Abstract # 579

NantOmics/NantHealth

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

CONTRIBUTING RESEARCHERS

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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 contexture, 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 **elucidating the immune compositions** in those cancers would reveal **biological insights and potentially therapeutic targets.**

METHODS

- **464 GI tumors with RNAseq** data (~200x10^6 reads per tumor) and **tumor/normal DNAseq** from a commercial database were available for analysis.
- Tumors were categorized into colorectal (CRC), gastroesophageal (GE), head neck and oral (H&N), and biliary (other) cancers.
- **Tumor mutational burden (TMB) was directly observed** from DNAseq as counts of non-synonymous exonic mutations
- A curated panel of 122 genes that discriminate between **28 immune cell-specific signatures** was identified. For each of these signatures, a database containing 1467 unselected tumors was used to define a distribution of expression. The study samples were then scored for their deviances within such distributions.
- Each of the 464 tumors were assigned to one of the colorectal **Consensus Molecular subtypes** (CMS).
- **Significant enrichment for immune subsets between locations and CMS was analyzed.**

RESULTS

Figure 1. **NantHealth clinical GI cases database**

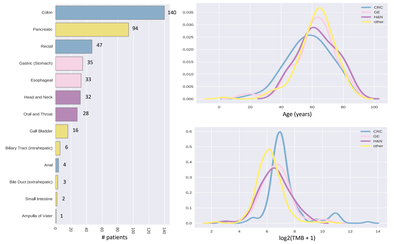
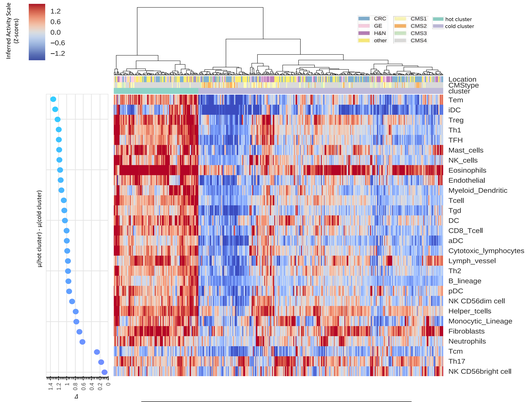


Figure 2. **CRC samples are associated with relatively lower inferred immune activity**



comparison	odds ratio	p	adj. p
CRC vs. cold cluster	1.889	0.004	0.025
Biliary (other) vs. hot cluster	1.774	0.006	0.025

Figure 3. **Inferred immune activity summarized across GI locations**

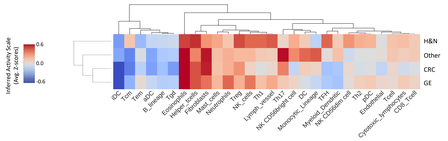
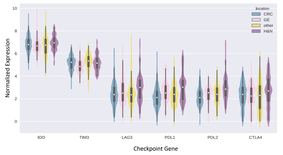
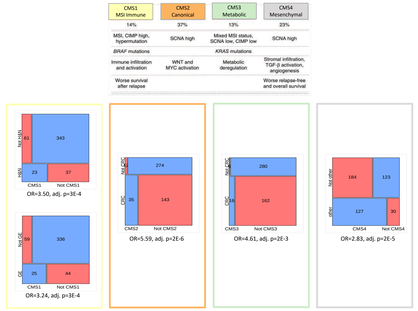


Figure 4. **H&N overexpresses key checkpoints, CRC has significantly lower expression**



group	t	p	adj. p
PDL2 & H&N	5.57	4.37E-08	0.000001
PDL1 & H&N	5.13	4.33E-07	0.000005
PDL1 & CRC	-5.55	6.73E-06	0.000054
TIM3 & GE	-3.62	3.30E-04	0.001733
PDL2 & CRC	-3.59	3.61E-04	0.001733
LAG3 & H&N	3.21	1.42E-03	0.005691

Figure 5. **H&N/GE are enriched in immune-active subtype, biliary location are enriched in stromal subtype**



KEY FINDINGS

- Despite slightly higher average TMB, CRC cancers have colder immuno-activity than other GI locations across almost all immune cell types
- CRC cancers also have significantly lower PDL1/2 expression
- Oral and throat cancers (H&N) have relatively high checkpoint expression
- Many HN and GE tumors are classified as the immune-active CMS1, biliary tumors are frequently classified as the stroma-rich CMS4
- Eosinophils are abundant in all GI cancers, Immature dendritic cells are often excluded from GI tumors, especially the GE & CRC locations

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.

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2. Bindea, Gabriela, et al. "Spatiotemporal dynamics of intratumoral immune cells reveal the immune landscape in human cancer." *Immunity* 39.4 (2013): 782-795.
3. Becht, Etienne, et al. "Estimating the population abundance of tissue-infiltrating immune and stromal cell populations using gene expression." *Genome biology* 17.1 (2016): 218.
4. Guinney, Justin, et al. "The consensus molecular subtypes of colorectal cancer." *Nature medicine* 21.11 (2015): 1350.

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