REGIONAL CENTRE FOR BIOTECHNOLOGY
Journal Club

Delivery of siRNA to the mouse brain by systemic injection of targeted exosomes

Lydia Alvarez-Erviti et al. (2011)Nature Biotechnology, Volume 29, 341-345.

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Wednesday, October 3, 2012
4:00 pm
Seminar Room

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To realize the therapeutic potential of RNA drugs, efficient, tissue-specific and nonimmunogenic delivery technologies must be developed. Here we show that exosomes—endogenous nano-vesicles that transport RNAs and proteins1,2—can deliver short interfering (si)RNA to the brain in mice. To reduce immunogenicity, we used self-derived dendritic cells for exosome production. Targeting was achieved by engineering the dendritic cells to express Lamp2b, an exosomal membrane protein, fused to the neuron-specific RVG peptide3. Purified exosomes were loaded with exogenous siRNA by electroporation. Intravenously injected RVG-targeted exosomes delivered GAPDH siRNA specifically to neurons, microglia, oligodendrocytes in the brain, resulting in a specific gene knockdown. Pre-exposure to RVG exosomes did not attenuate knockdown, and non-specific uptake in other tissues was not observed. The therapeutic potential of exosome-mediated siRNA delivery was demonstrated by the strong mRNA (60%) and protein (62%) knockdown of BACE1, a therapeutic target in Alzheimer's disease, in wild-type mice.