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Hypothesis

Do Neural Cells Communicate with Endo via Secretory Exosomes and Microvesicl

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Abstract

Neurons, glial, cells, and brain tumor cells tissues release small which may represent a novel mechanism by which neuronal embryonic and mature brain. If CNS-derived vesicles can enter th endothelial cells in the peripheral circulation and with cells concern

1. Introduction

About a year and a half ago, I reviewed evidence that cells withir containing RNAs and proteins among themselves in a novel emphasized the possible role of secretory exosomes as a mechanis molecules across synapses, corresponding to the morphological a long noted by neuroanatomists. However, there are numerous ad of molecules by vesicles moving freely from cell to cell or by cyto into another. For example, astrocytes can provide neuroprotective cells can provide polyribosomes to the axons that they ensheath possibility that central nervous system-(CNS-) derived vesicles m the brain, and that they may potentially find their way to the bloo

cells and with cells of the immune system.

Secretory exosomes are formed by a specific process of invaginat formation of multivesicular bodies [4], or on the cell surface, res plasma membrane [5]. Microvesicles are little fragments that are Microvesicles are generally thought to be larger than exosomes, bu distinct [6], and there may be additional types of vesicles that ca and microvesicles have been shown to be shed in a regulated fash [8] and astrocytes [9]; they have cell-adhesion molecules on the certain target cell types and to be internalized (e.g., [9, 10]).

In several cases, the internalized mRNAs have been shown to be gene transfer to the target cells [9–11]. Studies of endothelial ce can alter their gene expression and activate thrombogenicity, apop

2. Do CNS-Derived Vesicles Interact with Endotheli

Secretory exosomes have been detected within the cerebrospinal 17], and neuron-enriched microRNAs have been detected in the c that neural cells do release vesicles into the extracellular space concurrently within the developing brain [19, 20]; both invo differentiation, and both respond to some of the same patternin growth factor), and so forth. Endothelial cells interact with neu "neurovascular unit" [21], and these interactions are necessa junctions that underlie the blood-brain barrier [22]. Transfer of v may interact with endothelial cells during embryogenesis. More mature brain and can be stimulated in response to neuronal activ arena in which neural-derived cues interact with endothelial ce glioblastoma-derived microvesicles can stimulate angiogenesis of that would be expected to support tumor growth in vivo [11].

3. Can CNS-Derived Vesicles Reach the Bloodstrean

Blood plasma or serum is an abundant source of microRNAs a secretory exosomes and/or microvesicles (e.g., [24–33]). Mar contribute vesicles to the bloodstream. Placental-derived microR pregnancy [24], whereas vesicles bearing tumor-specific antigen related to the tumor cells from which they derive (e.g., [25]). Ace well as other organs, results in elevated levels of the liver-specific

To date, no evidence has been published demonstrating that vesic bloodstream. (Glioblastoma cells have been reported to shed vesic blood vessels may be aberrant and not representative of norm causes elevated levels of numerous microRNAs in the blood that a was interpreted by the authors as likely due to neural damage pro Chief Scientific Officer of Xenomics, Inc., presented unpublish conference on "microRNA in Human Disease and Development microRNAs characteristics of brain expression were detectable in l were elevated in individuals poststroke in a time-dependent mann Alzheimer disease, though it was not examined whether the microR

What mechanisms might permit CNS-derived vesicles to reach the

prevent movement of large molecules into and out of the brain, transported across capillaries. However, the blood-brain barrier exosomes may be free to communicate with the blood at developn that clearance of the cerebrospinal fluid into the blood ma circumventricular regions of the brain appear to be devoid of a b postrema, choroid plexus, subfornical organ, supraoptic crest, Furthermore, exit of vesicles may be expected to occur under patl is compromised, for example, following trauma, cell death, or infla

4. Conclusion

There is a growing appreciation that secretory exosomes, micrc vesicles comprise a physiological channel for cell-cell communica bloodstream. Neurons and glial cells in the brain also appear tc trophic interactions and synaptic plasticity [1]. CNS-derived se potential to interact with endothelial cells during developmental brain. These interactions should have functional significance, inso coordinated responses both in the developing and mature brain [2(

Recent studies also raise the possibility that CNS-derived vesicl endothelial cells in the peripheral circulation. This would repres nervous system and the cardiovascular system. Circulating vesicle surveillance and activation [7]. Perhaps future issues of *Cardiovas* that provide evidence for this channel and that explore the meanin

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