

Diverse role of homeostatic mucosa-associated chemokines in breast cancer

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BACKGROUND: Homeostatic mucosa-associated chemokines (HMAC) consist of CCL28 (MEC), CXCL14 (BRAK), CXCL17 (VCC-1) and so on, that exhibits antibacterial activity against a panel of pathogenic and opportunistic bacteria in gastrointestinal and respiratory tract. They not only take part in mucosal immunity, but also mediate direct killing of invading pathogens.

HYPOTHESIS: HMAC may be also involved in innate immunity and sterility of human mammary gland, which open via multiple lactiferous ducts in nipple and is apt to be infected. This study is aimed to disclose the role and possible mechanism of HMAC in breast cancer.

METHODS: Gene expression and protein level of CCL28, CXCL14 and CXCL17 were detected by RT-PCR and Western blot in normal breast epithelial cell lines and breast cancer cell lines. Their effects on the proliferation, invasion, tumor growth and metastasis were tested using specific overexpressing cell lines and orthotopic xenograft model in SCID or BALB/c nude mice. Furthermore, we detected their protein level in breast cancer patients by immunohistochemistry and discussed the correlation between HMAC and the prognosis of breast cancer.

RESULTS: Our preliminary results show that CCL28 is higher, but CXCL14 is lower in breast cancer cell lines with high pulmonary metastatic potential. Both of breast cancer cell line MCF-7 and MDA-MB-231 express CXCL17 and its receptor CXCR8. rhCXCL17 can suppress migration of breast cancer cell lines *in vitro* due to epithelial-mesenchymal transition (EMT) inhibition. CCL28 can promote proliferation and inhibit apoptosis of breast cancer cell lines, accompanying with up-regulation of bcl-2 and activation of MAPK signaling pathway. Overexpression of CXCL14 inhibited cell proliferation and invasion *in vitro* and attenuated xenograft tumor growth and lung metastasis *in vivo*. CXCL14 is positively correlated to the overall survival of breast cancer patients, and it has a negative correlation with the lymph node metastasis.

CONCLUSION: We conclude that homeostatic mucosa-associated chemokines play an important role in the pathogenesis of breast cancer partly by influencing cellular biological behavior and host microenvironment, although their role is pretty diverse and complex. Needless to say, the precise function of HMAC, the relationship among pathogens, immune cells and HMAC should be clarified in the future.