

miR-148a-3p、miR-128、miR-588在乳腺癌中的表达情况及其与耐药性的关系

《现代肿瘤医学》[ISSN:1672-4992/CN:61-1415/R] 期数: 2019年12期 页码: 2108-2113 栏目: 论著 (胸部肿瘤) 出版日期: 2019-05-08

Title: The differential expression of miR-148a-3p,miR-128,miR-588 and their association with chemo-resistance in breast cancer

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关键词: microRNA; 耐药; 差异性表达; 肿瘤标志物; microRNA芯片; 生物信息

Keywords: microRNAs; chemo-resistance; differential expression; tumor biomarker; microRNA chips; bioinformatics

分类号: R737.9

DOI: 10.3969/j.issn.1672-4992.2019.12.018

文献标识码: A

摘要: 目的:了解microRNA在乳腺癌中的表达情况,以及其对肿瘤化疗药物耐药性的影响。方法:获取GEOGSE71142的microRNA表达数据,通过edgeR和热图寻找乳腺癌耐药和药物敏感两组中差异性表达的microRNA。收集我院2012年至2015年100例病理诊断为乳腺癌的患者的癌及癌旁组织。使用qRT-PCR检测microRNA在癌和癌旁中的表达情况以及在MCF-7中的表达情况;应用配对t检验分析microRNA和T、N、M分期之间的关系。使用倾向值匹配模型(PSM),将患者分为耐药组和非耐药组,使用qRT-PCR检测microRNA的表达情况。使用Logistic回归模型进行多因素分析。按照microRNA的表达情况,进行亚组分析。结果:使用edgeR对GSE71142进行差异性表达分析,共筛选出了1432个差异性表达的microRNA。应用qRT-PCR,配对样本t检验发现miR-148a-3p ($P < 0.05$)、miR-128 ($P < 0.05$)、miR-466 ($P < 0.05$)、miR-31-5p ($P < 0.05$)、miR-588 ($P < 0.05$)在癌和癌旁中差异性表达。卡方检验提示T分期、N分期、Her-2表达以及Cyclin-D1的表达情况与紫杉醇(PTX)耐药性有关($P < 0.05$)。PSM匹配后,在PTX耐药及PTX敏感中,qRT-PCR发现miR-148a-3p、miR-128、miR-588呈差异性表达($P < 0.05$)。ROC曲线提示miR-148a-3p (AUC: 0.864, 95%CI:0.737-0.991, $P < 0.05$)、miR-128 (AUC: 0.859, 95%CI: 0.733-0.986, $P < 0.05$)和miR-588 (AUC: 0.777, 95%CI: 0.623-0.930, $P < 0.05$)。Logistic回归提示miR-148a-3p (OR=18.36, $P < 0.05$)和miR-128是PTX耐药的保护因素(OR=5.26, $P < 0.05$);而miR-588是PTX耐药的危险因素(OR=0.35, $P < 0.05$)。miR-148a-3p的亚组分析提示其高表达和低表达均与Cyclin-D1的表达有关。结论:miR-148a-3p、miR-128、miR-466、miR-31-5p、miR-588有成为乳腺癌肿瘤标志物的可能;miR-148a-3p、miR-128、miR-588与乳腺癌的PTX耐药性有关;miR-148a-3p、miR-128可以用于判断患者的PTX耐药情况。miR-148a-3p可能通过Cyclin-D1调控PTX耐药性,但需要进一步的分子学机制研究证实。

Abstract: Objective:To understand the expression profile of microRNAs in breast cancer and their roles in the chemo-resistance.Methods:Download microRNA expression data from GEOGSE71142.Perform differential expression analysis through edgeR and plot heatmap by heatmap2.Recruit 132 histologically diagnosed breast cancer patients from 2012 to 2015 in our hospital.Evaluate the expression of microRNAs in MCF-7 cell line and breast cancer patients by qRT-PCR, and understand their expression's relationships with T,N and M stage.Evaluate the expression of microRNAs in chemo-sensitive and chemo-resistant patients.Results:1432 differentially expressed microRNAs were detected in total.We have selected 5 microRNAs based on breast cancer tissue expression level,which were miR-148a-3p,miR-128,miR-466,miR-31-5p and miR-588.And their expression was correlated to T,N and M stage.In addition,miR-148a-3p,miR-128 and miR-588 were found relevant with chemo-resistance.Conclusion:miR-148a-3p,miR-128,miR-466,miR-31-5p and miR-588 have the potential to be

biomarkers. And miR-148a-3p, miR-128 and miR-588 are associated with chemo-resistance in breast cancer. Further molecular mechanisms are needed.

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备注/Memo: National Natural Science Foundation of China(No.81702430);国家自然科学基金青年科学基金项目(编号:81702430)

更新日期/Last Update: 1900-01-01