Immunoglobulin Variable Region Gene Cloning and Sequencing of Tumor-infiltrating Plasma Cells: Evidence of Germ Cell Expansion in Invasive Ductal Breast Carcinoma

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ABSTRACT

Breast cancer is the most common invasive cancer in women in the United States. About 80% of all the breast cancers are Invasive Ductal Carcinomas (IDC). Breast cancers often show detectable lymphocytic infiltrates, and only about one-fourth of them contain moderate to heavy infiltration of B cells and plasma cells. B cells are the effector cells of humoral immunity and can terminally differentiate into antibody secreting plasma cells. In the present study, we have analyzed the immunoglobulin variable genes of tumor-infiltrating plasma cells from 2 IDC patients. This was done to determine the clonal character of the plasma cells and their possible role in the tumor immunity. Fresh malignant breast tumors were obtained following surgery, and their frozen sections were screened for the lymphocytic infiltration. The tumor samples from 2 patients which showed good plasma cell-infiltration were used for this study. Both malignant breast tumors, A55 (estrogen receptor-positive 80%; progesterone receptor-positive >90%) and A91 (estrogen receptor-positive 70%; progesterone receptor positive 90%), were categorized as invasive ductal carcinomas. Using a laser capture microdissection technique, clusters of plasma cells in the tumors were collected. The plasma cells were processed for human immunoglobulin variable gene analysis using appropriate RT-PCR primer sets. The analyses of variable regions (V_{Heavy} and V_{Light}) of immunoglobulin genes show a *very limited* number of plasma cell clones in both the tumors. These results indicate their origin from a possible B-cell germ center within the tumor. These plasma cells may be secreting antibodies relevant to the tumor-specific antigens, we plan to clone these VH and VL genes and produce antibodies *in-vitro;* to examine their binding to the tumor from which they were derived. This work can be extended to the production of patient-specific antibodies, and may be the future of personalized breast cancer therapy.