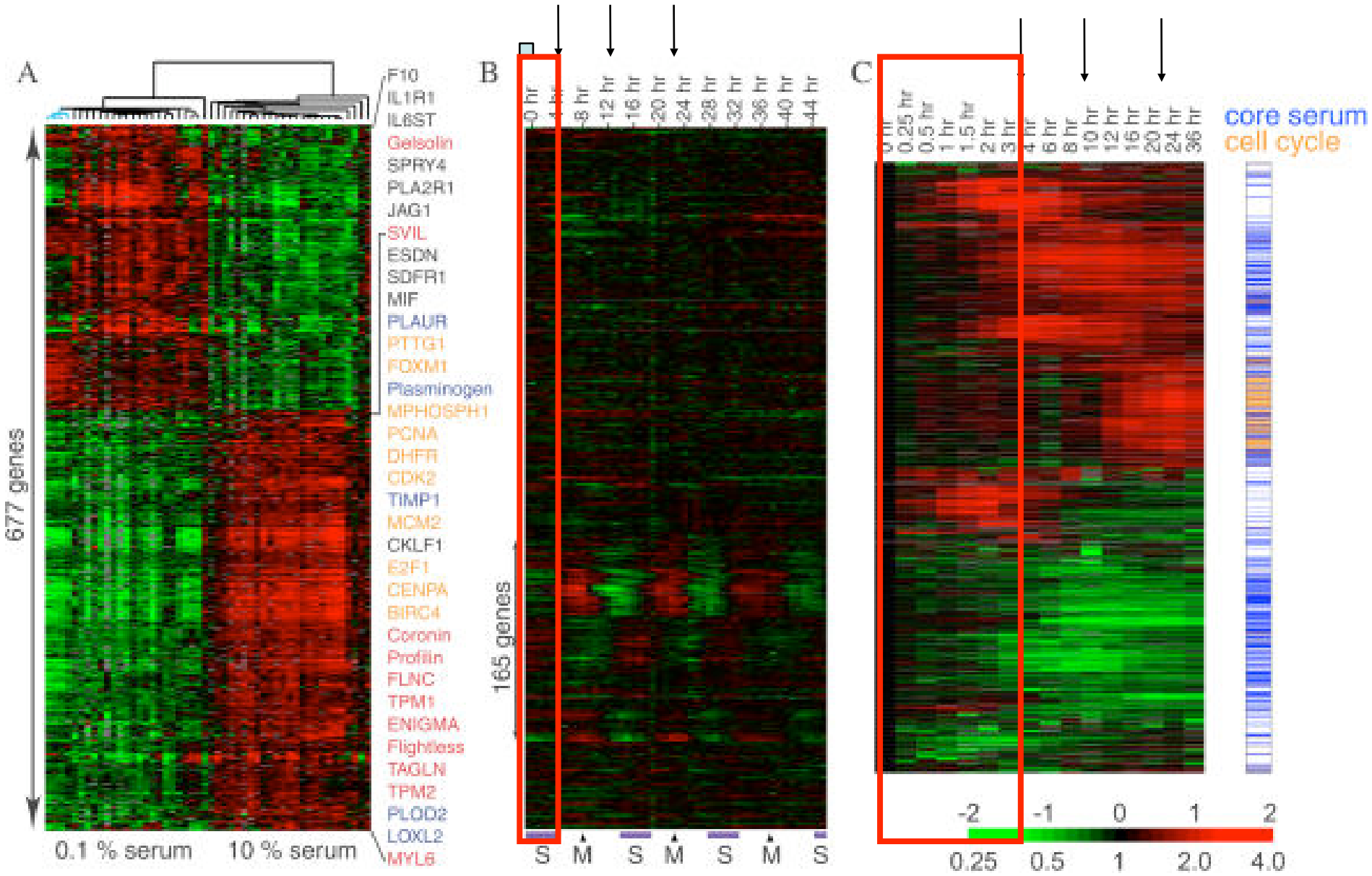
RNA expression analysis

- transcription vs stability effects
- tumor typing, prognostic indicator signitures
- useful reference collections
  - GNF Symatlas http://symatlas.gnf.org
  - Shyamsundar et al 2005 (SK)

