

ILC MANUSCRIPT: Figures Outline

FIGURE 1

- **Panel A:** ILC genomic features
 - recurrently events: mutations + CNA + methylation(?) + miRNA (?) + heatmap entries for selected mRNA (CDH1/PTEN/GATA3) and protein (Akt)
- **Panel B:** comparison of recurrent events (mut/cna) between
 - IDC vs ILC
 - Luminal IDC vs ILC
 - LumA IDC vs LumA ILC

[We should choose 2 of these]

FIGURE 2: E-cadherin loss

- CDH1 mutations in ILC (lollipop plot) + copy number status
- DNA methylation: no solid evidence for epigenetic silencing, can we make a case for “lack of DNA methylation”?
[Peter/Suhn are looking into that, hard to go against previous literature without experimental validation]
- miRNA [Gordon/Reanne]

FIGURE 3: FOXA1

- FOXA1 mutations across all breast tumors (hotspot clusters emerge)
- Highlight DNA binding mutations + 3D plot
- FOXA1 binding sites are demethylated in FOXA1 expressing samples (composite heatmap with mutations, DNA methylation, mRNA expression, PAM50, purity)
- Differential expression analysis for different mutation classes
- Differentially expressed signatures (enrichment for mitotic genes)
- Methylation status of mitotic targets and/or inhibited targets?

FIGURE 4: PTEN/Akt

- PTEN alteration status in ILC (vs Luminal IDC)
- Akt pathway alteration and pAKT levels
- PTEN mRNA levels in normals
- pAKT vs tumor purity
- miRNA targeting PTEN

FIGURE 5: mRNA subtypes

- mRNA expression subtypes
- associations with RPPA and survival

FIGURE 6: Unsupervised Classifiers

- Mixed tumors and non-LumA-ILC (NLA) molecular alterations
- ILC-vs-IDC classifiers
 - how it performs with ILC/IDC
 - how does it classify mixed and NLA tumors
- OncoSign analysis
 - develop molecular classifiers from oncogenic signatures
- CoCA