

Therapeutic effects upon tumor microenvironment in breast cancer: The changes of neoangiogenesis and tumor infiltrating lymphocytes subtypes before and after the neoadjuvant therapy of endocrine therapy and neoadjuvant chemotherapy in breast cancer patients - A Comparative study

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# 学 位 論 文 要 約

博士論文題目 Therapeutic effects upon tumor microenvironment in breast cancer: The changes of neoangiogenesis and tumor infiltrating lymphocytes subtypes before and after the neoadjuvant therapy of endocrine therapy and neoadjuvant chemotherapy in breast cancer patients - A Comparative study (術前治療による乳癌局所微小環境への治療検討:化学療法と内分泌療法による血管新生と腫瘍内浸潤リンパ球サブタイプに対するの影響)

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Carcinoma cells, including breast cancer, develop in a complex and dynamic microenvironment where the tumor cells are embedded in a supporting framework composed of tissue specific types of extracellular matrix (ECM), different cellular components including fibroblasts, lymphatics, vasculatures including endothelial cells, inflammatory cells and others and various kinds of cytokines. Tumor-stroma reciprocal cellular pathways, interactions and crosstalks play indispensable roles in tumorigenesis, development, disease progression, subsequent invasion and metastasis, and also in determining the therapeutic response. This tumor stroma micro-milieu hence is generally considered an imperative and integrated part of the solid cancer development and progression.

Neoangiogenesis and tumor infiltrative lymphocytes (TIL) are two important stromal components as stated above. It is therefore important to evaluate the effects of different therapeutic agents upon the tumor stroma, which could provide new insights into how breast carcinoma responds or why the state of clinical resistance to a particular treatment developed in the treated patients with breast cancer. Therefore, in this study, I assessed the effects of different therapeutic agents upon the tumor micro-milieu, with particular emphases on the tumor neoangiogenesis and infiltrative lymphocytes. The differences in the changes of neoangiogenesis and TIL subtypes in response to neoadjuvant AI and chemotherapy as reported in my present studies did firstly demonstrate that not only the tumor cells but also other cells in the tumor stroma microenvironment (neoangiogenesis and TIL in this respect) responded differently to the therapeutic agents as reflected by the change in mitotic index in the AI group and the histopathological changes of cytotoxic effects in the chemotherapy group.

Considering the complex reciprocal interactions and cross-talks among different cellular pathways of carcinoma cells and their microenvironment, these results here in my study clearly indicated that not only features of carcinoma cells but also those of adjacent stromal cells in the tumor microenvironment should be incorporated when assessing the response to any therapeutic agent given. The importance of considering the carcinoma cells and tumor microenvironment as a whole in the treatment of breast cancer was clearly confirmed in my present study.