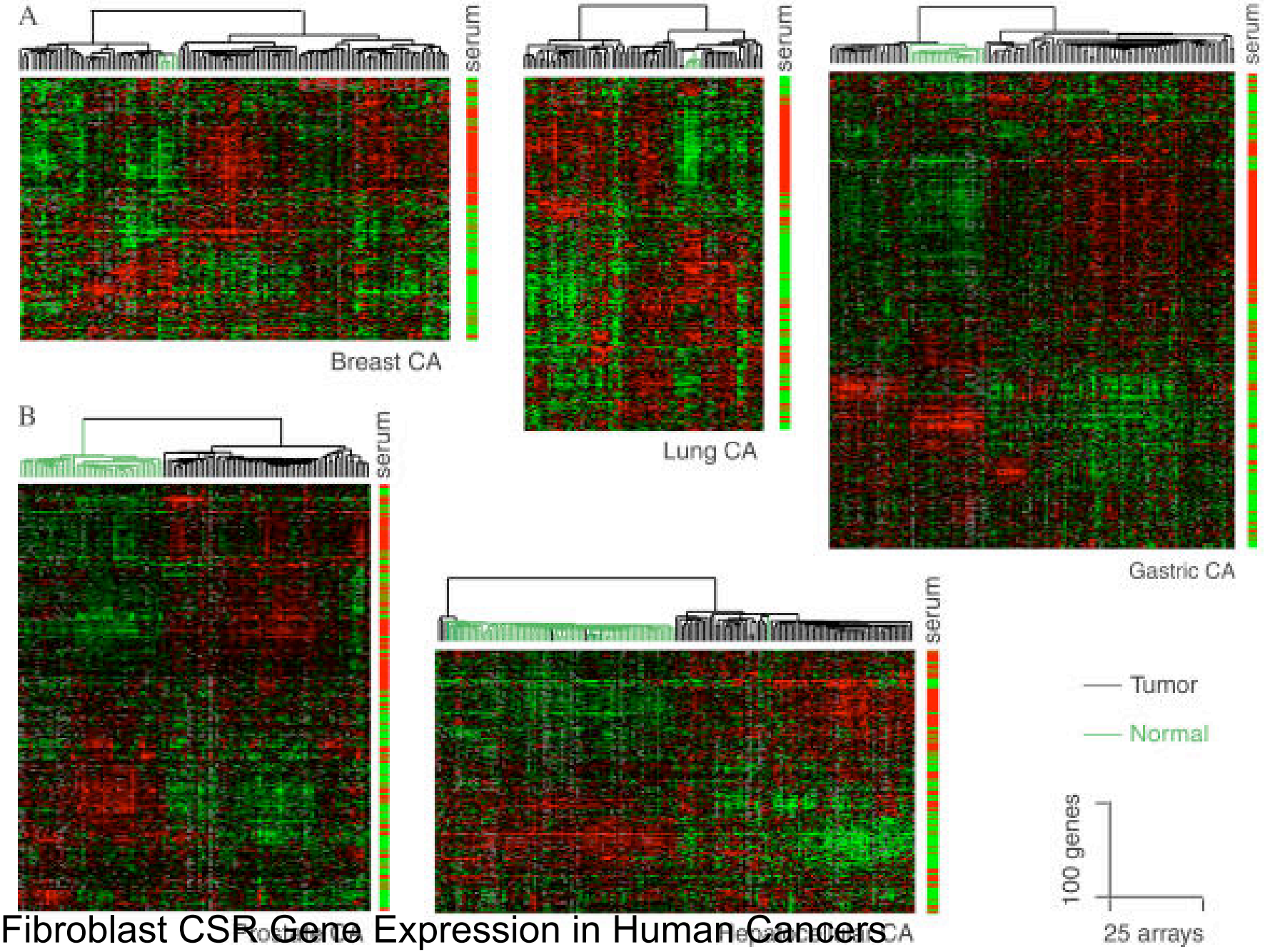
RNA ananlysis of serum response P. Brown and colleagues



