癌变.畸变.突变 ISSN: 1004-616x CN:44-1063/R 2009; 21(2) :119-122

论著

p53基因249编码子突变对p53功能的影响

吴智群,李庆霞,李 臻,于翠娟,罗亚宁,胡 静,王 红

第四军医大学唐都医院介入科,陕西 西安 710038

收稿日期 2008-9-9 修回日期 2008-11-14 网络版发布日期:

摘要 背景与目的： 研究p53基因249编码子突变对p53基因功能的影响。 材料与方法： 利用基因打靶技术在小鼠胚胎干细胞(ES)p53基因249编码子中引入点突变，使编码子249由精氨酸(Arg)变成丝氨酸(Ser)，然后将含突变的ES细胞显微注射到Hprt-/-小鼠囊胚中，将注射过的囊胚植入假孕的雌性小鼠子宫，到第14 d取小鼠胚胎纤维母细胞(EF)，用含HAT的培养液筛选出从ES细胞分化而成的鼠EF细胞，经测序证实细胞含有由249 Arg到Ser的突变。用不同剂量的电离辐射(IR)或紫外光(UV)分别照射ES或EF细胞，然后利用流式细胞仪检测该突变对小鼠ES细胞周期及对ES和EF细胞凋亡的影响，并利用Western blot检测相关蛋白的表达。 结果： 用IR处理ES细胞后，含p53基因249编码子突变的ES细胞对IR诱导的G1/G0细胞周期阻滞作用减弱 (P<0.05)。用IR或UV处理ES和EF细胞后，含p53基因249编码子突变的ES及EF细胞凋亡百分数较含野生型p53者明显减少(P<0.05)。含p53基因249编码子突变的ES及EF细胞p53的表达与含野生型p53 者差别不明显(P>0.05)；但其bax和p21的表达，较含野生型p53 的细胞表达减少(P<0.05)。 结论： p53基因249编码子突变可减弱p53在细胞周期阻滞和凋亡中的作用，但对p53的表达无明显影响。

关键词 肝癌； 发病机制； p53基因； 突变

Effect on the Function of 249 Arg to Ser Mutation in the p53 Gene

WU Zhi-qun, LI Qing-xia, LI Zhen, YU Cui-juan, LUO Ya-ning,HU Jing, WANG Hong

Department of Interventional Radiology, Tangdu Hospital, The Fourth Military Medical University, Xi'an 710038,Shaanxi, China

Abstract BACKGROUND AND AIM: To explore the effect on the function of 249 Arg to Ser mutation in the p53 gene in mice. MATERIALS AND METHODS: Arg to Ser mutation was introduced into the 249 position of the p53 gene by knock-in method. These ES cells with this mutation were selected according to the homologues-recombination with PCR and Southern blot. The positive ES cells without a selection marker were injected into blastocysts recovered from Hprt-/- mice, which were derived from Hprt-deficient ES cells. The injected blastocysts then were implanted into pseudopregnant females. At embryonic day 14, MEFs were recovered from the embryos and cultured under the selection of HAT (0.016 mg of hypoxanthine/ml, 0.01 mmol/L aminopterin, 0.0048 mg of thymidine thymidine/ml)， and the cell cycle, apoptosis, and the relative protein expressions were analyzed by flow cytometry and Western blot. RESULTS: The ES cells with 249 Arg to Ser mutation were more resistant to the IR-induced cell cycle arrest compared to the wild type ES cell(P<0.05).The ES and EF cell with 249 Arg to Ser mutation were more resistant to the IR- or UV-induced apoptosis compared to the wild type ES and EF cell(P<0.05). The mutation did not affect the expression of p53 after IR or UV, but decrease the expression bax and p21 after IR or UV. CONCLUSION: The p53 249 Arg to Ser mutation could disable the function of p53, but did not change the expression of p53.

Keywords hepatoma carcinogenesis p53 gene mutation

DOI

扩展功能

本文信息

Supporting info

[PDF全文](2716k)

[HTML全文](94k)

参考文献

服务与反馈

把本文推荐给朋友

加入我的书架

Email Alert

相关信息

本刊中 包含“肝癌； 发病机制； p53基因； 突变”的 相关文章

本文作者相关文章

- 吴智群
- 李庆霞
- 李臻
- 于翠娟
- 罗亚宁
- 胡静
- 王红

通讯作者 tdjrfsk@fmmu.edu.cn