753 THE IMMUNE LANDSCAPE OF PAPILLARY THYROID CANCER AND ITS ASSOCIATION WITH NEOANTIGEN LANDSCAPE AND DNA REPAIR GENE MUTATIONS

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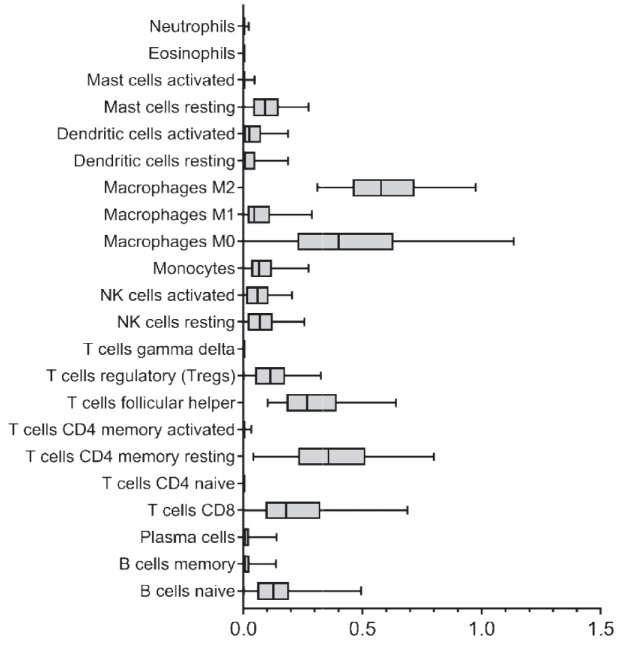
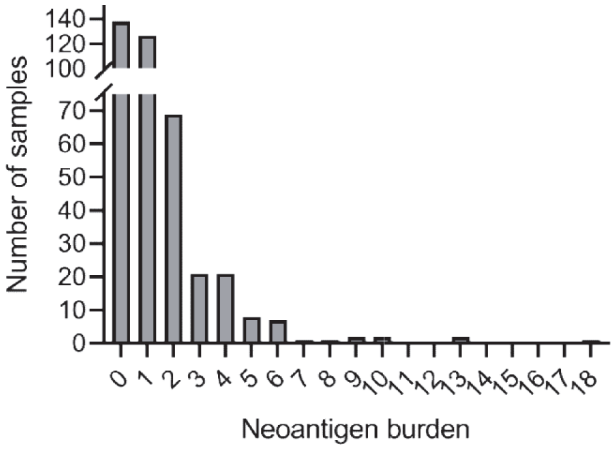
Background Tumors with high tumor mutational burden (TMB) or defects in mismatch repair (dMMR) respond well to immune checkpoint inhibitors (ICIs).[1 2] TMB and DNA repair gene mutations including dMMR are closely related to the increase of neoantigens, which are recognized by immune cells to trigger an immune response.[1 3] Although not a standard of care in thyroid cancer treatment, there are ongoing clinical trials for ICI use in differentiated thyroid carcinoma. However, not much has been explored concerning the neoantigen landscape and its association with immune traits in papillary thyroid cancer (PTC). We aim to analyze the immune landscape of PTC in association with neoantigen burden, TMB, and DNA repair gene mutations.

Methods We used the PTC cohort data from The Cancer Genome Atlas (TCGA). The mutation counts and data for neoantigen prediction were acquired from TCGA mutation calling. CloudNeo pipeline was used for neoantigen prediction. TMB was calculated as the sum of missense and indel mutation counts per megabase pairs covered by whole-exome sequencing. Tumor-infiltrating immune cells were estimated using CIBERSORT.

Results Out of the 496 PTC patients from cBioPortal, a subset of 400 patients with available mutation counts and predicted neoantigen burden was included in the study. Immune cell infiltration estimated by CIBERSORT showed macrophage M2 as the most abundant, followed by macrophage M0 and other T cells (figure 1). The TMB ranged from 0.03 to 2.05 with a median value of 0.2. Neoantigen burden ranged from 0 to 18 with a median value of 1, which is relatively low compared to the median value of 18 in non-small cell lung cancer (NSCLC)[1] (figure 2). One or more DNA repair gene mutations were discovered in 32 patients (8%). The mutation status of repair genes was not related to TMB or neoantigen burden. TMB or neoantigen burden was not related to immune traits such as infiltration of CD8+ T cells or regulatory T cells, cytolytic activity score, and PD-L1 expression.



Abstract 753 Figure 1 Immune cell infiltration estimated by CIBERSORT



Abstract 753 Figure 2 Histogram of neoantigen burden

Conclusions This is the first study to report the immune landscape of PTC in the context of neoantigen. The lack of association between TMB or neoantigen burden with immune traits may be due to the relatively low number of neoantigens in PTC compared to other immunogenic cancers such as NSCLC. Our results suggest that mutations in DNA repair genes or TMB are likely to have limited value in predicting response to ICI treatment in PTC.

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754 DYSREGULATION OF SOLUBLE IMMUNE CHECKPOINT PROTEINS IN NEWLY – DIAGNOSED EARLY BREAST CANCER PATIENTS

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Background Checkpoint proteins regulate the immune system. Breast cancer (BC) cells exploit the up-regulation or down-regulation of these proteins to evade anti-tumor immune responses. Soluble forms of immune checkpoint molecules (ICM) can be measured in human plasma. However, their biological and clinical significance remains mostly unknown. The aim of the present analysis was to measure the levels of pre-