IMP3 expression determines aggressive superficial urothelial carcinoma

Predicting the risk of tumor progression in superficial urothelial carcinoma is currently difficult. Sitnikova *et al.* have examined the utility of using IMP3—an oncofetal protein—as a biomarker to distinguish between tumors with a high probability of progression and those that are unlikely to become invasive.

The researchers examined the expression of IMP3 in 214 patients with superficial urothelial carcinoma. IMP3 expression was noted in 20% of primary superficial urothelial carcinomas and in 93% of metastatic urothelial carcinomas. IMP3 expression was significantly associated with disease recurrence ($P=0.029$), tumor stage ($P=0.016$) and tumor grade ($P<0.0001$). Progression-free and disease-free survival times were significantly longer in patients with non-IMP3-expressing carcinomas than in patients with carcinomas expressing this protein ($P=0.0002$ and $P=0.0067$, respectively). The 5-year progression-free and disease-free survival rates for IMP3-negative patients were 91% and 94%, compared with 64% and 76% for IMP3-positive patients. Multivariate analyses adjusted for age, tumor size, tumor stage and grade, multiplicity and treatment with bacillus Calmette-Guérin revealed IMP3 expression to be a strong independent predictor of clinical outcome. The hazard ratio for progression-free survival in IMP3-positive versus IMP3-negative patients was 6.46 (95% CI 2.19–19.05; $P=0.001$), and the hazard ratio for disease-free survival was 2.82 (95% CI 1.18–6.71; $P=0.019$).

The authors conclude that IMP3 expression has prognostic value in superficial urothelial carcinoma and could be used to identify those patients who are likely to show progression and who would, therefore, benefit from aggressive treatment.

Original article Sitnikova L *et al.* (2008) IMP3 predicts aggressive superficial urothelial carcinoma of the bladder. *Clin Cancer Res* **14:** 1701–1706

SATB1 expression generates gene-expression profiles that promote breast tumor metastasis

Gene-expression analyses of human breast cancer cell lines that are associated with a poor outcome have revealed characteristic expression patterns that can predict metastasis (or metastatic risk), but how such gene-expression profiles confer metastatic potential is unclear. Han *et al.* have described a genome organizer protein—SATB1—that when expressed in breast cancer cells can establish a pattern of gene expression that is consistent with invasive behavior.

Initial investigations involving breast epithelial cell lines and breast-tumor specimens revealed that SATB1 is expressed only in metastatic cancer cell lines. To determine the prognostic significance of SATB1 expression, tissue microarrays comprising 1,318 breast cancer samples were scored on the basis of expression levels of SATB1 protein in tumor cell nuclei. Kaplan–Meier analysis of data from 985 patients with ductal breast carcinomas revealed a correlation between higher levels of SATB1 expression and shorter overall patient survival ($P<0.001$). To determine whether SATB1 expression is required to establish an invasive phenotype, the researchers used an RNA interference technique to knock down SATB1 expression in a highly metastatic cell line. SATB1 knockdown in this cell line to levels that were barely detectable by immunoblotting markedly decreased *in vitro* proliferation, restored anchorage-dependent growth and breast-like acinar polarity, and inhibited tumor growth and metastasis *in vivo*. Consistent with these findings, ectopic expression of SATB1 in a nonmetastatic cell line was sufficient to confer invasive activity *in vivo*. Global gene-expression profiling showed that expression of SATB1 altered the expression patterns of over 1,000 genes. Further analysis revealed that SATB1 modified the epigenetic status of all SATB1-dependent genes analyzed.

The authors conclude that SATB1 establishes gene-expression profiles that promote tumor growth and metastasis.

Original article Han HJ *et al.* (2008) SATB1 reprogrammes gene expression to promote breast tumour growth and metastasis. *Nature* **452:** 187–193

Pfetin predicts outcome for patients with gastrointestinal stromal tumors

The molecular background of gastrointestinal stromal tumors (GISTs) has been investigated through genome and transcriptome studies, but the proteomic profile of these tumors has not