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Cell fate change induced by extracellular vesicles

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Extracellular vesicles, encompassing exosomes and microvesicles, are capable of altering cell fate of cell species. Lung-derived microvesicles enter target murine marrow cells inducing expression in the marrow cells of mRNA for surfactants A, B, C and D clara cell protein and aquaporin 5. These cells also show expression of surfactant protein and show increased capacity to form epithelial lung cells after transplantation into lethally irradiated mice. Our studies have shown that initially originator lung cell mRNA is transferred to marrow cells along with a transcriptional regulator which induces the murine marrow cells to produce lung-specific mRNA. However in cytokine supported liquid culture the originator cell mRNA is rapidly degraded, but the transcriptionally induced lung mRNA persists at high levels out to 13 weeks. Thus there has been a stable long term epigenetic change induced in the marrow cells. This phenomena appears to be RNAase sensitive leading to the conclusion that the active agent is a non coding RNA. The vesicles contain mRNA, microRNA, protein and some DNA. Similar results have been obtained studying liver derived vesicles and expression of albumin mRNA in target marrow cells. We have found that tissue specific changes occur with brain derived and cardiac derived vesicles and marrow cells. We have also observed that mesenchymal stem cell derived vesicles have the capacity to reverse pulmonary hypertension in a mouse monocrotaline model. Extracellular vesicles have great therapeutic potential.

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