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)

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