LobSig4 is a superior and readily implementable ILC-specific prognostic biomarker set.

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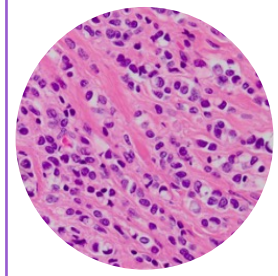
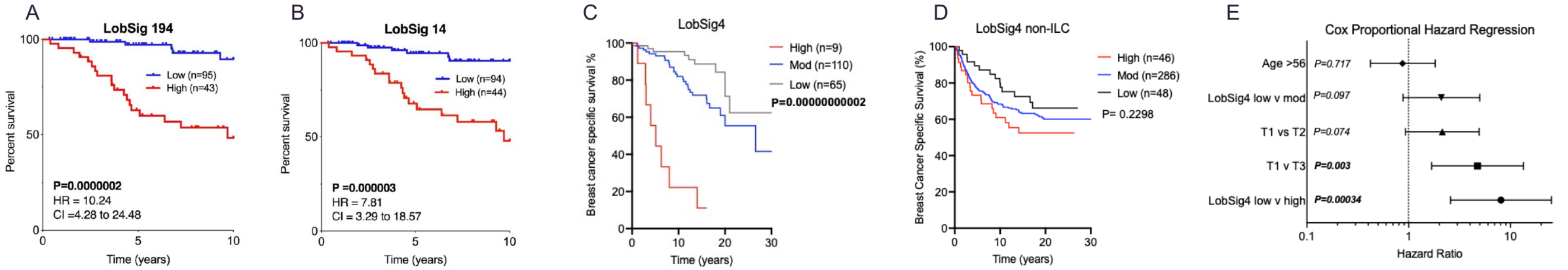
Invasive Lobular Carcinoma (ILC) is the most common special histological subtype of breast cancer. Despite clinical and biological differences, including diverse sites of metastasis, ILC are managed in the same way as the more commonly diagnosed, Invasive Carcinomas of no special type. Previously, we derived the LobSig lobular specific gene signature in an attempt to prognosticate within an otherwise homogeneous tumour category. We showed that this set of genes could stratify Grade 2 and Nottingham Prognostic Index moderate tumours into high and low risk groups. Using a CoxBoost analysis we further refined the geneset to 14 genes of interest which we examined using Immunohistochemistry on a large panel of ILC with clinical follow up data. Four targets showed a significant association with breast cancer specific survival, with high levels correlating with the poorest outcomes. Considering the expression data for these 4 candidates together with a Cox Proportional Hazard Regression we present a combined prognostic power of (P=0.00034, HR=8.07 (CI 2.58-25.30)), which has superior prognostic power over variables including tumor size and patient age. 'LobSig4' represents a readily implementable and informative biomarker set for prognostication in Invasive Lobular Carcinoma.

Invasive Lobular Carcinoma



- 2nd most common Br Ca
- Mostly ER+
- Mostly Grade 2
- Spread to atypical organs (e.g. ovary, orbit, gut)
- No specialised treatments



Further refinement of (A) LobSig149 to 14 genes using a Cox-Boost analysis stratifies ILC with equivalent prognostic power to LobSig194 (B) (Kaplan Meier survival curves (and log rank P values)). We performed Immunohistochemistry for the LobSig14 candidates and found protein expression significantly associated with survival outcomes for 4 of the proteins. By combining these 4 candidates, we found a significant stratification of survival outcomes, as shown in (C) Kaplan Meier survival curves (and log rank P values) of C) the LobSig4 set is prognostically significant only in ILC, not in unselected non-ILC breast cancers (D). Cox proportional hazards forest plots of models E) including age, tumour size and LobSig4 expression status Hazard ratio is plotted on a log scale, with the 5%- 95% Confidence Interval. We are working to further validate.

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