VIROLOGY

Inducing instability

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An intriguing paper in a recent issue of *Current Biology* shows that the non-cytolytic virus Mason–Pfizer monkey virus (MPMV) can cause cancer by inducing chromosomal instability through cell fusion.

Most human tumours are associated with chromosomal instability, but whether this is a cause or a consequence of cancer remains unclear. However, the molecular mechanisms that are responsible for chromosomal instability in sporadic cancers are now beginning to be elucidated. One theory, which dates back more than 100 years, is that chromosomal instability can be caused by cell fusion. In previous work, Duelli *et al.* found that MPMV could induce fusion of normal human cells, which did not proliferate upon fusion. If, however, one of the fusion partners expressed an oncogene then the resultant hybrid fused cells had a transformed, proliferative phenotype. The fusion activity could be purified from MPMV-infected cells in the exosome fraction, and is referred to as MPMV^{E}.

In this follow-up study, Duelli *et al.* established three populations of human D551 fibroblast cells. One population (D) was transduced with the *E1A* and *HRASV12* oncogenes and the second (DV) was infected with MPMV^{E} but not allowed to fuse and then transduced with both oncogenes. Finally, a test population of hybrid cells (DVH) was created by MPMV^{E}-mediated fusion of two cell populations that had been separately transduced with *E1A* and *HRASV12*. Karyotyping revealed the presence of substantial chromosomal instability only in the fused cells, with heterogeneity in chromosome number and an increase in both numerical and structural aberrations. The full extent of the chromosomal instability present was revealed by spectral karyotyping, a karyotyping method that uses fluorescent probes for greater sensitivity and that showed that each of the ~90 DVH cells examined had a unique karyotype.

The key question was whether the MPMV^{E}-fusion-induced chromosomal instability promoted tumorigenesis and this was addressed in a mouse model. Tumour formation in nude mice was induced only by the DVH population and not by either of the control populations, thus establishing a link between tumorigenesis and virus-induced cell fusion. Further analysis showed that the DVH fibroblast cells induced the formation of tumours that were more characteristic of aggressive epithelial-derived carcinomas than of fibroblast-derived malignancies. As contamination with an epithelial cell line was ruled out, the authors conclude that this shows "the randomizing power of cell fusion". Finally, in support of the idea that cancers can evolve, the authors determined that explanted cells induced a more aggressive tumorigenic phenotype than the parental hybrids.

The link between viruses and cancer is well known, with viruses thought to be involved in an estimated 10–20% of all cancers. However, this work raises the possibility that fusogenic viruses that were not previously thought to be carcinogenic might in fact be able to cause cancer by inducing chromosomal instability through cell fusion.

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ORIGINAL RESEARCH PAPER Duelli, D. M. *et al.* A virus causes cancer by inducing massive chromosomal instability through cell fusion. *Curr. Biol.* **17**, 1–7 (2007)
FURTHER READING Duelli, D. M. *et al.* A primate virus generates transformed human cells by fusion. *J. Cell Biol.* **171**, 493–503 (2005)