GLOSSARY

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Method

No link between *AIB1* variation and increased breast cancer risk in *BRCA1/2*-mutation carriers

Although germline alterations in the breast cancer susceptibility genes *BRCA1* and *BRCA2* are known to be associated with a high overall lifetime risk of breast and ovarian cancer, there is a great deal of variability in cancer-risk estimates between different analyses. Research has suggested that breast cancer risk in *BRCA1/2*-mutation carriers might be modified by variations in the poly-Q coding repeat of the nuclear receptor coactivator *AIB1*, and that breast cancer risk is increased in *BRCA1/2*-mutation carriers with at least 28 polyglutamine repeats. A recent large study, however, has challenged these findings.

Hughes and colleagues genotyped the *AIB1* repeat length polymorphisms in 851 women with *BRCA1* germline mutations and 324 with *BRCA2* germline mutations. They found no increase in risk of breast cancer in women who carried alleles with 28 or more polyglutamine repeats compared with those with fewer repeats, and no relationship between average repeat lengths and increased risk. They suggest that the risk associations reported in earlier studies were probably a result of the small size of the sample populations.

The authors caution that the findings in *BRCA2*-mutation carriers should be confirmed in a larger series. Nevertheless, they conclude that the data strongly suggest that there is no significant effect of *AIB1* genetic variation in *BRCA1*-mutation carriers, and indicate that the same is probably true for *BRCA2*-mutation carriers.

Carol Lovegrove

Original article Hughes DJ *et al.* (2005) Breast cancer risk in *BRCA1* and *BRCA2* mutation carriers and polyglutamine repeat length in the *AIB1* gene. *Int J Cancer* 117: 230–233

Galectin-1: a novel hypoxia-induced protein linked with tumor immune privilege

A novel hypoxia-induced secreted protein found in head-and-neck squamous cell carcinomas (HNSCC) and linked to prognosis has been characterized in a recent study.

Using surface-enhanced laser desorption ionization time-of-flight mass spectrometry, Le and colleagues identified a 15 kDa, hypoxia-induced

protein in HNSCC cell lines. Further characterization showed this protein to be galectin-1, which is known to be associated with several aspects of cancer biology, including apoptosis, cell migration and adhesion, and immune response. Immunohistochemistry was then used to determine the expression of galectin-1 in tumor tissue from 101 HNSCC patients, and the results correlated with carbonic anhydrase IX (a marker of hypoxia), CD3 (a T-cell marker), and with treatment outcome. There was a significant association between galectin-1 and carbonic anhydrase IX staining ($P=0.01$), further establishing the link between galectin-1 and hypoxia. There was also a strong inverse correlation between galectin-1 and CD3 expression ($P=0.01$), implying a role for galectin-1 in immune modulation. Galectin-1 and CD3 expression were both significant predictors of overall survival ($P<0.05$). When staining patterns of the two markers were combined, the authors were able to define three prognostic groups: favorable (negative-weak galectin-1; strong CD3), intermediate (strong or negative-weak staining of both galectin-1 and CD3) and unfavorable (strong galectin-1; negative-weak CD3). These three groups were prognostic indicators for freedom from relapse, cancer-specific survival and overall survival.

The authors conclude that this study gives new insights into the role of hypoxia in malignant progression and treatment response by modulation of immune privilege, and provides a rationale for combining hypoxia-targeted drugs and immunotherapy in the treatment of HNSCC.

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Original article Le Q-T *et al.* (2005) Galectin-1: a link between tumor hypoxia and tumor immune privilege. *J Clin Oncol* [doi:10.1200/JCO.2005.02.0206]

OncoSurge: rating treatment for patients with metastatic colorectal cancer

A recent paper in the *Journal of Clinical Oncology* reports on OncoSurge, a new computer-based decision model for the treatment of metastatic colorectal cancer. An international, multidisciplinary team created this model using RAM to determine the appropriateness of resection, chemotherapy, and local ablation, and various combinations of these