# Development of Cell membrane-coated oil in water nano-emulsions as biomimetic nanocarriers

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## Introduction

Oil in water nano-emulsions (O/W NEs or NEsoSOme) are an ideal system for the encapsulation of lipophilic molecules. The kinetic stability of O/W NEs is usually increased via layer-by-layer strategies [1, 2]. However, they have some limitations including short circulation time, immune recognition, poor tumor accumulation or penetration. Recently, improving nano-carrier circulation times has gained considerable attention and, one of the most innovative is based on biomimetic systems deriving by extracted cell-membrane[3]; this coating strategy is known to elude the immune system, improving therapeutic efficacy and drug accumulation[4]

## Experimental

Here, we report for the first time a new cell membrane (CM) coated nanomaterial - composed by membranes extracted from glioblastoma cancer cells (U87-MG) - deposited on NEsoSOmes through a liquid–liquid interface method to produce highly controllable membrane caked nano-capsules, namely CM-NEsoSOmes. CM-NEsoSOmes were fully characterized by different techniques including Cryo-transmission electron microscopy (CRYO-TEM), nanoparticle tracking analysis (NTA), stimulated emission depletion (STED) and Confocal Microscopy. Furthermore, CM-NEsoSOmes cytotoxicity and uptake were tested on human dermal fibroblast (HDF)[3].

