1411 BREAST CANCER IMMUNOPEPTIDOMES CONTAIN NUMEROUS SHARED TUMOR ANTIGENS

[1]Eralda Kina*, [1]Jean-Philippe Laverdure, [1]Chantal Durette, [1]Joël Lanoix, [1]Mathieu Courcelles, [1]Qingchuan Zhao, [1]Anca Apavaloaei, [1]Jean-David Larouche, [1]Marie-Pierre Hardy, [1]Krystel Vincent, [1]Patrick Gendron, [1]Leslie Hesnard, [1]Maria Virginia Ruiz Cuevas, [2]Gregory Ehx, [1]Pierre Thibault, [1]Claude Perreault. [1]*University of Montreal, Montreal, Canada*; [2]*University of Liege, Liege, Belgium*

Background Hormone-receptor-positive breast cancer (HR+) is an immunologically cold cancer that has not benefited from advances in immunotherapy. In contrast, triple-negative breast cancer (TNBC) displays high levels of leukocytic infiltration and responds to immune checkpoint inhibitors. CD8 T cells, the main effectors of anti-cancer responses, recognize MHC I-associated peptides (MAPs). Our work aimed to characterize the repertoire of MAPs presented by HR+ and TNBC tumors.

Methods Using a proteogenomic approach relying on mass spectrometry, we identified 57 094 unique MAPs in 26 primary breast cancer samples (14 HR+, 12 TNBC).

Results MAP source genes showed a high overlap between both subtypes (>70%). We identified 25 tumor-specific antigens (TSAs) derived from various genomic regions, of which 24 were unmutated. TSAs were mainly identified in TNBC samples (70%) and were more highly shared among TCGA TNBC than HR+ samples. In the TNBC TCGA cohort, the predicted number of TSAs positively correlated with leukocytic infiltration ($p<0.05$) and overall survival ($p<0.05$, figure 1), suggesting that these TSAs are immunogenic in vivo. We also identified 49 overexpressed tumor-associated antigens (TAAs), some of which derived from cancer-associated fibroblasts. FEST assays confirmed the in vitro immunogenicity of our TSAs and TAAs.

Conclusions Well-defined antigens were identified in both subtypes of breast cancer and represent attractive targets for cancer immunotherapy. The higher prevalence and immunogenicity of TSAs in TNBC tumors provide a molecular rationale for the responsiveness of TNBC to immune checkpoint inhibitors.

Ethics Approval Approved by the comity for clinical research of University of Montreal (CERC-20-012-D)

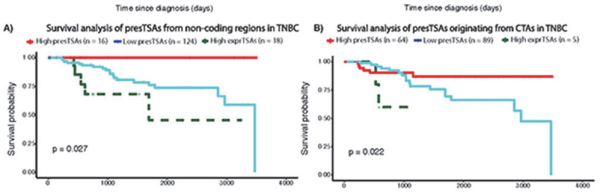

Figure 1. Aberrantly expressed TSAs predicted presentation confers a survival advantage to patients with TNBC tumors.
For each individual tumor, TSAs were considered presented (presTSAs) if their coding sequence and an adequate HLA allele for presentation were expressed. High groups (red) correspond to the first quartile of patients with the highest number of presTSAs. Low groups (turquoise) correspond to the 2nd to 4th quartile.
A-B) High levels of presTSAs originating from non-coding regions and CTAs confer a survival advantage to patients with TNBC tumors. To distinguish the impact of expression as opposed to presentation of aeTSAs, an additional curve was computed with expressed antigens who lacked an appropriate HLA allele for presentation (exprTSAs). High expression of aeTSAs alone, without potential presentation, was insufficient to reiterate a survival benefit.

Abstract 1411 Figure 1 Aberrantly expressed TSAs predicted presentation confers a survival advantage to patients with TNBC tumors

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