Characterizing B-Lymphocyte Response to Neoantigen Exposure in Early-Stage Pancreatic Cancer

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Even in its earliest stages, pancreatic ductal adenocarcinoma (PDAC) remains a highly lethal disease, with a five-year survival rate of < 10%. This is especially puzzling, given the known presence of neoantigens that should be acted upon by the host adaptive immune response. These epitopes are not recognized as “self” by the thymus, and are thus vulnerable to immune surveillance and attack. During the course of pancreatic cancer progression, immune surveillance is altered, even though the specific components responsible for altering anti-tumor immune responses have not yet been identified. Using a genetically engineered mouse model of PDAC that recapitulates human PDAC progression and secretes chicken ovalbumin (OVA), a moderately immunogenic epitope that models neoantigenicity, we investigated changes in the immune infiltrate in response to neoantigen exposure in early-stage pancreatic cancer. This was done using immunofluorescent staining and immune cell quantitation via HALO software. B cell infiltration was correlated to both tissue transformation and tumor grade to examine the relationship between antigen exposure and PDAC pathogenesis. Additionally, the induction of inflammatory response was examined by comparing B cell quantitation to granulocyte count. Our investigation revealed that infiltration of B220+ B lymphocytes increased in early stage tumors expressing OVA and corresponded with disease stage, progression, and inflammation, demonstrating an early host adaptive immune response against neoantigen in pancreatic lesions. Future studies will explore these parameters in later stage disease tissue to observe changes in the immune infiltrate and whether or not adaptive immune activation declines over time. These findings may further support why advances in immunotherapy have yet to yield results in treating patients with pancreatic cancer.