Abstract # 579

Comprehensive profiling of immune landscape in gastrointestinal (GI) and head and neck (HN) cancers via computational deconvolution

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BACKGROUND

Immune context has been shown to play a dynamic role in response or resistance to immunotherapy. Understanding the composition of local immune microenvironment may provide useful insights for immunotherapy personalization. Conventional methods for characterizing the immune context, such as imaging techniques and flow cytometry, are limited by throughput. Computational immune deconvolution using transcriptomic data offers an efficient alternative. The immune profiles of other human gastrointestinal (GI) and head & neck (HN) cancers than colorectal cancer (CRC) have not been clearly defined by computational approaches. We propose that dissecting the immune compositions in those cancers would reveal biologic insights and potentially therapeutic targets.

METHODS

- 464 GI tumors with RNAseq data (~200x10⁶ reads per tumor) and 48 normal GI tissues from a commercial database were available for analysis.
- Tumors were categorized into colorectal (CRC), gastrointestinal (GI), head and neck (HN), and biliary (other) cancers.
- Tumor mutational burden (TMB) was directly observed from RNAseq as counts of non-synonymous somatic mutations.
- A curated panel of 122 genes that discriminate between 20 immune subpanels signatures was identified. For each of these signatures, a database containing 467 unselected tumors was used to define a distribution of expression. The study samples were then scored for their deviations within such distributions.
- Each of the 464 tumors were assigned to one of the colorectal, gastrointestinal, biliary, or normal immune subtypes (CMS).
- Significant enrichment for immune subsets between locations and CMS was analyzed.

RESULTS

- Figure 1: NantOmics dataset of the 464 GI tumors was used to define a distribution of expression. The study samples were then scored for their deviations within such distributions.
- Figure 2: CRC samples are associated with regulation lower immune activity.
- Figure 3: CMS are associated with enrichment higher immune activity.

CONCLUSIONS:

Upper and lower GI tumors are distinct in their tolerated immune-cell infiltration. IO therapies should be tailored based on location to take advantage of the innate immune apparatus present. Specifically, upper GI cancers appear especially fit for checkpoint therapy despite having lower average TMB.

KEY FINDINGS:

- Despite slightly higher average TMB, CRC cancers have colder immune-activity than other GI locations across almost all immune cell types
- CRC cancers also have significantly lower PD1/L2 expression
- Oral and throat cancers (H&N) have relatively high checkpoint expression
- Many HN and GE tumors are classified as the immune-active CMS3, biliary tumors are frequently classified as the stroma-rich CMS4
- Eosinophils are abundant in all GI cancers, Immune dendritic cells are often excluded from GI tumors, especially the GE & CRC locations