Comprehensive molecular analysis of several prognostic signatures using molecular indices related to hallmarks of breast cancer: proliferation index appears to be the most significant component of all signatures

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Although the development of high-throughput gene expression technologies has led to the identification of several “molecular signatures” predicting clinical outcome, no attempt has yet been made to perform a comprehensive analysis integrating well characterized biological processes and gene expression data. Here we aim to elucidate the relationship of gene expression patterns defined by several biologically relevant indices with previously reported prognostic signatures and their interaction with prognosis.

Defining Molecular Indices (Sotiriou et al ASCO 2006)

Van’t veer et al. Nature 2002, 70 genes
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Materials & Methods

- Selection of prototype genes related to several biological processes in breast cancer (hallmarks of cancer) such as basal/luminal phenotype, ERBB2, proliferation, fully captured by the gene expression grade index, angiogenesis, immune response (Sotiriou et al ASCO 2006)
- Use of a model selection procedure based on cross-validation error estimation in order to select the genes that are able to predict significantly and specifically one of the prototypes (molecular indices)
- Application to several previously reported prognostic signatures (70-gene, 76-gene, wound healing, p53, genomic grade and recurrence score) and their impact on survival using several microarray datasets
- Characterization of dependency patterns between these indices for each prognostic signature and their impact on survival using several microarray datasets

Survival Analysis DMFS (original data sets)

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Survival Analysis DMFS, TRANSBIG VALIDATION N=198

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Conclusions

Proliferation seems to be the common denominator of many existing prognostic gene signatures, recapitulating their prognostic power.

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