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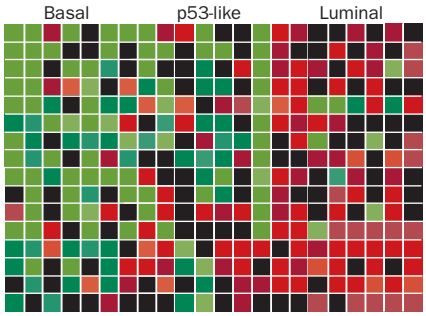
GENETICS

What do breast and bladder cancer have in common?

Muscle-invasive bladder cancers (MIBCs) are heterogeneous tumours associated with rapid progression to metastatic disease. Current staging systems are inadequate for identifying those patients who would benefit most from chemotherapy, and no new systemic therapies have been approved over the past 20 years. David McConkey and colleagues have now discovered three molecular subtypes of MIBC (basal and luminal) that share biomarkers with several breast cancer subtypes. As McConkey highlights, "the most significant findings were firstly, that bladder cancers form intrinsic subtypes that are remarkably similar to breast cancers, and secondly that 'p53-ness' is associated with chemotherapy resistance."



The researchers performed whole-genome mRNA sequencing and unsupervised hierarchical cluster analysis on 73 primary fresh-frozen MIBCs. The basal subtypes of bladder cancer shared a similar molecular profile to basal breast cancers, and were characterized by p63 activation. Luminal bladder cancers were associated with overexpression of PPARγ, ER transcription and *FGFR3* mutations, and p53-like tumours were associated with resistance to chemotherapy. McConkey notes, "it was clear that our findings in bladder cancer were entirely consistent with the experience in breast cancer."

In a second study, William Kim and coauthors wanted to better define the molecular heterogeneity within high-grade bladder cancers. Using relatively well established bioinformatic tools, the researchers showed that "two molecular subtypes of high-grade bladder cancer, which we have termed 'basal-like' and 'luminal,' could be accurately distinguished by a set of 47 genes as part of a gene signature termed BASE47. These subtypes had differences in overall survival and are therefore prognostic." At the molecular level, the subtypes had strong similarities to the intrinsic subtypes of breast cancer previously described.

"The BASE47 subtype could be integrated into decisions about risk of relapse, neoadjuvant or adjuvant therapy," notes Kim. As no targeted agents have been approved for MIBCs, "hopefully this new information can rapidly correct this problem," concludes McConkey.

Lisa Hutchinson

Original articles Choi, W. *et al.* Identification of distinct basal and luminal subtypes of muscle-invasive bladder cancer with different sensitivities to frontline chemotherapy. *Cancer Cell* **25**, 152–165 (2014) | Damrauer, J. S. *et al.* Intrinsic subtypes of high-grade bladder cancer reflect the hallmarks of breast cancer biology. *Proc. Natl Acad. Sci. USA* doi:10.1037/pnas.1318376111