2 way hierarchical clustering

Cyclic transcript subset

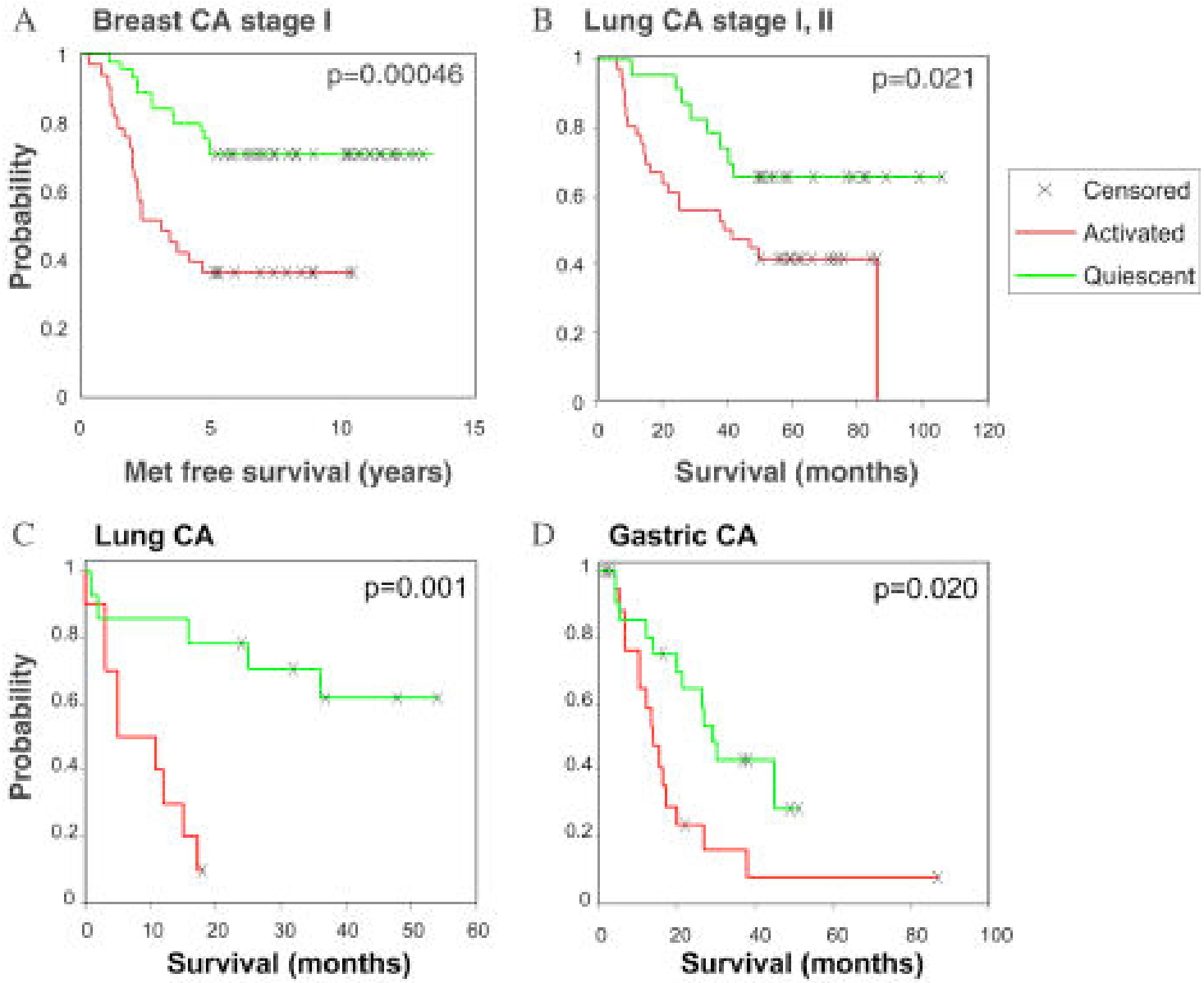
“Core” serum fibroblast Response transcripts



