The role of lymph node germinal centers and the B cell response in triple-negative breast cancer

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Lymph nodes play a pivotal role in triple-negative breast cancer (TNBC) as both the first site of metastasis and the potential orchestrator of antitumor immune responses, including the germinal center (GC) response; the site of memory B cells and plasma cell maturation. At the primary tumor, increased B cell density demonstrates prognostic and predictive value, however the source of tumor-infiltrating B cells (TIL-B) and their functional role is yet to be fully explored. We were the first to show that in low tumor-infiltrating lymphocytes (TILs) TNBC patients, more and smaller GCs in cancer-free (CF) LNs are associated with longer distant metastasis-free survival (DMFS). TNBC patients with high TILs at their primary tumor present with more lymph node GCs, suggesting crosstalk between the LN and tumor that warrants further investigation. Here, the tumor draining lymph nodes (td-LNs), non-tumor draining lymph nodes (ntd-LNs) and tumor immune cell infiltration during cancer evolution and progression were studied in four orthotopic mouse models of TNBC. On day 7, all models presented significantly more GC B cells in td-LNs than in ntd-LNs. The most aggressive model exhibited a steady decline in td-LN GC B cells until day 21, whereas the least aggressive model maintained high GC B cell levels up to day 28 post-inoculation. Only the fastest growing tumor model displayed class-switched plasma cell production despite consistent evidence of GC formation across all models. Finally, the level of TIL-B infiltration fluctuated between models, with the model sustaining GC B cells the longest demonstrating the highest TIL-B density. This is the first study to link tumor formation and TIL infiltration with GC B cells and highlights the need further to study the role of B cell antitumor immunity.