Expression-based immune signatures as predictors of neoadjuvant targeted-chemo-therapy response: Experience from the I-SPY 2 TRIAL of ~1000 patients across 10 therapies

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Background

Expression-based signatures have been shown to predict neoadjuvant therapy response, but further studies are needed to deconvolute the contribution of different immune cell types.

Objective: In this study, we compared published T/B-cell related signatures at 3 different levels of resolution as predictors of response in I-SPY 2 [Savas 2018].

I-SPY 2 TRIAL

†An investigational combination of one or more agents may be used to replace all or some of the standard therapy for breast cancer.

I-SPY 2 TRIAL SABCS Abstract: P3-10-06

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Methods

Pre-treatment expression data available for 989 I-SPY 2 patients from 9 previously reported experimental arms and shared controls

Immune Signatures Evaluated

Overall, proportions of gene overlap between signatures are small.

Although the proportions of gene overlap are small, expression levels of most signatures are well correlated.

- Subpopulation-specific signature tends to cluster more closely together
- Most cell signature is not well correlated with others

Association with Response

In the population as a whole, immune signatures predict response across multiple classes of agents, including the checkpoint inhibitor Pembrolizumab.

Higher mast cell signature expression is associated with lower pCR rates, as opposed to other immune signatures where higher levels associates with better response.

Conclusions

- Our exploratory study suggests that immune signatures are associated with response to multiple I-SPY 2 experimental agents and implicates different immune cell types as response-predictive within breast cancer subtypes.

- Single cell sequencing derived population specific signatures may help further de-covariate how different immune cell types contribute to therapy responsiveness.

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References:


2. “I-SPY 2 ITRIAL: Phase II trial using response-adaptive randomization in biomarker defined cohorts to evaluate novel agents when added to standard neoadjuvant chemotherapy for women with high-risk stage III breast cancer.”

3. I-SPY 2 ITRIAL: Phase 2 trial using response-adaptive randomization in biomarker defined cohorts to evaluate novel agents when added to standard neoadjuvant chemotherapy for women with high-risk stage III breast cancer.

4. “Pre-treatment expression data available for 989 I-SPY 2 patients from 9 previously reported experimental arms and shared controls.”

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