Background

- Immunotherapies such as checkpoint inhibitors, CAR T cells, and therapeutic vaccines are revolutionizing cancer medicine with remarkable responses in some patients.
- Several cancers have FDA approval for the use of check point inhibitors. And publications have suggested that mutational burden and neoepitope burden predict response to check point inhibitors.
- Cancers such as TNBC have few treatment options and would greatly benefit from novel immunotherapy approaches.

We analyzed whole genome sequencing (WGS) and RNA sequencing (RNAseq) sites from TCGA Cancer Genome Atlas (TCGA) to identify neoepitopes tumor-specific antigens derived from somatic tumor mutations that could be exploited to develop next-generation, patient-specific cancer immunotherapies.

Methods

- TCGA WGS and RNASeq data were obtained from the University of California, Santa Cruz (UCSC) Cancer Genomics Hub (https://cghub.ucsc.edu).
- Neoepitopes were identified by creating all possible permutations of either 9-mer or 15-mer amino acid strings derived from somatic single nucleotide variants (SNVs) or insertions/deletions (indels) in coding regions.
- Potential neoepitopes were filtered against all possible variation in 9-mer and 15-mer sequences from reference human coding genes, insertions/deletions (indels) in coding regions.
- Potential neoepitopes were filtered against all possible 9-mer and 15-mer amino acid strings derived from somatic tumor mutations that could be exploited to develop next-generation, patient-specific cancer immunotherapies.

Results

Cancer Neoepitope Loads Across TCGA Dataset

Neoepitopes (via WGS)

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Conclusions

- Nearly all identified neoepitopes are patient-specific. TNBC samples do not share any common neoepitopes.
- Neoepitope-MHC interactions restrict more commonly shared mutations.
- Development of personalized immunotherapies is dependent on accurate DNA and RNA sequencing.
-Checkpoint inhibitor markers such as neoepitope load or PD1 expression will need to be screened before suggesting use of immunotherapy for breast cancer patients.

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