Introduction

Hormone-receptor positive breast cancer (HR+) is considered an immunologically cold cancer and has not benefited from advances in immunotherapy. In contrast, the triple negative breast cancer (TNBC) subtype has demonstrated its immunogenicity through high levels of leucocytic infiltration and clinical benefits to immune checkpoint blockade. As T cells recognize antigens presented by MHC-I molecules (MAPs), we aimed to characterize the repertoire of MAPs presented in both subtypes and identify actionable targets for immunotherapy.

Methods

Immunoprecipitation of HLA-I molecules
Mass spectrometry analysis
RNA and smRNA sequencing of primary breast tumors

Identification of novel tumor antigens
Canonical proteome
ERE proteome
smRNA proteome
Cancer-specific proteome

Genomic origin of tumor specific antigens
Non coding
Exonic
mTSA (n=1)
Exonic other (n=3)
Exonic CTA (MAGE family, n=14)
Non-coding RNA (n=3)
Intergenic (n=4)

Results

Highly similar immunopeptidomes of HR+ and TNBC tumors

Sharing of TSAs in TCGA

TSAs predicted presentation is associated to a survival benefit in patients with TNBC tumors

Conclusion and Relevance

Immunopeptidomes of HR+ and TNBC tumors are highly similar with the exception of the number of identified TSAs, which were more prevalent in TNBC. TSAs showed in vitro and in vivo immunogenicity. These findings provide a molecular rationale for differences in observed immunogenicity phenotypes between both subtypes. Identified tumor antigens with our pipeline represent interesting targets for vaccine immunotherapy and engineered T cells. Further in vivo testing will confirm their clinical relevance.