LANA is encoded on a tricistronic transcript with the viral cyclin (v-cyclin; *ORF72*) and FLICE inhibitor protein (v-FLIP; *K13*) homologues. The KSHV v-cyclin induces p53-dependent growth arrest; in p53-null mice, however, v-cyclin induces lymphomas[9]. LANA's interference with p53 function might therefore allow v-cyclin to also have a key role in tumor formation. This would explain the coordinated expression of these two latent KSHV proteins from a common transcript. The induction of cellular cyclin D1 by LANA, as shown by Fujimuro *et al.*[3], also infers that v-cyclin does not provide all the necessary cues, allowing early S-phase entry. Oncogenic viruses often block cellular differentiation to form tumors; the stabilization of β-catenin by LANA could be the main mechanism that KSHV uses to achieve this[5].

Apart from the 'oncogenic cluster' of LANA, v-cyclin and v-FLIP, KSHV encodes other proteins such as interferon regulatory factor and interleukin-6 homologues that could promote tumorigenesis through dysregulation of growth signaling pathways or through immune-evasion strategies. The pathogenesis of KS is more complicated; some of the lytic viral proteins (such as the G-protein-coupled receptor homologue v-GPCR) expressed in a fraction of tumor cells appear to contribute to tumor formation by inducing angiogenesis and cell proliferation through paracrine mechanisms[10,11].

Oncogenic viruses often provide clues to how non-virally induced cancers might develop. The work presented by Fujimuro *et al.* should be of interest not only to aficionados of Wnt signaling: dysregulated shuffling of GSK-3β between the cytoplasm and nucleus could be a universal mechanism involved in other virally and non-virally induced cancers, particularly where mutations in *APC*, *CTNNB1* and *AXIN* are not present but β-catenin stabilization is seen[4].

1. Chang, Y. *et al.* Identification of herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma. *Science* **266**, 1865–1869 (1994).
2. Boshoff, C. & Weiss, R.A. AIDS-related malignancies. *Nat. Rev. Cancer* **2**, 373–382 (2002).
3. Fujimuro, M. *et al.* A novel viral mechanism for dysregulation of β-catenin in Kaposi's sarcoma-associated herpesvirus latency. *Nat. Med.* **9**, 300–306 (2003).
4. Polakis, P. Wnt signaling and cancer. *Genes Dev.* **14**, 1837–1851 (2000).
5. Kielman, M.F. *et al.* Apc modulates embryonic stem-cell differentiation by controlling the dosage of β-catenin signaling. *Nat. Genet.* **32**, 594–605 (2002).
6. Ballestas, M.E., Chatis, P.A. & Kaye, K.M. Efficient persistence of extrachromosomal KSHV DNA mediated by latency-associated nuclear antigen. *Science* **284**, 641–644 (1999).
7. Friborg, J., Kong, W., Hottiger, M.O. & Nabel, G.J. p53 inhibition by the LANA protein of KSHV protects against cell death. *Nature* **402**, 889–894 (1999).
8. Radkov, S.A., Kellam, P. & Boshoff, C. The latent nuclear antigen of Kaposi sarcoma-associated herpesvirus targets the retinoblastoma-E2F pathway and with the oncogene *Hras* transforms primary rat cells. *Nat. Med.* **6**, 1121–1127 (2000).
9. Verschuren, E.W., Klefstrom, J., Evan, G.I. & Jones, N. The oncogenic potential of Kaposi's sarcoma-associated herpesvirus cyclin is exposed by p53 loss *in vitro* and *in vivo*. *Cancer Cell* **2**, 229–241 (2002).
10. Bais, C. *et al.* G-protein-coupled receptor of Kaposi's sarcoma-associated herpesvirus is a viral oncogene and angiogenesis activator. *Nature* **391**, 86–89 (1998).
11. Montaner, S. *et al.* Endothelial infection with KSHV genes *in vivo* reveals that vGPCR initiates Kaposi's sarcomagenesis and can promote the tumorigenic potential of viral latent genes. *Cancer Cell* **3**, 23–36 (2002).

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Kohn to Kaposi

"The disease leads to death, and it does so within a short period of two to three years...The disease must, from our present experience, be considered from the onset not only as incurable but also as deadly."—Moritz Kaposi, 1872

Moritz Kaposi was born Moritz Kohn, in the village of Kaposvar in the Austro-Hungarian Empire. By the time he went to study dermatology in Vienna, he was known as Moritz Kaposi. It is still debated as to why he changed his name; it is unlikely to be due to the pressures of anti-Semitism, but more likely because many other dermatologists at the time in Vienna were called Kohn and he wanted to stand out. Kaposi described sarcomatous skin lesions on the legs and arms of elderly men in 1872 (ref. 1). This became known as 'classic Kaposi sarcoma' and is predominantly found in men of Mediterranean, Eastern European or Jewish heritage. For over 100 years, Kaposi sarcoma (KS) remained a rare curiosity to cancer researchers, until it shot to prominence as the sentinel of the AIDS epidemic[2]. The particularly aggressive form of KS in HIV-1–infected individuals prompted Robert Gallo and colleagues to study the role of the HIV-1 Tat protein in KS tumor growth. They showed a synergistic effect of Tat with cytokines to promote KS formation. However, the observation that KS is present mainly in gay men infected with HIV-1, and not in individuals who acquired HIV-1 through a blood transfusion or intravenous drug use, impelled husband-and-wife team Yuan Chang and Patrick Moore, pathologist and epidemiologist respectively, to search for an infectious agent in KS. In 1994, with their colleagues at Columbia University (New York), they identified sequences of a new human herpesvirus, which they called KSHV, in an AIDS-KS lesion[4].

KAPOSI (1837-1902).

Courtesy of Károly Nagy, National Institute of Dermato-Venereology, Budapest, Hungary.

1.Kaposi, M. Idiopathisches multiples pigmentsarcom der haut. *Arch. Dermatol. und Syphillis* **4**, 265–273 (1872).
2.Kaposi's sarcoma and *Pneumocystis* pneumonia among homosexual men—New York City and California. *MMWR Morb. Mortal. Wkly. Rep.* **30**, 305–308 (1981).
3.Ensoli, B. *et al.* Synergy between basic fibroblast growth factor and HIV-1 Tat protein in induction of Kaposi's sarcoma. *Nature* **371**, 674–680 (1994).
4.Chang, Y. *et al.* Identification of herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma. *Science* **266**, 1865–1869 (1994).

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