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TARGETED THERAPIES

New targets in Burkitt lymphoma?

Burkitt lymphoma is a disease that, as for diffuse large B-cell lymphoma (DLBCL), is thought to originate from the normal germinal centre B cell, and can be cured using aggressive chemotherapy regimens. Unfortunately, these regimens cannot be used to treat elderly patients or those patients with endemic Burkitt lymphoma in developing countries. Two studies have now drilled down into the molecular biology of this disease and identified targets for potential clinical assessment.

One study used high-throughput RNA sequencing and RNA interference screening on samples from patients with Burkitt lymphoma and on cell lines to identify the molecular pathways that control carcinogenesis in these patients. The pathways were then compared with those that regulate DLBCL. The second group adopted a completely different strategy; they developed and analysed a mouse model of Burkitt lymphoma by co-expressing MYC and constitutively active PI3K in germinal centre B cells.

Both studies identified regulatory proteins that interact with MYC and are essential for the development of Burkitt lymphoma, and showed that PI3K pathway activation is a key element in the malignant transformation of the B cells. Furthermore, the first study showed that mutations in the transcription factor *TCF3* and its negative regulator *ID3*, and stabilizing mutations in *CCND3* (coding for cyclin D3) were highly prevalent in Burkitt lymphoma, but not DLBCL. The recurrent mutations in *CCND3* were also seen in the second study.

The functional information and the mouse model may, in time, help to target therapy for this disease.

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Original articles Schmitz, R. *et al*. Burkitt lymphoma pathogenesis and therapeutic targets from structural and functional genomics. *Nature* doi:10.1038/nature11378 | Sander, S. *et al*. Synergy between PI3K signaling and MYC in Burkitt lymphomagenesis. *Cancer Cell* doi:10.1016/j.ccr.2012.06.012