Survey of Fibroblast CSR Gene Expression in Human Cancers

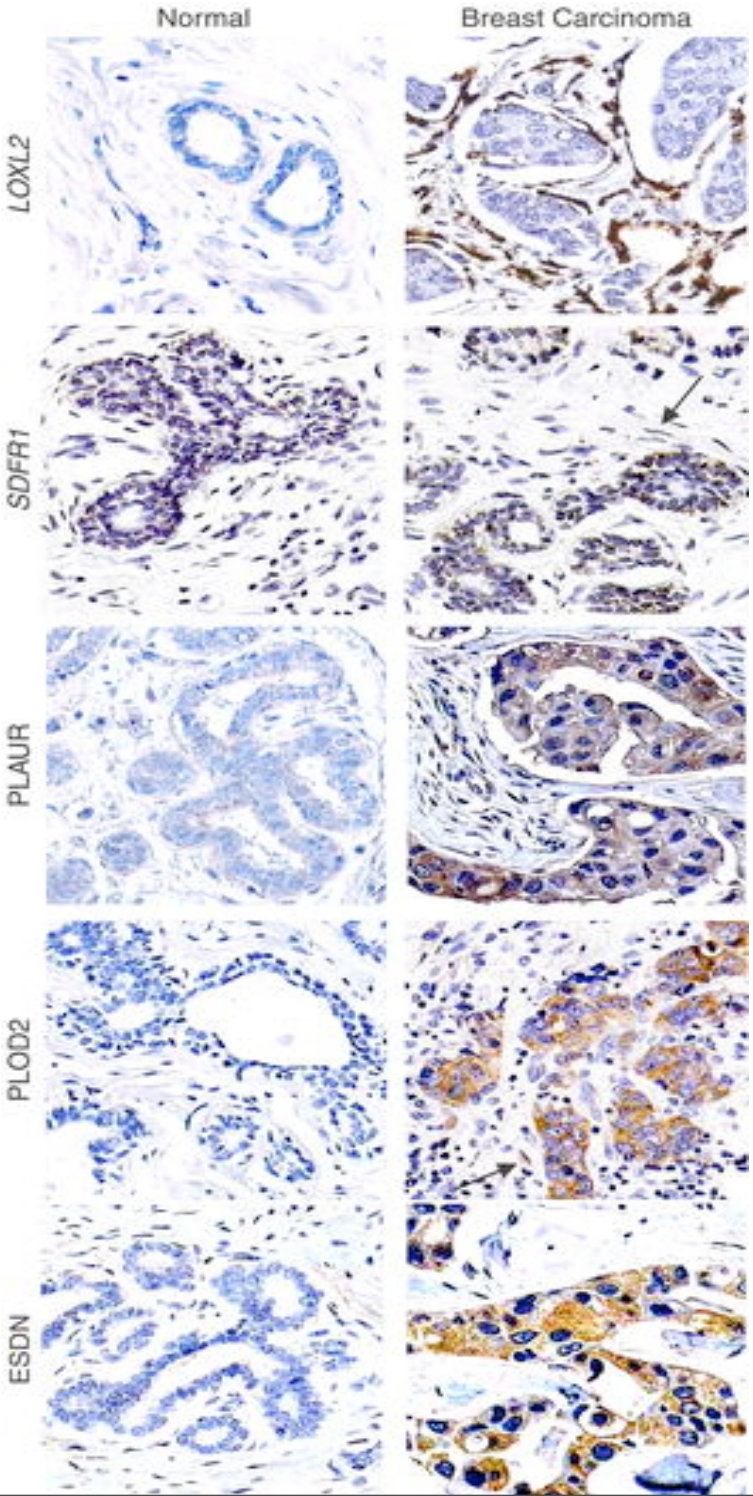
Expression patterns of CSR genes in over 500 tumors and corresponding normal tissues organized by 2-way hierarchical clustering. Tumors in black tree; normal tissues green

