Characterization of the pre-metastatic niche in lymph node, in experimental and clinical settings

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BACKGROUND AND OBJECTIVES

Clinical issue: Lymph node status (N+/N−) is a strong prognostic factor of patient’s cancer specific survival which is widely used to guide therapeutic decisions. A pelvic and/or para-aortic lymph node dissection remains mandatory in order to confirm the histological nodal status. However, this surgical staging is associated to therapeutic morbidity (lymphoedema). The latter risk is particularly marked when an adjuvant radiation therapy is administered after the surgery to patients diagnosed N+. A specific dialogue between the primary tumor and the lymph node leads to the formation of a supportive microenvironment for metastasis, the pre-metastatic niche. A better understanding of pre-metastatic modulations that occur in the sentinel lymph node (SLN), the first tumor draining lymph node, is needed. A digital image analysis methodology assisted by computer was used to determine objectively whole slide densities and spatial distributions of immunostained structures (D2/40+ lymphatic vessels, CD8, Foxp3, CD20 and PD1).

Current view: We aim at getting new insights into the lymphatic vessel dynamics and immune microenvironment in the sentinel lymph node (SLN) on human early cervical cancers (FIGO stage IB1, n=50). We also set up an in vivo model reproducing the pre-metastatic lymphangiogenic niche in lymph node.

Objectives: We will highlight the presence of a pre-metastatic lymphangiogenic network that may facilitate the transport of tumor cells from the primary tumor to the SLN. In addition to the presence of a regulatory and cytotoxic lymphocyte rich microenvironment in the paraarterial space of the SLN, our data indicate a modulation of humoral immunity (B lymphocytes) in the superficial cortex, which is associated to a subcapsular lymphangiogenic network. All together, our data bring out that, in addition to provide a physical route for tumor cell dissemination, lymphatic vascular network could play a role in the modulation of the humoral pro/anti-tumoral immune response in the SLN prior metastasis.

CONCLUSIONS

A. CLINICAL RESULTS

Pre-metastatic lymphangiogenesis

B. PRE-ClinICAL RESULTS

Pre-metastatic immune modulations

Figure 1: Characterization of pre-metastatic lymphangiogenesis.

Figure 2: Characterization of pre-metastatic immune modulations.