FBXW7调控非小细胞肺癌上皮间质转化的作用机制

《现代肿瘤医学》[ISSN:1672-4992/CN:61-1415/R] 期数: 2019年16期 **页码:** 2839-2843 **栏目:** 论著（基础研究） **出版日期:** 2019-07-08

Title: **Mechanism of FBXW7 regulating epithelial-mesenchymal transformation in non-small cell lung cancer**

作者: 杜 宁[1]; 王培礼[2]; 王 猛[1]; 任 宏[1]; 刘大鹏[1]
1.西安交通大学第一附属医院胸外科，陕西 西安 710061;2.河南省肿瘤医院乳腺外科，河南 郑州 450003

Author(s): Du Ning[1]; Wang Peili[2]; Wang Meng[1]; Ren Hong[1]; Liu Dapeng[1]
1.Department of Thoracic Surgery,The First Affiliated Hospital of Xi'an Jiaotong University,Shaanxi Xi'an 710061,China;2.Department of Breast Surgery，Henan Tumor Hospital,Henan Zhengzhou 450003,China.

关键词: 非小细胞肺癌; FBXW7; 上皮间质转化; Snail1

Keywords: NSCLC; FBXW7; EMT; Snail1

分类号: R734.2

DOI: 10.3969/j.issn.1672-4992.2019.16.009

文献标识码: A

摘要: 目的：研究FBXW7在非小细胞肺癌上皮间质转化(epithelial-mesenchymal transformation,EMT)过程中发挥的作用。方法：收集100对非小细胞肺癌组织和对应的癌旁组织，利用免疫组化检测FBXW7在癌组织和癌旁组织中的表达。利用Western blot检测FBXW7在细胞系中的表达及FBXW7对EMT部分标志蛋白的影响。利用Transwell实验检测FBXW7对NSCLC细胞迁移能力的影响。免疫共沉淀实验和泛素化的Western blot验证FBXW7与Snail1的关系。结果：FBXW7在NSCLC组织中的表达明显低于对应癌旁组织中的表达。FBXW7在正常肺上皮细胞中的表达也明显高于4种非小细胞肺癌细胞系中的表达。FBXW7过表达显著抑制A549细胞的迁移能力。FBXW7过表达也明显抑制NSCLC细胞的EMT。机制研究发现，FBXW7可以直接结合并泛素化降解Snail1蛋白，并且Snail1部分逆转FBXW7对NSCLC细胞EMT标志蛋白的影响。结论：FBXW7对NSCLC细胞EMT的调控部分依赖于泛素化降解Snail1蛋白。

Abstract: Objective:To study the role of FBXW7 in epithelial-mesenchymal transformation of non-small cell lung cancer (NSCLC).Methods:Total of 100 pairs of non-small cell lung cancer tissues and corresponding para-cancerous tissues were collected.The expression of FBXW7 in cancer tissues and para-cancerous tissues was detected by immunohistochemistry.The expression of FBXW7 in cell lines and the effect of FBXW7 on some marker proteins of EMT were detected by Western blot.Transwell assay was used to detect the effect of FBXW7 on the migration of NSCLC cells.Verification of the relationship between FBXW7 and Snail1 by immunoprecipitation test and ubiquitin Western blot.Results:The expression of FBXW7 in NSCLC tissues was significantly lower than that in corresponding para-cancerous tissues.The expression of FBXW7 in normal lung epithelial cells was also significantly higher than that in four non-small cell lung cancer cell lines.Overexpression of FBXW7 significantly inhibited the migration ability and EMT in A549 cells.FBXW7 could directly bind to and ubiquitin degrade Snail1 protein,and snail1 partially reversed the effect of FBXW7 on EMT marker protein in NSCLC cells.Conclusion:The regulation of EMT by FBXW7 in NSCLC cells depends partly on ubiquitin degradation of Snail1 protein.

参考文献/REFERENCES

[1] Siegel RL,Miller KD,Jemal A.Cancer statistics,2015 [J] .Ca A Cancer J for Clinicians,2015,65(1):5-29.
[2] Xu C,Xiao G,Zhang B,et al.CCAT1 stimulation of the symmetric division of NSCLC stem cells through activation of the Wnt signalling cascade [J] .Gene Therapy,2018,25(1):4-12.
[3] Davis R,Welcker M,Clurman B.Tumor suppression by the Fbw7 ubiquitin ligase:mechanisms and opportunities [J] .Cancer Cell,2014,26(4):455-464.
[4] Wang Z,Inuzuka H,Zhong J,et al.Tumor suppressor functions of FBW7 in cancer development and progression [J] .Febs Lett,2012,586(10):1409-1418.
[5] Xiao G,Gao X,Sun X,et al.miR-367 promotes tumor growth by inhibiting FBXW7 in NSCLC [J] .Oncol Rep,2017,38(2):1190.
[6] Díaz VM,de Herreros AG.F-box proteins:Keeping the epithelial-to-mesenchymal transition (EMT) in

check［J］.Semin Cancer Biol,2016(36):71-79.
［7］ Yang H,Lu X,Liu Z,et al.FBXW7 suppresses epithelial-mesenchymal transition,stemness and metastatic potential of cholangiocarcinoma cells［J］.Oncotarget,2015,6(8):6310.
［8］ Li H,Wang Z,Zhang W,et al.Fbxw7 regulates tumor apoptosis,growth arrest and the epithelial-to-mesenchymal transition in part through the RhoA signaling pathway in gastric cancer［J］.Cancer Lett,2016,370(1):39-55.
［9］ Sun X,Jiao X,Pestell TG,et al.MicroRNAs and cancer stem cells:the sword and the shield［J］.Oncogene,2014,33(42):4967-4977.
［10］ Vinas-Castells R,Beltran M,Valls G,et al.The Hypoxia-controlled FBXL14 ubiquitin ligase targets SNAIL1 for proteasome degradation［J］.J Biol Chem,2010,285(6):3794-3805.
［11］ Sun X,Xiao G,Zhang B,et al.miR-367 stimulates Wnt cascade activation through degrading FBXW7 in NSCLC stem cells［J］.Cell Cycle,2017，16(24):2374-2385.
［12］ Yokobori T,Yokoyama Y,Mogi A,et al.FBXW7 mediates chemotherapeutic sensitivity and prognosis in NSCLCs［J］.Mol Cancer Res,2014,12(1):32-37.
［13］ Flügel D,G□rlach A,Kietzmann T.GSK-3β regulates cell growth,migration,and angiogenesis via Fbw7 and USP28-dependent degradation of HIF-1α［J］.Blood,2012,119(5):1292-1301.
［14］ Wang M,Li Y,Xiao GD,et al.H19 regulation of oestrogen induction of symmetric division is achieved by antagonizing Let-7c in breast cancer stem-like cells［J］.Cell Proliferation,2019,52(1):e12534.
［15］ Horvay K,Casagranda F,Gany A,et al.Wnt signaling regulates Snai1 expression and cellular localization in the mouse intestinal epithelial stem cell niche［J］.Stem Cells and Development,2010,20(4):737-745.

备注/Memo: National Natural Science Foundation of China(No.81602597);国家自然科学基金面上项目（青年）(编号：81602597)

更新日期/Last Update: 1900-01-01