Note: All Done using previously published, publicly downloadable data



Prognostic Value of Fibroblast CSR in Epithelial Tumors

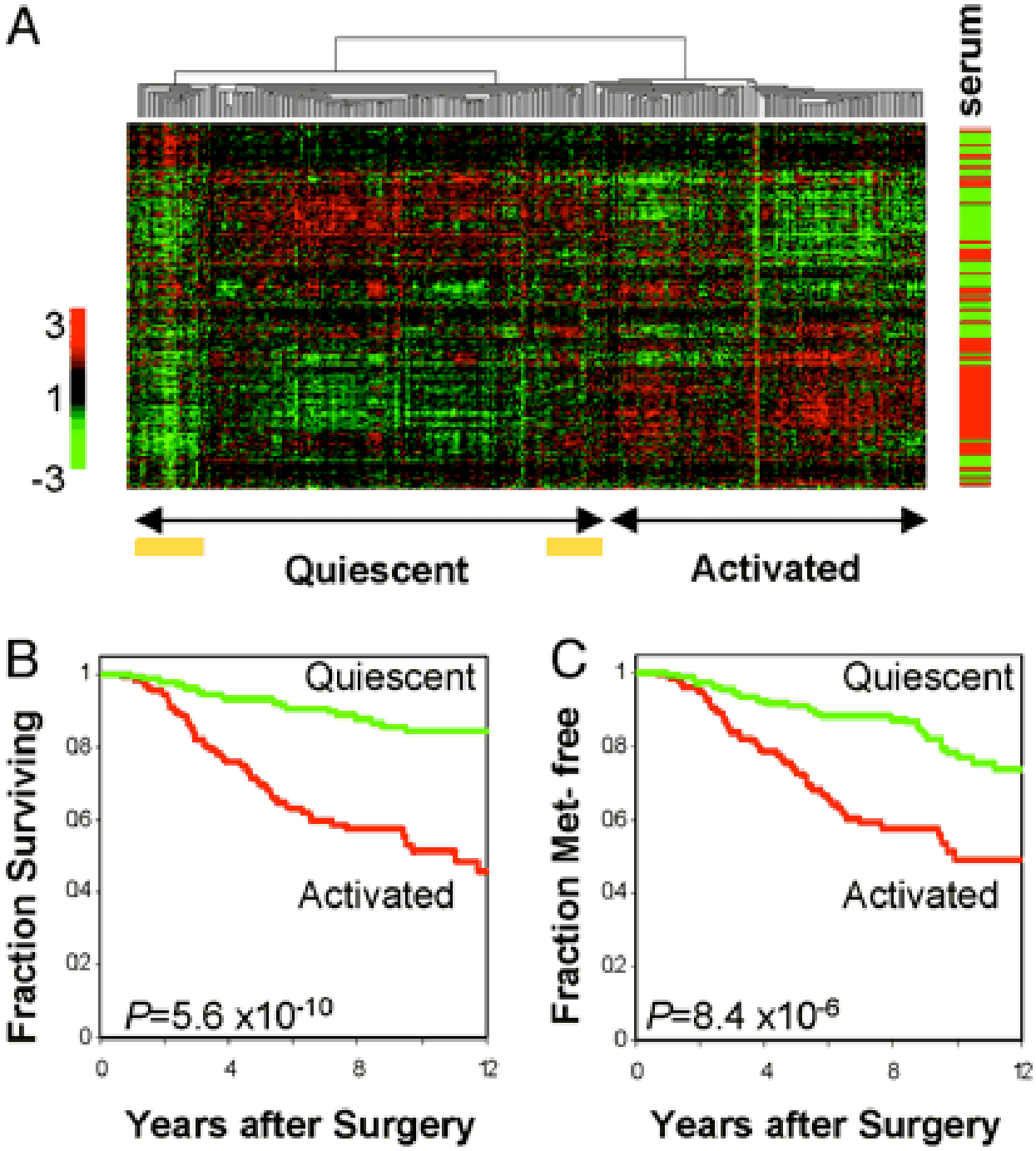
Kaplan–Meier survival curves of tumors stratified into two classes using the fibroblast CSR Activation to classify. Appears to be highly prognostic across a range of tumors.



Tissue arrays - example result
Histological Architecture of CSR Gene Expression in Breast Cancer

Representative ISH of LOXL2 and SDFR1 and IHC of PLOD2, PLAUR, and ESDN are shown

Panels for LOXL2, PLAUR, PLOD2, and ESDN represent cores of normal and invasive ductal breast carcinoma from different patients on the same tissue microarray. Panels for SDFR1 demonstrate staining in adjacent normal and carcinoma cells on the same tissue section.

