IN BRIEF

LEUKAEMIA

The *TEL–AML1* leukemia fusion gene dysregulates the TGF-β pathway in early B lineage progenitor cells

Ford, A. M. *et al. J. Clin. Invest.* 16 Mar 2009 (doi:10.1172/JCI36428)

The concept that certain gene fusions, such as TEL–AML1, enable pre-leukaemic changes but not leukaemia has provoked much interest. Mel Greaves and colleagues show that progenitor B cells expressing TEL–AML1 proliferated more slowly than their normal counterparts *in vivo*, but did not arrest in the presence of transforming growth factor-β (TGFβ). A similar growth advantage in the presence of TGFβ was evident in human cord blood cells expressing TEL–AML1 and this led to the outgrowth of pre-leukaemic early B lineage cells. Thus, early B cells that acquire TEL–AML1 might be selected for in conditions under which there is prolonged expression of TGFβ. These data indicate a plausible mechanism through which a deregulated immune response, as a result of delayed exposure to infection, could promote the selection of a pre-leukaemic TEL–AML1 clone.

ANGIOGENESIS

Edema control by cediranib, a vascular endothelial growth factor-targeted kinase inhibitor, prolongs survival despite persistent brain tumor growth in mice

Kamoun, W.S. *et al. J. Clin. Oncol.* 30 Mar 2009 (doi:10.1200/JCO.2008.19.9356)

Precisely how agents that target vascular endothelial growth factor (Vegf) pathways can increase the survival of some patients with glioblastoma is not known. This paper indicates that cediranib significantly improves the survival of mice with this disease by reducing oedema, rather than slowing the growth rate of the tumour. Oedema is controlled as a result of rapid changes within the tumour vasculature, including reduction in vessel diameter and permeability, and normalization of perivascular cell coverage.

THERAPY

Response of small intestinal epithelial cells to acute disruption of cell division through CDC25 deletion

Lee, G., White, L. S., Hurov, K. E., Stappenbeck, T. S. & Piwnica-Worms, H. *Proc. Natl Acad. Sci. USA* **106**, 4701–4706 (2009)

The CDC25 protein phosphatases are involved in regulating the cell cycle. In mice, disruption of *Cdc25b*, *Cdc25c* or both has no effect, promoting the long-awaited outcome of the single *Cdc25a* knockout and the triple knockout (TKO; *Cdc25a*;*Cdc25b*;*Cdc25c*). This paper shows that *Cdc25a*-null mice are embryonic lethal, whereas conditional deletion of *Cdc25a* in adult tissues has no effect. Deletion of all three CDC25 phosphatases in adult tissues results in the death of the animals. Examination of the TKO mice showed significant changes in the small intestine including G1 or G2 arrest of epithelial cells, epithelial cell differentiation and loss of the absorptive surface of the villi. Interestingly, the crypt stem cells were preserved and this was associated with increased Wnt signalling. As most cancer therapies induce side effects owing to inducing changes in the intestinal tract, it might make sense to use Wnt agonists to potentially protect intestinal stem cells, enabling them to more efficiently repopulate the intestinal tract after chemotherapy.