# Potential roles of extracellular vesicles in brain cell-to-cell communication

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Extracellular vesicles (EVs) are released into the extracellular space from both cancer and normal brain cells, and are probably able to modify the phenotypic properties of receiving cells[1]. EVs released from astrocytes and neurons contain FGF2 and VEGF[2-3] and induce a 'blood-brain barrier' (BBB) phenotype in cultured brain capillary endothelial cells (BCECs, unpublished results), On the other hand, EVs from G26/24 oligodendroglioma induce apoptosis in neurons and astrocytes[4-5]. These effects are probably due to Fas Ligand and TRAIL, present in G26/24 vesicles[4-5]. Moreover, G26/24 EVs contain extracellular matrix remodeling proteases (such as ADAMTS)[6], H1.0 histone protein, and H1.0 mRNA[7]. In particular, we previously hypothesized that G26/24 cells, and tumor cells in general, can escape differentiation cues, and continue to proliferate by eliminating proteins, such as the H1° linker histone (and its mRNA) [7], which could otherwise block proliferation.
To study vesicle release in a system that can better resemble *in vivo* conditions, astrocytes and BCECs were cultured on poly-L-lactic acid (PLLA) scaffolds and tested for their ability to grow and survive on this three-dimensional structures. We analyzed in parallel the cell growth in 2D and 3D culture systems and observed the differences in cell morphology by fluorescence analysis: three-dimensional scaffolds have the ability to guide cell growth, provide support, encourage cell adhesion and proliferation. Astrocytes[8] and BCECs (unpublished results) adapted well to these porous matrices, not only remaining on the surface, but also penetrating inside the scaffolds.
EVs released by astrocytes in these scaffolds are probably exosomes, as suggested by transmission electron microscopy pictures, and by the presence of intracellular structures resembling multivesicular bodies. This 3D cell culture system could be further enriched to host different brain cell types, in order to set , for example, an *in vitro* model of BBB, that may be useful for drug delivery studies, and for the formulation of new therapeutic strategies for the treatment of neurological diseases.

**References**

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