, 200032 ; ² Shanghai Medical College, Fudan University, Shanghai, China ; ³ Department of Biostatistics, School of Public Health, Fudan University, Shanghai, China and ⁴ Department of Thoracology, Zhongshan Hospital, Fudan University, Shanghai, China .

Body: Purpose: To test the role of FoxM1 in the metastasis of non-small cell lung cancer. Experimental design: FoxM1 expression was examined in 175 NSCLC patients with or without nodal metastasis by immunohistochemistry. By lenti-virus transduction, the role of FoxM1 in metastasis was also tested by in vitro methods using different NSCLC cell lines. Results: In this study, the FoxM1 expression was found to be significantly associated with nodal metastasis and the cumulative 5-year survival rate. Thus, an increased expression of FoxM1 is the indicator of shortened survival and high risk of metastasis of NSCLC patients. Furthermore, we also found that increased FoxM1 expression could enhance the migratory and invasive abilities of lung cancer cells, while inhibition of FoxM1 expression could reduce the migratory and invasive properties of lung cancer cells, which are the two important parameters of metastasis biology. In addition, cells with high FoxM1 expression were presented with phenotypic changes reminiscent of EMT, which was further proved by the results of immunoblotting with down-regulation of E-cadherin and ZO-1 while up-regulation of N-cadherin and Vimentin. Conclusion: These results suggested that FoxM1 plays an important role in lung cancer metastasis and elevated FoxM1 expression could be used as an indicator of poor prognosis and high risk of metastasis of NSCLC patients.