NEWS AND VIEWS

Small RNA expression profiling as a cancer diagnostic

One of the most promising therapeutic benefits of microarray and genome-wide expression profiling has been in the understanding of the molecular taxonomy of cancer. Detection of the up-regulation of particular transcripts has allowed the diagnosis of poorly defined cancers and opened up a new range of pharmaceutical targets for halting tumour progression. Furthermore, evidence has been uncovered that non-coding RNA transcripts may also play a significant role in tumourgenesis. He et al (2005) have demonstrated that a fragment of chromosome 13 (13q31-32), accumulated in certain lymphomas and known to encode seven miRNA precursors, dramatically increases the frequency and rate of development of cancer in genetically engineered leukaemia-prone mice. Although the mechanism is not clearly understood, this offers the first evidence of a non-coding oncogene. In the same issue of the journal Nature, Odonnell et al (2005) further strengthen the relationship between this miRNA cluster and cancer. Using a lymphoma cell line with an inducible *myc* oncogene they identified 6 miRNAs upregulated by increased expression of c-Myc – two of which lie in the Chr13q31-32 cluster. The predicted target of these miRNAs is transcription factor E2F1, a key cell-cycle regulator, and known to be upregulated by c-Myc. They postulate that the miRNAs act to fine tune the cell cycle, acting as a dampener to the E2F1 inducing ability of c-Myc – acting like a tumour-suppressor.

The complex miRNA regulatory networks evidenced by the dual tumour inducing and repressing capacity of the Chr13q31-32 cluster present a significant challenge to understanding the subtle influences on gene expression of these small RNAs. Given that each miRNA may influence a number of targets, a few hundred miRNAs might be able to regulate several thousand protein coding genes, playing important roles in cell division and differentiation. Lu et al (2005) demonstrate the feasibility of monitoring the expression of such a number of miRNAs. Their analysis of 217 miRNAs involved in human cancers by bead-based hybridisation allowed them not only to discriminate between tumours of different lineages, and identify difficult to diagnose cancers of histologically uncertain origin, but also indicated a global down-regulation of miRNA expression in tumours relative to normal tissue. Such differences add to the hypothesis that global miRNA expression may be indicative of, and perhaps capable of influencing the state of cellular differentiation.

Whilst further work is required in establishing the utility of miRNA expression profiling in a clinical diagnostic setting, such research provides an unexpected insight into the mechanisms of cell division and differentiation that are disrupted in cancer and that may be responsible for the maintenance and pathological development of tumours. This may equally offer a further avenue for pharmacological intervention especially given the promising progress of in anti-RNA therapeutics.

REFERENCES

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