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Altered intercellular diffusion of misfolded proteins in neuroglia

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Intercellular communication is a physiological mechanism underlying cellular and systemic homeostasis. This occurs either through direct cell to cell contact (e.g. trogocytosis and tunneling nanotubes) or it involves vesicles secretion (e.g. endosome-derived exosome and microvesicles) (1,2). The release of extracellular vesicles is recruited in physiological processes while it plays a crucial role in protecting cells from accumulation of dangerous or waste compounds. Recent evidence suggests that altered intercellular communication of misfolded proteins is involved in tumors and neurodegeneration as well, thus posing cell-to-cell communication as an unconventional mechanism of disease spreading (3,4). In the present study we performed ultrastructural dissection of cell-to-cell communication in *vitro* using an experimental model of Glioblastoma Multiforme (GBM). Ultrastructural analysis was carried out by using transmission electron microscopy (TEM), which is the gold standard for vesicles detection, identification and size determination. This experimental approach was combined with immunocytochemistry and staining for glycated end products. Evidence is provided here showing increased amount of misfolded proteins including prion protein and alpha synuclein which are released in the form of glycated compounds. Release of glycated misfolded proteins can be modulated by altering specific protein clearing pathways. These studies set the stage for further investigations into multiple roles of cell-to-cell communication in neurodegeneration and disease progression.

References

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Keywords

Cell-to-cell communication; ultrastructure; electron microscopy; U87MG.