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SIGNALLING

Vesicle vehicles of genetic information

Exosomes are a type of extracellular vesicle that can transfer cellular cargo between cells and have emerging importance in cell–cell communication. The exosome-mediated transfer of genetic information in the form of microRNAs (miRNAs) or mRNAs has been primarily shown *in vitro*; a new study now suggests that such transfer occurs between the haematopoietic system and the brain *in vivo*.

Ridder *et al.* used a transgenic reporter mouse model in which tissue-specific promoters drive the expression of the Cre recombinase in the haematopoietic system, and Cre-mediated recombination then activates the expression of *GFP* or *lacZ* reporter genes. This enabled the tracking of cells and tissues that expressed Cre. Crucially, in addition to the expected reporter activation in the haematopoietic system, reporter-positive cells were also identified from tissue sections in the liver, lung and small intestine, as well as in the Purkinje neurons of the brain.

Focusing on the Purkinje neurons, the authors investigated the source of the Cre activity. They found no binuclear reporter-positive cells, which indicated that fusion with haematopoietic cells was not the cause. Additionally, alternative transgenic mice with *Cre* driven by different tissue-specific promoters and the transplantation of Cre-expressing haematopoietic cells into non-Cre-encoding hosts further suggested that Cre activity was derived from the haematopoietic system rather than from 'leaky' expression of Cre in non-haematopoietic tissues.

Turning to whether extracellular vesicles might have mediated an extracellular transfer of Cre recombinase, Ridder *et al.* purified exosomes from the peripheral blood of the transgenic mice and detected *Cre*-encoding mRNA, but not the Cre protein itself, inside the exosomes. Furthermore, injecting exosomes that contained *Cre* mRNA into the brain led to reporter gene expression in non-Cre-encoding mice.

Although the source cells and anatomical transfer routes of *Cre* mRNA into the brain remain unclear, various forms of inflammation increased the efficiency of reporter gene activation in several neuronal cell types, which indicated that cytokine signalling and/or vascular permeability might influence exosome-mediated RNA transfer.

Finally, the authors showed that Purkinje neurons with activated reporter genes contained a different repertoire of expressed miRNAs relative to adjacent unactivated cells. The miRNAs overrepresented in the reporter-expressing cells included haematopoietic-specific miRNAs that were also detected in blood exosomes; thus, in addition to the *Cre* mRNA, exosomes are likely to transfer endogenous miRNAs to alter the properties of recipient cells.

It will be interesting to further decipher the pervasiveness and physiological roles of the exosome-mediated transfer of endogenous RNAs *in vivo*, and whether this study has implications for optimizing drug delivery to the brain.

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ORIGINAL RESEARCH PAPER Ridder, K. *et al.* Extracellular vesicle-mediated transfer of genetic information between the hematopoietic system and the brain in response to inflammation. *PLoS Biol.* **12**, e1001874 (2014)