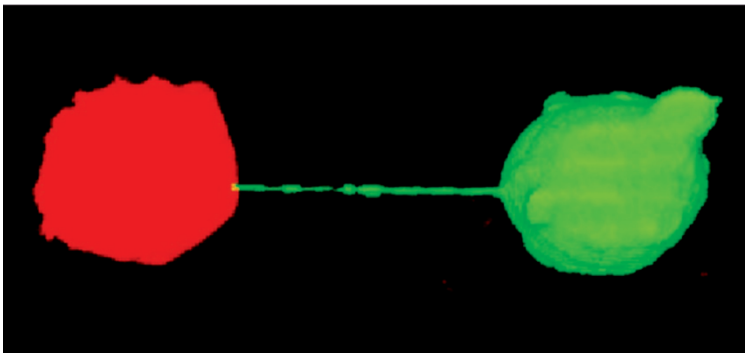
CELL BIOLOGY

Tube travel for HIV?

Retrovirus-infected cells are more infective than naked viruses. Understanding how retroviruses move directly from cell to cell is important, as infection by this route might shield viruses from the immune response. Now, Sowinski *et al.* report in *Nature Cell Biology* that membrane nanotubes can connect T cells and that these tubes can transport HIV-1 from infected to non-infected cells.

Previous observations from the laboratory of Walther Mothes used fluorescence microscopy to show that murine leukaemia virus (MLV), avian leukosis virus and HIV-1 can move from infected to non-infected cells in culture by 'surfing' along the outside of viral cytonemes. Viral cytonemes were formed by long, thin filopodial-membrane projections that extended from the target cell and became tethered to the infected cell by viral proteins.

Using confocal laser scanning microscopy, Sowinski and colleagues observed that numerous nanotubes connect fluorescently labelled cultured T cells. These nanotubes were different to viral cytonemes, as they formed independently of viral proteins through cells coming into contact and moving apart. Nanotubes were 5–10 times longer than the cytonemes that MLV used to surf from cell to cell and extended to more than 100 µm. By surrounding T cells with an extracellular matrix, Sowinski *et al.* simulated the environment of a mammalian tissue. Nanotubes were readily formed under these conditions, and intriguingly some of them were curved and able to negotiate obstacles in the matrix to connect different T cells.



Long membrane tethers — membrane nanotubes — readily form between Jurkat T cells labelled with the membrane dyes DiO (green) and DiD (red). Image kindly provided by Daniel Davis, Imperial College, UK.

Labelled cell-membrane proteins of different T cells did not intermix along nanotubes, but instead revealed a dynamic junction that moved along the nanotubes. Cytosolic green fluorescent protein also flowed into nanotubes, but the junction prevented it from entering the adjoining T cell. Unlike the nanotubes that connect myeloid cells, T-cell nanotubes did not transport a calcium signal between cells, and the authors instead investigated whether HIV-1 could spread using nanotubes.

Sowinski *et al.* mixed T cells that contained labelled infectious HIV-1 with uninfected cells. Transfer of viral proteins to uninfected cells was detected within 1 hour of nanotube formation, whereas cells that were not physically connected by nanotubes remained uninfected. Labelled viral proteins moved rapidly from one T cell to another through nanotubes, and disrupting nanotubes by agitation prevented protein movement. Blocking the host receptor CD4 with antibody prevented labelled viral proteins from trafficking through nanotubes, which indicated that the intercellular spread of HIV-1 is receptor dependent.

By monitoring the movement of the virus through the labelling of its proteins, the authors inferred that nanotubes could transport HIV-1 between T cells. Interconnecting T-cell nanotubes have not yet been visualized *in vivo*, and how HIV-1 moves across the junction has not been addressed. However, this research is an important step towards defining a new mechanism to explain how persistent HIV-1, and perhaps other viruses, spread from cell to cell.

Susan Jones

ORIGINAL RESEARCH PAPER Sowinski, S. *et al.* Membrane nanotubes physically connect T cells over long distances presenting a novel route for HIV-1 transmission. *Nature Cell Biol.* **10**, 211–219 (2008)

FURTHER READING Sherer, N. M. *et al.* Retroviruses can establish filopodial bridges for efficient cell-to-cell transmission. *Nature Cell Biol.* **3**, 310–315 (2007)