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The biological effects and mechanism of TLR4-NF-κB activation on colon cancer with different APC genotypes

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The role of TLRs in tumor growth is paradoxical. In colon cancer, APC/GSK-3β/β-catenin pathway cross regulates TLRs/NF-Kb pathway through β-catenin, and possibly associated with APC genotype. It is speculated that the connection between TLRs and APC/GSK-3b/ β-Catenin may relate with APC gene mutation. This study aims to investigate the mechanism of TLRs/ NF-κB pathway activation in different APC status in colon cancer. SiRNA transiently targeting APC was transfected into human HCT116 cell with wild APC, while ShRNA-APC was stably transfected into HCT116 and human normal colon cell line NCM460 with lentiviral packaging system. Cell lines with different APC status were stimulated with LPS (lipopolysaccharide, TLR4 agonist). SKID xenograft models of HCT116 and HCT116-ShAPC cells were established, followed by intra tumoral injection of LPS (5µg, 10 µg, 20µg). p-β-catenin, NF-κB, p-NF-κB and caspase-3 expression in tumor tissues were tested with Western blot and immunohistochemistry. Cells proliferation of HCT116-SiAPC and HCT116-ShAPC treated with LPS increased similar to HT29 and SW480 with APC mutation, while proliferation of HCT116 cells was inhibited. Activation of TLRs/NF-KB signaling pathway by LPS was different between wild and mutated APC cell lines. Our data indicated that changes of APC phenotype produced different biological behavior by regulating the levels of β- Catenin.

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Immunomarkers used as a differentiation antigen in metastasis from breast carcinoma

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Background and Objectives: Carcinoma of unknown primary origin is a diverse group of cancers that is defined by the presence of metastatic disease with no identified primary tumor at initial presentation. Positive estrogen and progesterone receptors are suggestive of breast cancer. However, negative ER/PR do not exclude the diagnosis of breast cancer, but other malignancies such as colon, ovary, endometrium, kidney, and melanoma may show detectable ER/PR positivity. Carcinoembryonic antigen, CA125, and ER assay are not specific. This study aims to evaluate and compare mammaglobin and NY-BR-1 staining in identification of metastatic breast carcinoma with well known history as well as their staining in primary breast carcinomas and their simultaneous nodal metastasis.

Materials and Methods: Immunostaining of mammaglobin and NY-BR-1 were done for archival cases of 24 primary breast carcinomas and their simultaneous axillary nodal metastasis, 4 axillary nodal metastasis of occult carcinomas, 6 supraclavicular nodal metastasis, 14 cell blocks of positive pleural effusions and 8 tru cut biopsies of post mastectomy chest wall masses all with past history of breast carcinoma.

Results: NY-BR-1 showed more positivity rate in both primary and metastatic breast carcinomas than mammaglobin. There was no significant difference between NY-BR-1 and mammaglobin expression in primary breast carcinomas while there was a significant difference between both in metastatic breast carcinomas.

Conclusion: NY-BR-1 and mammaglobin can help in identification of mammary origin of metastatic carcinoma however NY-BR-1 is easier to use and interpret in suspected metastatic breast carcinomas.

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