PD-1及PD-L1在三阴性乳腺癌中差异性表达及与临床病理特征关系的研究

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Title: **Differential expression of PD-1 and PD-L1 in triple negative breast carcinoma and its correlation with clinicopathology**

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摘要: 目的：探讨PD-1及PD-L1在三阴性乳腺癌（triple negative breast carcinoma，TNBC）中的表达情况。方法:收集158例TNBC组织标本，应用免疫组化方法进行PD-1及PD-L1的染色，观察其在TNBC中的表达情况，分析PD-1及PD-L1的表达与各项临床病理因素的关系。结果:PD-L1在TNBC肿瘤细胞及间质淋巴细胞中的表达率分别为53.2%和74.7%，PD-1在间质淋巴细胞中的表达率为64.6%；PD-L1与PD-1的表达有相关性（P＜0.05）；PD-L1及PD-1的表达与TNBC的肿瘤体积大、高组织学级别、基底样型BC（basal like breast carcinoma，BLBC）、Ki67增殖指数高及肿瘤浸润淋巴细胞（tumor infiltrating lymphocyte，TIL）高百分比相关（P＜0.05），多因素回归分析提示肿瘤的大小、BLBC、Ki67高增殖指数及TIL高百分比是PD-L1和PD-1表达的危险因素；PD-L1及PD-1在伴髓样特征的癌、伴大汗腺特征的癌及化生性癌中高表达，在浸润性小叶癌、腺样囊性癌及腺泡细胞癌中不表达。结论:PD-L1及PD-1在TNBC中高表达，可以作为TNBC免疫治疗的靶标及预后标记物；肿瘤体积大、BLBC、Ki67增殖指数高及高TIL是PD-L1及PD-1表达的危险因素；PD-L1及PD-1表达在TNBC中存在组织学异质性。

Abstract: Objective:To investigate the expression of PD-L1 and PD-1 in triple negative breast carcinoma (TNBC).Methods:158 TNBC tissue specimens were collected.Immunohistochemical staining was used for PD-1 and PD-L1 staining to observe the expression of PD-1 and PD-L1 in TNBC,and to analyze the relationship between the expression of PD-1,PD-L1 and various clinicopathological factors.Results:The expression rates of PD-L1 in TNBC tumor cells and interstitial lymphocytes were 53.2% and 74.7%,respectively.The expression rate of PD-1 in interstitial lymphocytes was 64.6%.there was a correlation between the expression of PD-L1 and PD-1(P＜0.05).The expressions of PD-L1 and PD-1 were correlated with larger tumor size,high histological grade,basal like breast carcinoma (BLBC),high proliferation index of Ki67 and high percentage of tumor infiltrating lymphocyte (TIL) in TNBC（P＜0.05）.Multivariate regression analysis suggested that tumor size,BLBC subtype,high proliferation index of Ki67 and high percentage of TIL were risk factors for the expression of PD-L1 and PD-1,PD-L1 and PD-1 was highly expressed in carcinoma with medullary features,carcinoma with apocrine differentiation and metaplastic carcinoma,but not in invasive lobular carcinoma,adenoid cystic carcinoma and acinar cell carcinoma.Conclusion:PD-L1 and PD-1 are highly expressed in TNBC,which can be used as targets and prognostic markers for TNBC immunotherapy.Larger tumor size,BLBC subtype,high proliferation index of Ki67 and high TIL are risk factors for PD-L1 and PD-1 expression.The expressions of PD-L1 and PD-1 are histologically heterogeneous in TNBC.

参考文献/REFERENCES

［1］Geyer FC,Pareja F,Weigelt B,et al.The spectrum of triple-negative breast disease:High-and low-grade lesions［J］.The American Journal of Pathology,2017,187(10):2139-2151.
［2］editorial Committee.Guidelines for Immunohistochemical detection of breast cancer estrogen and

