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TECHNOLOGY

A targeted viewing

The killing part is easy; the real challenge — when it comes to dealing with cancer cells — is to find the cells to be removed, or indeed treated, and to be able to see how well you are doing. Researchers now have the tool for this purpose; a hybrid virus that combines the efficiency of adeno-associated virus (AAV) and the adaptability of a bacteriophage that can target specific cancer cells and deliver to them imaging or anti-cancer agents.

Eukaryotic viruses enter cells efficiently and specifically. This specificity is also a drawback, as their strong preference for particular molecules limits their versatility. Bacterial viruses, on the other hand, are not very accomplished at entering mammalian cells — but they are indifferent to cell type, which allows them to be engineered to target eukaryotic cell-surface markers. Renata Pasqualini, Wadih Arap and colleagues put two and two together and built a hybrid virus that delivers DNA as efficiently as a mammalian virus but, like a phage virus, can be targeted to a desired protein. The aim was to create a unique tool that would combine tumour targeting and molecular-genetic imaging.

The chimeric molecule consisted of the *cis*-regions of mammalian AAV and the ssDNA of the fd-tet phage, which is derived from M13. The phage portion of the construct was engineered to encode a peptide that would allow the hybrid DNA to bind to αv-integrins, which are cell-surface markers of tumour blood vessels, and to be internalized by such cells. Indeed, when the construct was injected into nude mice it was rapidly taken up specifically by the vasculature of tumour xenografts, as expected, and hybrid viruses that carried *GFP* also stained vascular cells specifically and stably. A qualitatively similar effect was seen in genetic mouse models of cancer. Similarly, delivery of the 'suicide' gene *HSVtk* using this tool reduced tumour size considerably, showing that anti-cancer agents could be delivered to therapeutic effect *in vivo*.

The success of the hybrid virus highlights its potential usefulness — and that of eventual derivatives — in both a clinical and research setting. Tumours could be found, highlighted and then monitored non-invasively and cost-effectively while being targeted with specific genes. The *HSVtk* marker is picked up by a routine PET (positron emission tomography) body scanner and so, from a practical point of view, this tool is potentially ready for clinical use.

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ORIGINAL RESEARCH PAPER Hajitou, A. *et al.* A hybrid vector for ligand-directed tumor targeting and molecular imaging. *Cell* **125**, 385–398 (2006)