

Transfer of genetic information between the hematopoietic system and the brain without cell fusion

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Bone marrow-derived cells (BMDCs) contribute to non-hematopoietic tissues after transplantation into lethally irradiated hosts by cell fusion. While being a rare event, chronic inflammation leads up to a several orders of magnitude increase in the formation of binucleated heterokaryon Purkinje neurons in the cerebellum. To what extent these cell fusion events occur under physiologically relevant conditions remains unclear. Here, we show that expressing Cre recombinase specifically in the hematopoietic compartment causes the induction of reporter gene expression in non-hematopoietic tissues, including Purkinje neurons in the brain without any evidence for cell fusion. We show that recombination is induced by the intercellular transfer of Cre recombinase messenger RNA. Biochemical analysis demonstrates that Cre RNA is contained in secreted membrane vesicles, specifically in exosomes. These observations reveal the existence of a previously unrecognized mechanism to communicate RNA-based signals between the immune system and various organs, including the brain, which is activated by peripheral inflammation.