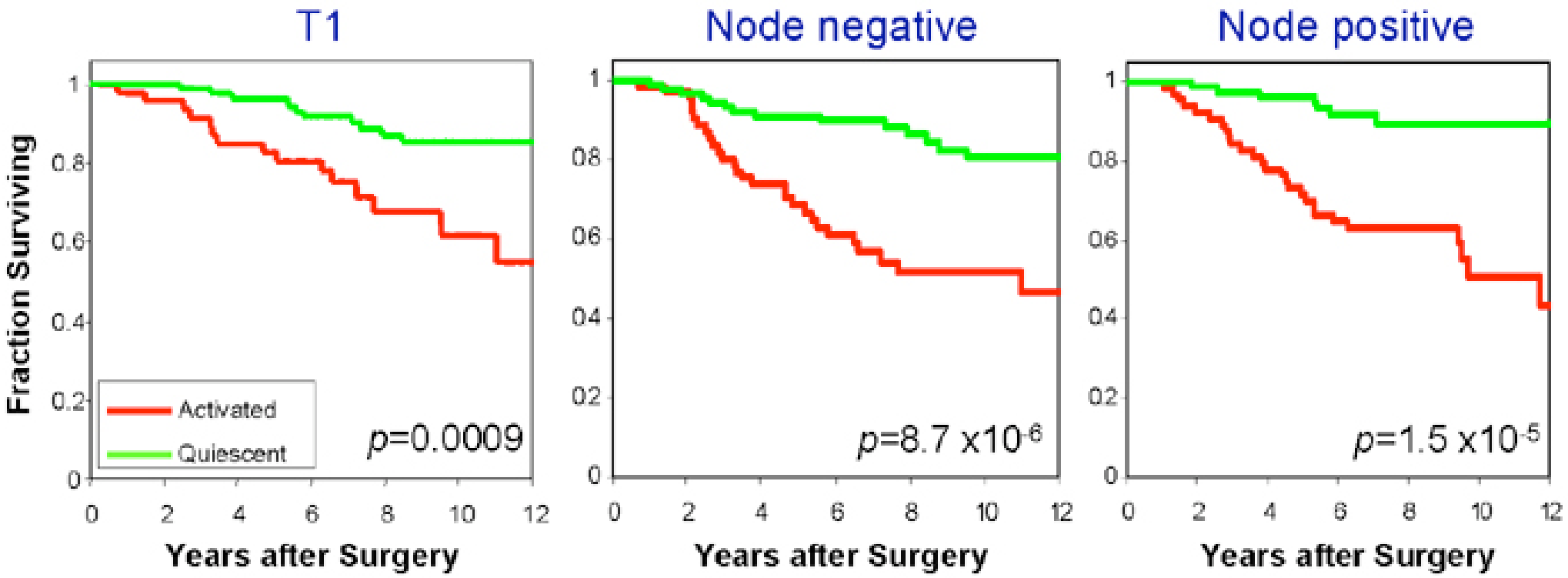


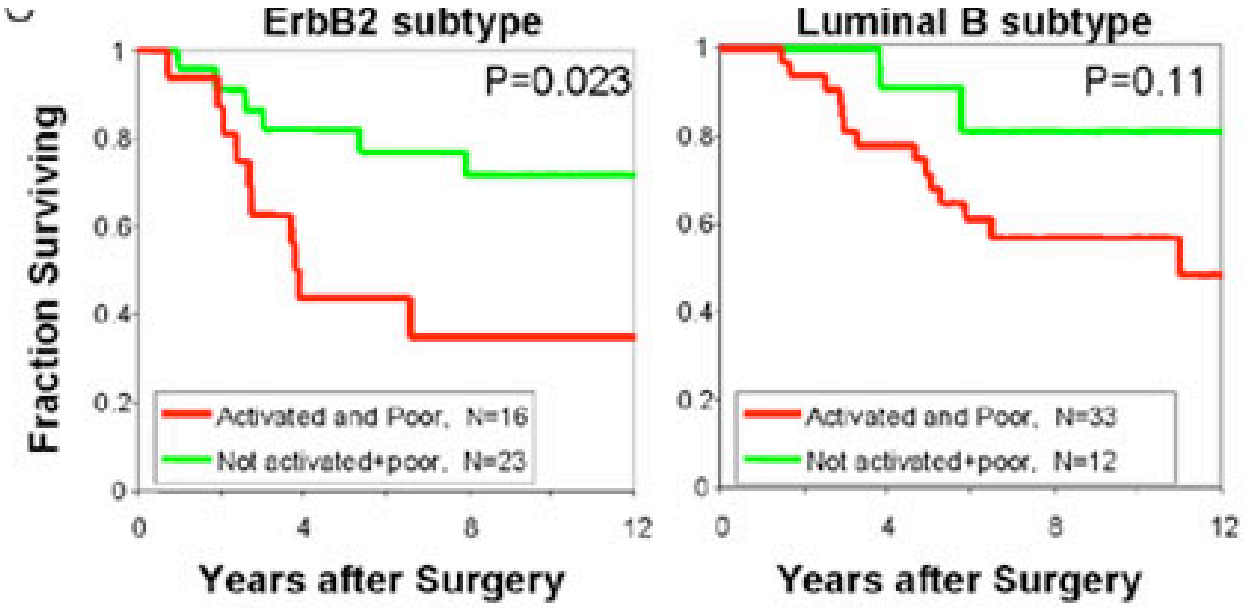
2005 - breast cancer follow-up

How predictive is The serum fibroblast Signature?

