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Prions hijack tunneling nanotubes for intercellular spread

Edwin Schiff, Karine Gousset, Duncan Browman, Christelle Langevin, Zrinka Marijanovic and Chiara Zurzolo*

Address: Unité Trafic Membranaire et Pathogenese, Institut Pasteur, 75015 Paris, France

Email: Chiara Zurzolo* - zurzolo@pasteur.fr

* Corresponding author

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In the infectious variant of Creutzfeldt-Jacobs disease (vCJD), prions (PrPSc) enter the body by oral exposure with contaminated foodstuffs. Prions may then spread from the intestinal entry site to the central nervous system (CNS) by intercellular transfer from the lymphoid system to the peripheral nervous system (PNS). Several mechanisms have been proposed for these intercellular transfer events, including hitch-hiking on membrane-coated viruses, transfer *via* exosomes or by GPI-painting and different cell types such as dendritic cells, follicular dendritic cells or macrophages have been proposed to be involved. However, the mechanism of cell-to-cell spread remains elusive.

Tunneling nanotubes (TNTs) have recently been identified as a novel means of cell-cell communication both *in vitro and in vivo*. Here we show that TNTs transfer cellular PrP (PrPc) and PrPSc between cells of the same and different origin. Significantly, we observed fluorescently-labelled PrPSc transferring *via* TNTs from dendritic cells (DCs) to primary neurons. Since DCs can interact with peripheral neurons in lymphoid organs, TNT mediated intercellular transfer would allow neurons to retrogradely transport prions to the CNS. We propose that TNTs are involved in the spreading of infectious prions from the peripheral site of entry to the PNS by neuroimmune interactions and within the CNS.