Kaposi’s sarcoma

Until recently, if someone had asked the cellular origin of the spindle cells of Kaposi’s sarcoma lesions, the answer would probably have been vague. In fact, the histogenesis of the spindle-cell component, the Kaposi’s sarcoma tumour cell, remains controversial. Most of these spindle cells express endothelial markers, but markers for smooth-muscle cells, macrophages, and dendritic cells are also present.1,2 Several aspects of the origin of the spindle cells in Kaposi’s sarcoma remain poorly understood. Although many studies favour an endothelial cell origin,3–6 some suggest a lymphatic-endothelial origin.3 A recent study by Hesei-Wei Wang and co-workers,5 from Chris Boshoff’s laboratory, suggests that Kaposi’s sarcoma herpesvirus; these viruses are characterised by their ability to replicate in lymphoblastoid cells.7 Members of this family, such as Epstein-Barr virus8 and herpesvirus saimiri,9 cause lymphoid neoplasms.

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malignancies. All clinical forms of Kaposi’s sarcoma have indistinguishable histological features. The sarcoma is composed of a variable mixture of irregularly shaped, round capillary, and slit-like endothelial-lined vascular spaces, and spindle-shaped cells accompanied by a variable inflammatory mononuclear-cell infiltrate (figure).

In their report Wang and colleagues show that Kaposi’s sarcoma neoplastic cells share a more similar gene-expression pattern with endothelial cells than any other cell type analysed. They then show that markers of lymphatic and vascular endothelial cells are present in Kaposi’s sarcoma spindle cells. This finding suggests that Kaposi’s sarcoma cells do not truly represent either cell lineage, although the spindle-cell component expresses mainly lymphatic endothelial cell markers. As Wang and colleagues point out, Kaposi’s sarcoma herpesvirus can infect both lymphatic and vascular endothelial cells and induce changes in their transcription pattern, making the gene-expression profile of both cell types closer to each other than to the corresponding uninfected cell type. At the core of these findings is the observation that Kaposi’s sarcoma herpesvirus causes transcriptional reprogramming of the infected cells, and induces over-expression of several cellular cytokines, chemokines, and their receptors. Among these molecules, those related to angiogenesis and lymphangiogenesis, such as angiopoietin-2, VEGF (vascular endothelial growth factor), and VEGF-D, have a particular clinical relevance; their concentrations are substantially higher in plasma of individuals with AIDS and Kaposi’s sarcoma than in healthy donors. In addition, plasma concentrations of angiopoietin-2 and VEGF-D decrease substantially during resolution of Kaposi’s sarcoma with antiretroviral therapy.

What do these results mean to the scientific and clinical community? Although the exact mechanisms whereby these lymphatic endothelial cells achieve the Kaposi’s sarcoma phenotype is not clear, Wang and colleagues’ study strongly suggests an involvement of lymphangiogenic molecules in the pathogenesis of the disorder. As the angiogenic phenotype of Kaposi’s sarcoma spindle cells is expected to be dependent on the upregulation of lymphangiogenic molecules, strategies to target these molecules might be useful. Thus one could speculate that neutralising antibodies to angiopoietin-2, VEGF, and VEGF-D might provide a suitable tool for antilymphangiogenic therapies. Wang’s work should be of interest to a wide readership: a reprogrammed cellular gene expression, which makes different cell types lose their own expression pattern driving the gene-expression profile of one closer to that of the other, is an important mechanism that could be involved in other virally induced cancers. This report will undoubtedly inspire follow-up studies that will further explore the proposed link between Kaposi’s sarcoma herpesvirus and lymphangiogenic molecules.

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I declare I have no conflict of interest.


Faecal occult-blood screening in Burgundy

Recently, Jean Faivre and colleagues reported a screening trial of over 90 000 French adults aged 45–74 who had been allocated by geographic area, in Burgundy, to receive or not receive an invitation to complete faecal occult-blood screening every 2 years. A total of six rounds of screening were offered, and the population was followed up for 11 years after study entry. Between 50% and 60% of the invited population completed tests at each round, with almost 70% of invitees completing at least one test over the course of the trial.

Faivre and colleagues found that allocation to the screening group was associated with a 16% reduction in mortality from colorectal cancer (mortality ratio 0.84, 95% CI 0.71–0.99). The frequency of colorectal cancer did not differ between groups, and all-cause mortality was not reported. The main methodological limitation was the use of geographic small-area allocation, rather than individual or household randomisation, of intervention and control status. This choice was made on practical grounds, and did not seem to result in unequal or dissimilar groups in terms of age, sex, or baseline frequency of colon cancer.

The results of Faivre and colleagues’ trial are consistent with the findings of four previous randomised trials of biennial faecal occult-blood screening of risk reductions for colorectal cancer mortality from 12% to 21%. The Faecal specimens were not rehydrated in the Burgundy trial and dietary restrictions were not used. Test-positive rates were similar to other trials that did not use rehydration: 2.1% were positive on the initial screen and 1.4%