295 tumor cases

How predictive compared with tumor size, node status, ErbB2?





scalable wound-response signature for chemotherapy

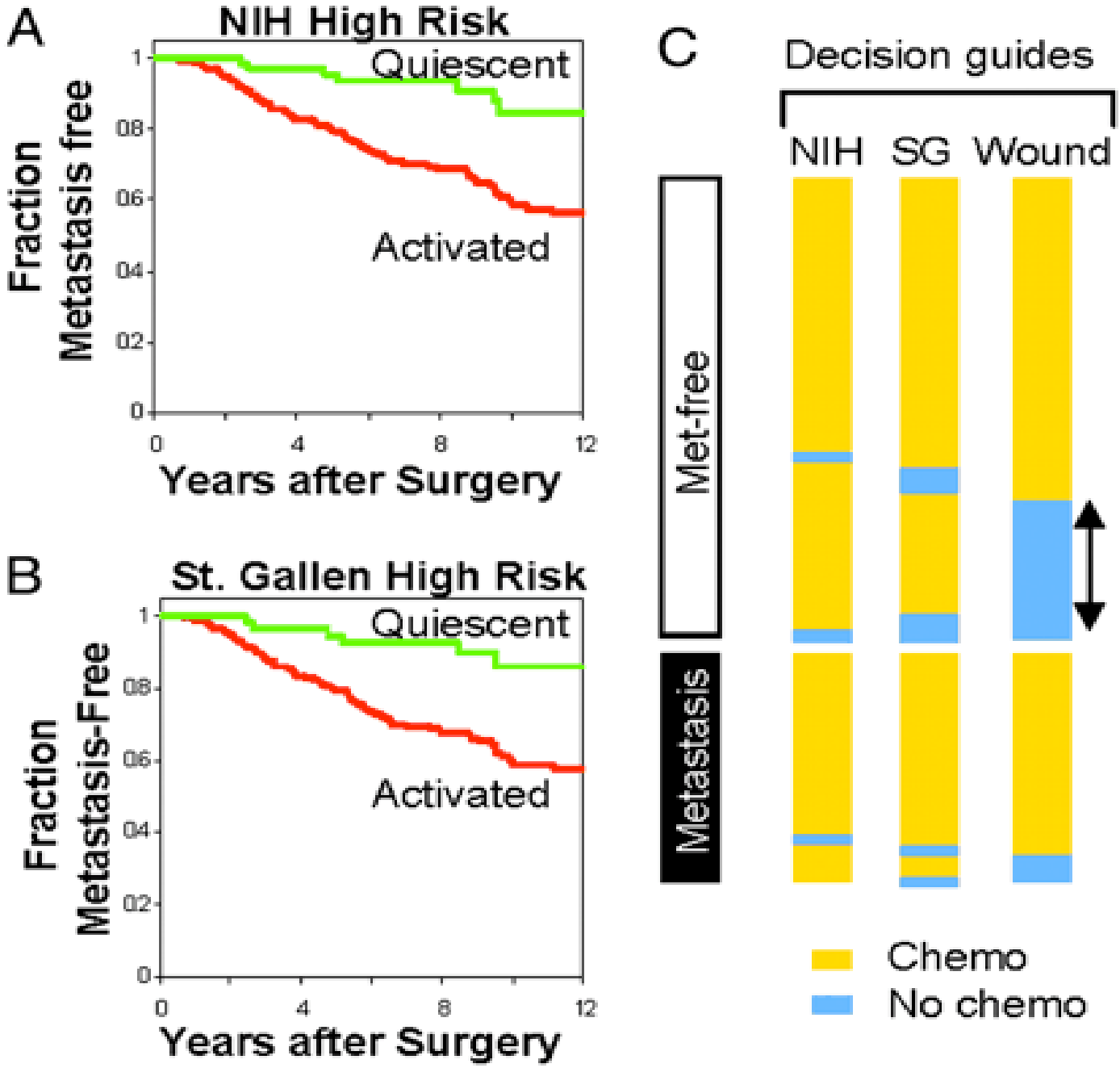
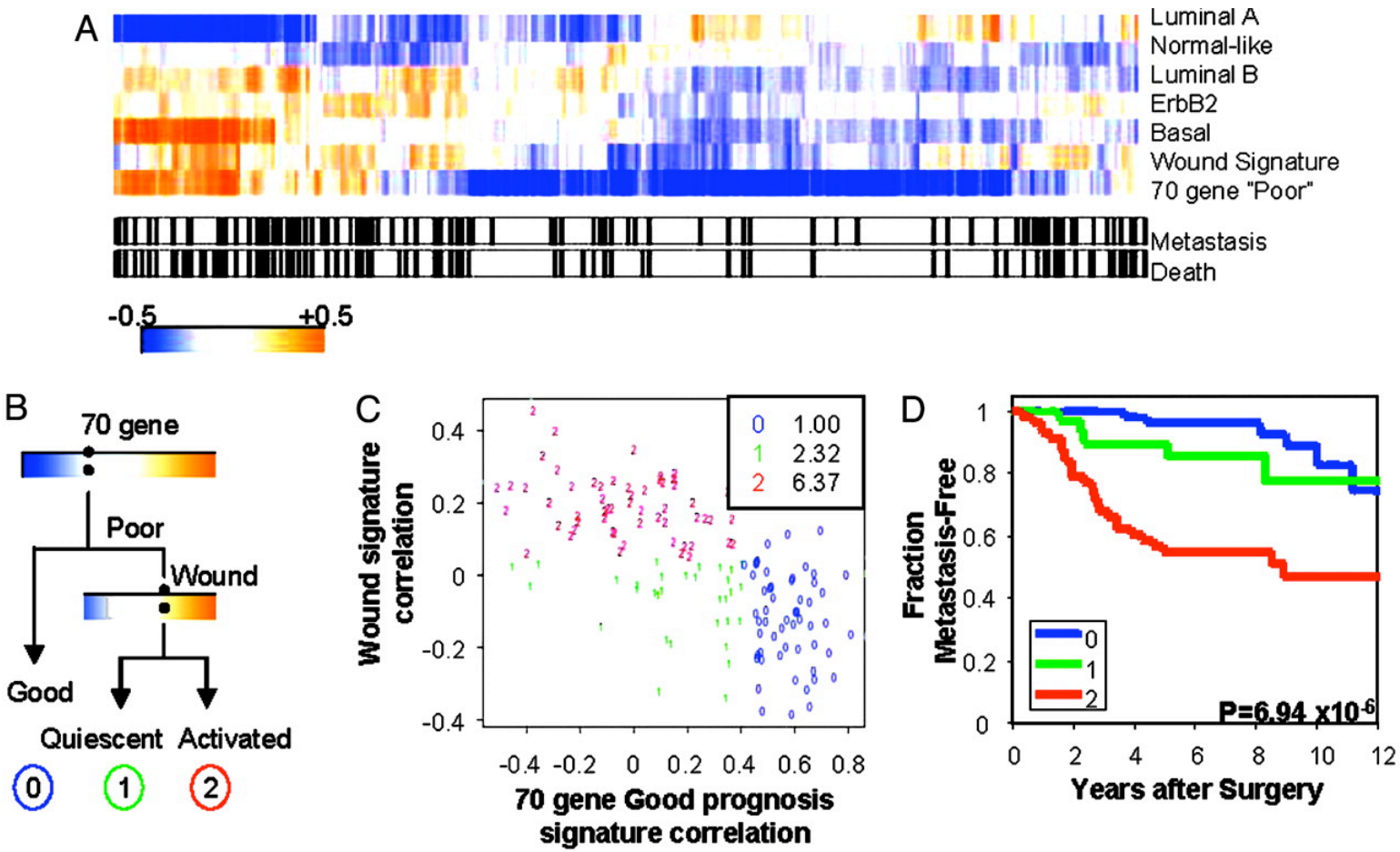


Fig. 3. Integration of diverse gene expression signatures for risk prediction



Chang, Howard Y. et al. (2005) Proc. Natl. Acad. Sci. USA 102, 3738-3743

Large scale expression signatures can be derived in different ways for cancer stratification

Multiple approaches “work” and can yield largely orthogonal groups of ~50- 500 gene scale that are each effective

Some capture already known clinical variation, others capture apparently novel information

Approaches for assembling the prognostic or diagnostic gene sets can be unsupervised, supervised, or hypothesis driven. However, the hypothesis itself may have its origin in a group defined or observed first on other cirteria.