112P Identification of a novel promiscuous anti-NY-ESO-1 immunogenic CD4+ peptide containing a CD8+ T-cell epitope highly present in metastatic gastric cancer responding to combined radiotherapy/anti-PD-1 immunotherapy

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Background: Immune checkpoint inhibitors offer the prospect of long term disease control in solid tumor types. NY-ESO-1 is a cancer-testis antigen expressed by 20% of advanced gastric cancers, known to induce humoral and cellular immune responses. Combination of anti-PD-1 with radiotherapy is currently investigated. Radiotherapy has the ability to promote immunogenic cell death leading to the release of tumor antigens, increasing infiltration and activation of T cells. In this study, we investigated the immune response to the NY-ESO-1 antigen in metastatic gastric cancer treated with anti-PD-1 (pembrolizumab).

Methods: T cells response to the NY-ESO-1 antigen was investigated by ELISPOT against NY-ESO-1 PepMix, against the 43 single peptides overlapping the NY-ESO-1 whole protein and the NY-ESO-1 HLA-A2 restricted peptide. The IEDB1 prediction database was used to predict the patient's HLA DR, DQ and DP binding to NY-ESO-1. We subsequently characterized the phenotypic and functional activity of the patient T cells using flow cytometry analysis.

Results: We have identified a novel promiscuous immunogenic NY-ESO-1 peptide restricted to the 4 HLA-DQ and HLA-DP alleles and containing the known NY-ESO-1 HLA-A2-02:01 (P157-165) immunogenic epitope. CD8+ T cells were increased during combined therapy and at disease resolution in which its PD-1+CD8+ subset was increased during combined therapy and resolution then decreased at disease progression. The CD107+ cytotoxic subset of the CD8+/HLA-A2-NY-ESO-1-dextramer+ T cells was markedly increased during combined therapy and at resolution then dramatically decreased at re-progression.

Conclusion: We have identified a novel promiscuous anti-NY-ESO-1 immunogenic CD4+ peptide containing the P157-165 HLA-A*02:01/CD8+ epitope that was highly presented at disease resolution and decreased at progression after combined radiotherapy/anti-PD-1 immunotherapy. Our study showed that radiation therapy combined with immune checkpoint blockade would enhance the immune response that correlates with the patient clinical outcome.

Legal entity responsible for the study: Hamad Medical Corporation.

Funding: Hamad Medical Corporation.

Disclosure: All authors have declared no conflicts of interest.