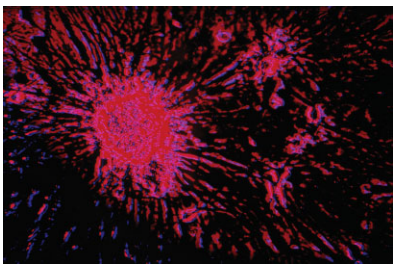
Highlights from this issue

Where does B-cell acute lymphoblastic leukemia originate?

A strategic question in battling B-cell acute lymphoblastic leukemia (B-ALL) is the cellular origin and subsequent evolutionary path of the disease. Chromosomal abnormalities in haematopoietic cells are the likely starting point. However, the cells which are capable of supporting disease progression vary in different B-ALLs and appear to be responsible for spreading, recurrence, and resistance to therapy. Since, B-ALL is often diagnosed at later stages, the typing of cancer cells as malignant counterparts to normal B-cell precursors is likely to be misleading. This is because the path of arrest in B-cell development in cancer may be due to a variety of factors related to oncogenic activation and tumor growth. B-cell plasticity and the ability to reacquire stem/early progenitor features further complicate the picture. On pages 600–609 of this issue, Cobaleda and Sánchez-Garciá discuss this dilemma, and its significance for the proposed cancer stem cell (CSC) hypothesis, which proposes the heterogeneous tissue organization of cancer, with cells capable of renewing the cellular diversity of the original tumor. It is argued that a given CSC phenotype should not be assumed to correlate with the cellular origin of the leukemia. The use of new mouse models of cancer which incorporate CSC theory, oncogenic reprogramming, and B-cell plasticity, may provide significant advantages in clarifying disease evolution and therefore successful therapeutic intervention.



United we age, divided we go out with a bang

Non-cooperating species make no compromises with resources: their members expand in the niche, take as much as they can get, develop quickly, and reproduce once, in massive numbers, before a banal calamity can undermine their vulnerable stand-alone existence (*e.g.*, a mayfly gets eaten by a bird): their life is so short that they do not ''age''. However, as individuals or other entities (*e.g.*, proteins) assemble into complex interacting networks, compromises are made, leading to sub-optimal distribution of maintenance resources to the network's subunits: each subunit therefore ages. This is the premise for the hypothesis of Kiss *et al.* on pages 651–664: in organisms that cooperate in a group society (the so-called ''K-strategists''), the scarcity of resources resulting from distribution in the group leads to individuals' gradual ageing – hand-in-hand with a relatively long life. Such species (*e.g.*, birds and humans) reproduce many times at intervals, and cooperate in communities, but each individual manages with less than ''enough'', in the interest of the group. Ageing appears to arise from the condensation of networks into cooperating units, also at the level of cells. Stem cells are forever young, and they contain a complete diversity of quietly humming genetic networks, just waiting to be reduced and condensed in discrete areas during the process of differentiation into a particular cell type. In differentiated cells, this reduction in network diversity, and condensation of the system into strictly cooperating subnetworks, dooms the cells to senescence, it is claimed. Again, cooperation (also at the level of the tissue) is accompanied by ageing. With numerous other examples, Kiss *et al.* extend their ideas from the level of protein interaction networks up to populations, and even human society.