ANGIOGENESIS

A complex picture

Inhibiting angiogenesis as a basis for anticancer therapy relies on the assumption that the vessel-forming endothelial cells recruited to the tumour are genetically stable and, therefore, less likely to cause the heterogeneity-associated problems that debilitate tumour-cell-targeted therapies. It is then a surprising and interesting finding by Streubel and colleagues that some microvascular endothelial cells from patients with lymphoma have the same genetic abnormalities as their tumour counterparts.

Angiogenesis is an essential process for any developing tumour and occurs through two mechanisms — the branching of new capillaries from pre-existing vessels, and the enlargement, splitting and fusion of pre-existing vessels driven in part through the proliferation of the endothelial cells. The authors were intrigued by their initial finding that in a patient presenting with post-transplant lymphoproliferative disorder — arising after a sex-mismatched liver transplant — the endothelial cells within the tumour had the same genetic defect (X0) as the tumour cells, indicating a genetic relationship between them. To investigate this phenomenon further, the authors studied an additional 27 B-cell lymphomas with known cytogenetic alterations. Paraffin sections of all the lymphomas were subject to combined fluorescent *in situ* hybridization (FISH) and immunohistological analysis. Endothelial cells were identified using several different antibodies to label endothelial-specific markers, in concert with FISH probes to known B-cell-lymphoma chromosomal translocation markers (primary alterations) and other, later arising, numerical chromosomal abnormalities (secondary alterations).

Streubel and colleagues found that for each specimen, a varying percentage — on average 37% — of the endothelial cells were positive for the primary and secondary chromosomal aberrations detected in the lymphoma cells. To confirm these findings, the authors analysed freshly cultured endothelial cells isolated from the tumour specimens (when available). They showed that the endothelial cells in culture retained the genetic abnormalities for three or more passages, albeit at a lower percentage than that detected in the original tumour sections, showing that the genetic aberrations were stably inherited.

What are the possible conclusions from this work? Primarily, they are that (through an as yet undetermined mechanism) a proportion of tumour-associated vascular endothelial cells have identical genetic aberrations to those of the tumour and, crucially, that the tumour vasculature is much more heterogeneous than originally thought and, therefore, might be dependent on the properties of the initiating tumour. These findings will undoubtedly provoke more detailed analysis of the mechanism of neoplastic angiogenesis and aid the development of more tumour-specific anti-angiogenic therapies.

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References and links

ORIGINAL RESEARCH PAPER Streubel, B. *et al.* Lymphoma-specific genetic abberations in microvascular endothelial cells in B-cell lymphomas. *N. Engl. J. Med.* **351**, 250–259 (2004)