ONCOGENOMICS

Compare and contrast

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Tumour cells are characterized by many genomic aberrations, so finding those that are instrumental in tumorigenesis is difficult. Two recent papers have used high-resolution array comparisons between the genomes of different tumours to look for regions of common amplification and thereby narrow the search for the key oncogenes, which were then identified by expression analysis.

Lynda Chin and colleagues generated two metastatic variants from a non-metastatic mouse model of melanoma. Profiling the genomic DNA of these variants with array-CGH (array comparative genomic hybridization) showed that they both had amplifications on chromosome 13, with an overlap of 850 kb that contained 8 genes. Expression patterns of these genes were studied

in a range of metastatic melanomas and non-transformed melanocyte cultures. *Ned9* (neural precursor cell expressed, developmentally down-regulated 9) was the only one that was consistently upregulated in the melanomas but not in the melanocytes. This pattern was also found in human samples.

Similarly, Scott Lowe and colleagues transplanted *Myc*-overexpressing liver cells into mice to obtain models of hepatocellular carcinoma (HCC). Analysing copy-number changes in the genomes of 7 such tumours identified a region on chromosome 9 that was amplified in 4 tumours, with a common overlapping region of 1 Mb. Cross-species comparison showed a syntenic region on human chromosome 11 that is amplified in HCCs, which allowed the overlapping region to be further narrowed. A combination of gene and protein expression analyses of the genes in this region in both species showed that only overexpression

of YAP1 (Yes-associated protein 1) and BIRC2 (baculoviral IAP repeat-containing 2) were consistently associated with HCCs.

Both sets of authors validated their findings by knocking down expression of their candidate oncogenes in tumour cells, and overexpression in non-transformed cells, showing necessity and in some genetic contexts sufficiency. This research has uncovered important new oncogenes, but it has also demonstrated the power of comparative oncogenomics for finding the genomic aberrations that matter. Importantly, it has demonstrated the usefulness of cross-species comparisons and therefore the relevance of mouse models to human cancer.

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ORIGINAL RESEARCH PAPERS Kim, M. et al. Comparative oncogenomics identifies NEDD9 as a melanoma metastasis gene. *Cell* **125**, 1269–1281 (2006) | Zender, L. et al. Identification and validation of oncogenes in liver cancer using an integrative oncogenomic approach. *Cell* **125**, 1253–1267 (2006)