progesterone receptors［J］.Chinese Journal of Pathology,2015,44(4):237-239.［《乳腺癌雌、孕激素受体免疫组织化学检测指南》编写组.乳腺癌雌、孕激素受体免疫组织化学检测指南［J］.中华病理学杂志,2015,44(4):237-239.］
［3］.Breast cancer HER2 (2014) test guide［J］.Chin J Pathol,2014,43(4):262-267.［《乳腺癌HER2（2014版）检测指南》编写组.乳腺癌HER2（2014版）检测指南［J］.中华病理学杂志,2014,43(4):262-267.］
［4］Lakhani SR,Ellis LO,Schnitt SJ,et al.WHO classification of tumours of the breast.4th edition［M］.Lyon:IARC,2012:10-11.
［5］Erik A Dill,Alejandro A Gru,Kristen A Atkins,et al.PD-L1 expression and intratumoral heterogeneity across breast cancer subtypes and stages an assessment of 245 primary and 40 metastatic tumors［J］.Am J Surg Pathol,2017(41):334-342.
［6］Salgado R,Denkert C,Demaria S,et al.The evaluation of tumor-infiltrating lymphocytes (TILs) in breast cancer:recommendations by an International TILs Working Group 2014［J］.Ann Oncology,2015,26(2):259-271.
［7］ZHANG Li,LIU Fangfang,FU Li.Significance and evaluation method of interstitial infiltrating lymphocytes in breast cancer［J］.Chin J Pathol,2016,45(4):282-284.［张丽,刘芳芳，付丽.肿瘤间质浸润淋巴细胞在乳腺癌中的意义及评价方法［J］.中华病理学杂志,2016,45(4):282-284.］
［8］Kwa MJ,Adams S.Checkpoint inhibitors in triple-negative breast cancer (TNBC):Where to go from here［J］.Cancer,2018,124(10):2086-2103.
［9］Karnik T,Kimler BF,Fan F,et al.PD-L1 in breast cancer:comparative analysis of 3 different antibodies［J］.Human Pathology,2018(72):28-34.
［10］Mittendorf EA,Philips AV,Meric-Bernstam F,et al.PD-L1 expression in triple-negative breast cancer［J］.Cancer Immunology Research,2014,2(4):361-370.
［11］Barrett MT,Lenkiewicz E,Malasi S,et al.The association of genomic lesions and PD-1/PD-L1 expression in resected triple-negative breast cancers［J］.Breast Cancer Research:BCR,2018,20(1):71.
［12］Zhou T,Xu D,Tang B,et al.Expression of programmed death ligand-1 and programmed death-1 in samples of invasive ductal carcinoma of the breast and its correlation with prognosis［J］.Anti-Cancer Drugs,2018,29(9):904-910.
［13］Aierken N,Shi HJ,Zhou Y,et al.High PD-L1 expression is closely associated with tumor-infiltrating lymphocytes and leads to good clinical outcomes in chinese triple negative breast cancer patients［J］.International Journal of Biological Sciences,2017,13(9):1172-1179.
［14］Ghebeh H,Mohammed S,Al-Omair A,et al.The B7-H1 (PD-L1) T lymphocyte-inhibitory molecule is expressed in breast cancer patients with infiltrating ductal carcinoma:correlation with important high-risk prognostic factors［J］.Neoplasia,2006,8(3):190-198.
［15］Ali HR,Glont SE,Blows FM,et al.PD-L1 protein expression in breast cancer is rare,enriched in basal-like tumours and associated with infiltrating lymphocytes［J］.Ann Oncology,2015,26(7):1488-1493.
［16］Li F,Ren Y,Wang Z.Programmed death 1 Ligand 1 expression in breast cancer and its association with patients' clinical parameters［J］.J Cncer Research and Therapeutics,2018,14(1):150-154.
［17］Thompson ED,Taube JM,Asch-Kendrick RJ,et al.PD-L1 expression and the immune microenvironment in primary invasive lobular carcinomas of the breast［J］.Modern Pathology,2017,30(11):1551-1560.
［18］Joneja U,Vranic S,Swensen J,et al.Comprehensive profiling of metaplastic breast carcinomas reveals frequent overexpression of programmed death-ligand 1［J］.Journal of Clinical Pathology,2017,70(3):255-259.
［19］Schutz F,Stefanovic S,Mayer L,et al.PD-1/PD-L1 pathway in breast cancer［J］.Oncology Research and Treatment,2017,40(5):294-297.

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