Treating Brain Diseases: Curcumin Loading of Exosomes

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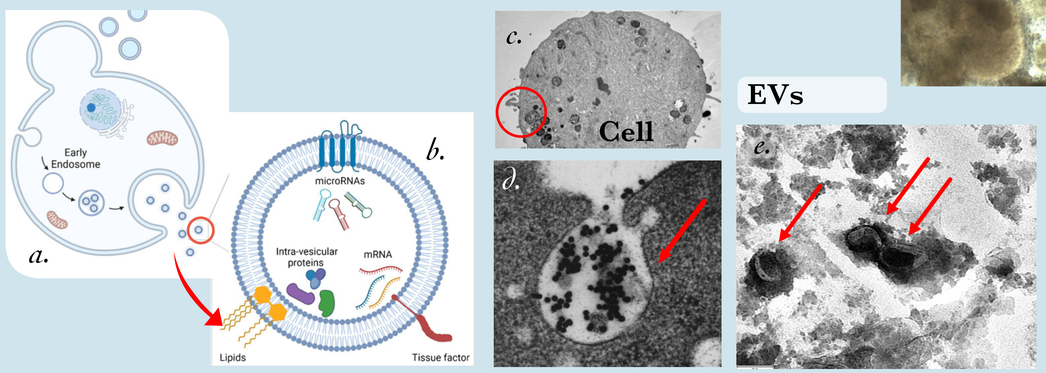
Background

•Maladies of the brain, such as Alzheimer's disease, Parkinson's disease, and brain tumors, are among the most difficult to treat as most medications cannot diffuse into the blood brain barrier (BBB).

• Administering medication via extracellular vesicles (EVs) would bypass this issue as they have an intrinsic ability to penetrate most biological barriers, do not elicit acute immune rejection, can be produced in large quantities, and are highly engineerable.

•One major obstacle that currently stands in the way of utilizing exosomes as drug delivery systems is how to effectively load them.

•The goal of this study is to determine the loading efficiency of curcumin into choroid plexus derived EVs using sonication, incubation, and freeze-thaw cycling.



Figures 1. a-e. EVs exiting the cell: diagram vs micrograph
Harding, C. V., Heuser, J. E., & Stahl, P. D. (2013). Exosomes: Looking back three decades and into the future. Journal of Cell Biology, 200(4), 367–371.

Methods

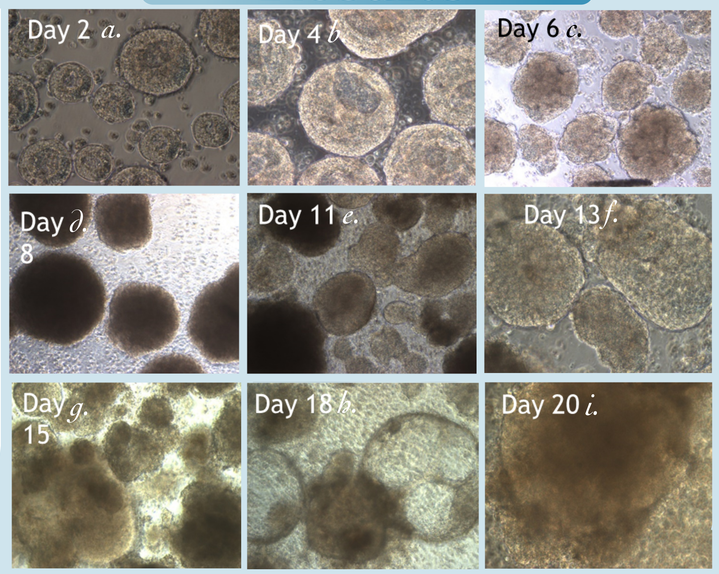
Undifferentiated stem cell cultures were treated with growth factors to become choroid plexus (ChP) in vitro. Throughout the culture period, cell media was collected and used to isolate the human induced pluripotent stem cell (hiPSC) derived EVs.

The EVs were loaded with curcumin in 3 different manners: sonication, incubation, and freeze-thaw cycling.

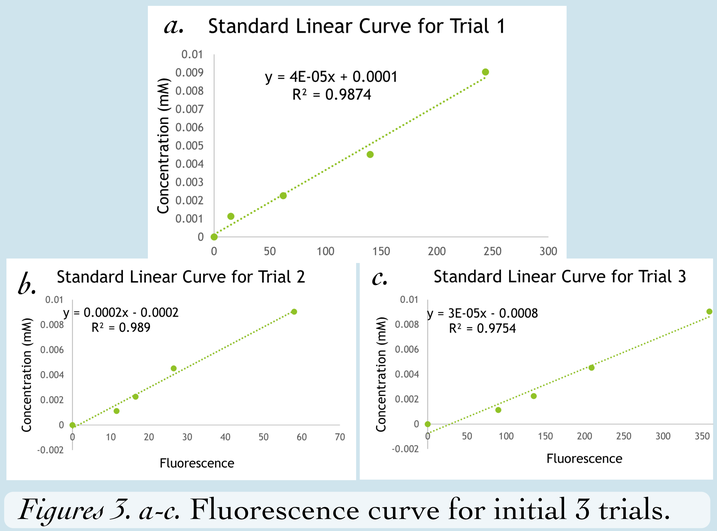
Loaded EV samples were then placed in a microplate reader to create a curcumin vs fluorescence plot, the slope of which is used to determine the loading efficiency of each technique.

EVs are then added to organoids treated with A-Beta cells to assess the anti-inflammatory response of the loaded EVs.

Results



Figures 2. a-j. Growing choroid plexus



Figures 3. a-c. Fluorescence curve for initial 3 trials.

Discussion

Preliminary data has been collected to determine the loading efficiency of loading curcumin into mesenchymal stem cells (MSC)-derived isolated exosomes via sonication. This was done as proof of concept in order to examine the loading capabilities of curcumin, to develop an effective curcumin solution, and to test loading protocols.

The following observations and results were obtained:

• Curcumin is highly hydrophobic and therefore difficult to make into a solution: most likely causing the variance in measured fluorescence for the dilutions of curcumin.
• Trial 1 loading efficiency: 34.8%.
• Trial 2 loading efficiency: 12.69%.
• Trial 3 loading efficiency: 30.27%.
• Previous studies show that the loading efficiency of sonication ranges between 8-30%.

Future works

•Increase solubility of curcumin by dissolving it in a more basic solution rather than PBS .

•Increase bioavailability of curcumin by adding piperine to the solution.

•Observe potential synergistic effect in anti-inflammatory response of a curcumin & vitamin D3 solution to more effectively clear plaque linked to brain diseases.

Reference

Muok L., Liu, C., Chen, X., Esmonde, C., Arthur, P., Wang, X., Singh, M., Driscoll, T., & Li, Y. (2023). Inflammatory Response and Exosome Biogenesis of Choroid Plexus Organoids Derived from Human Pluripotent Stem Cells. Int J Mol Sci, 24(8):7660.

Acknowledgement

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