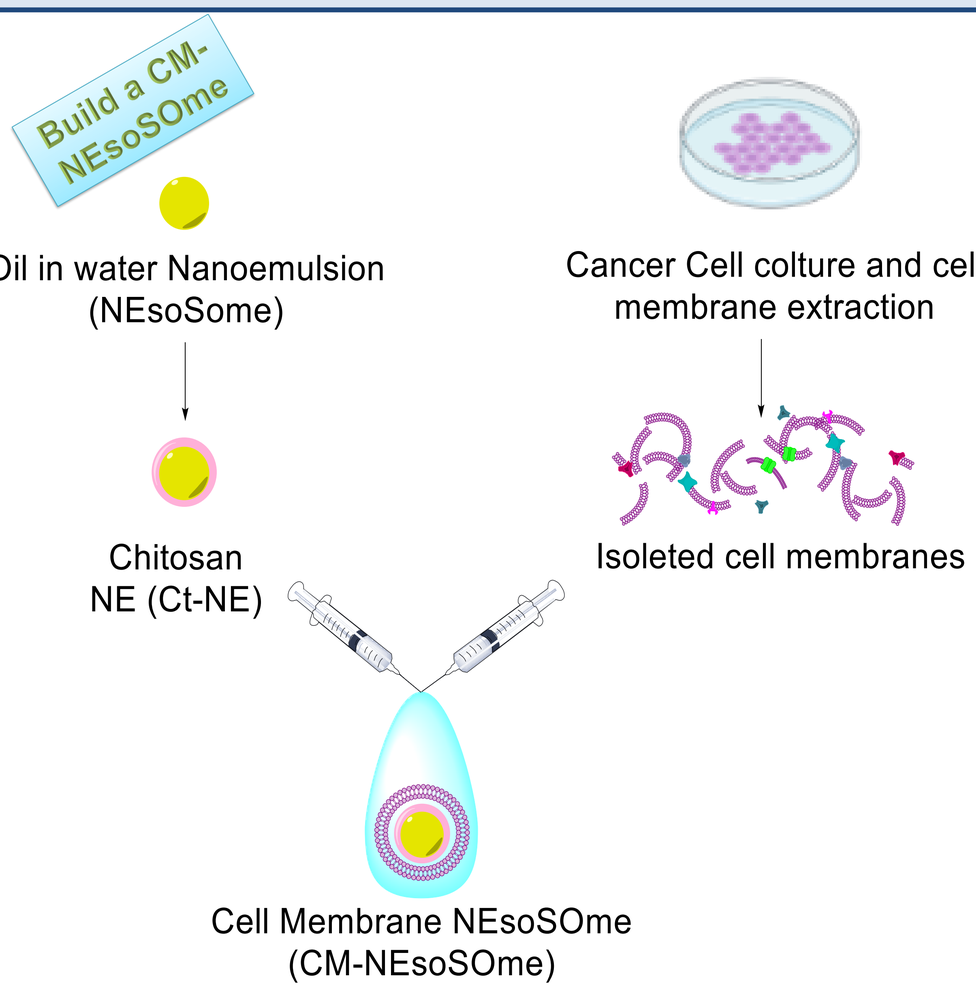


**Fig 1** A brief schematization of CM-NEsoSome production process

## Results

### Nanocarrier Physiochemical characterization

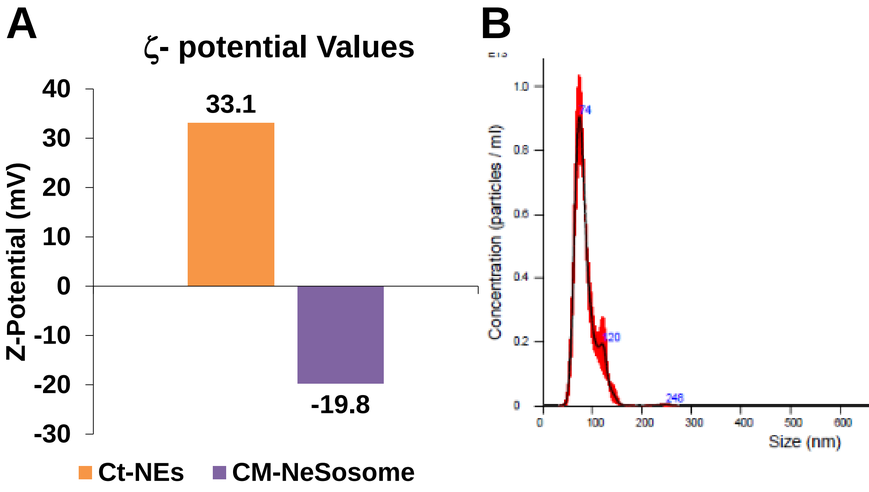


**Fig 2** . **A)** ζ-potential values of Ct-NEs, (***orange***) and CM-NEsoSOme(***violet***) and NTA analysis of **B)** Ct-NEs,and **C)** CM-NEsoSOme.

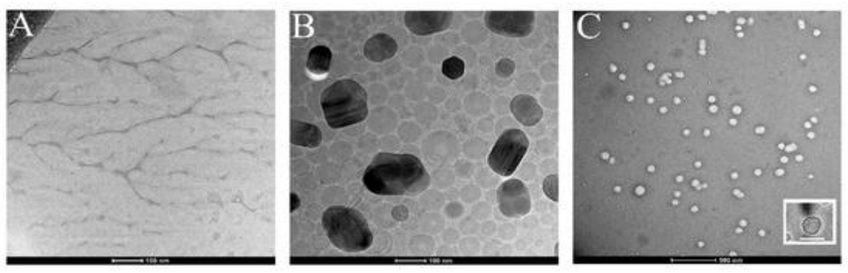


**Fig 3** Cryo-Tem images of **A)** extracted U87 cell membrane, **B)** Ct-NEs and **C)** CM-NEsoSOme (Scale bar 100nm).

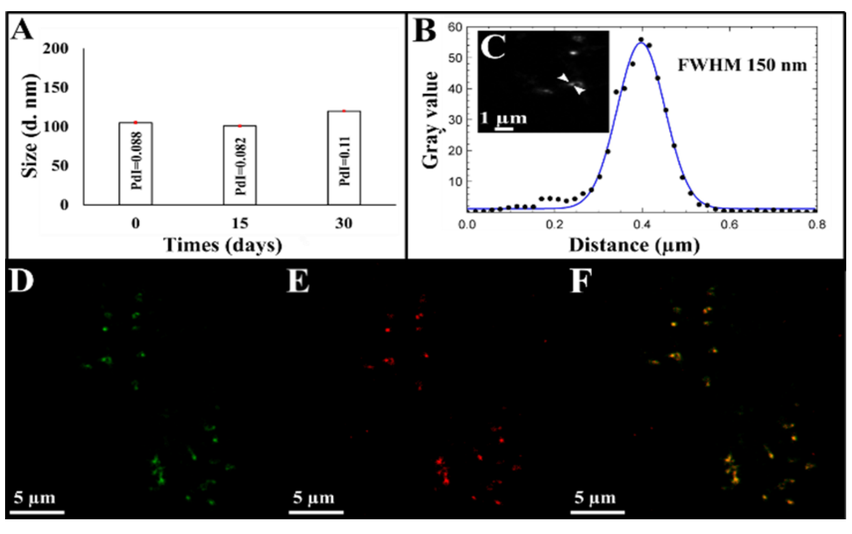


**Fig 2 A)**Time stability of CM-NEsoSOme, **B)** the corresponding line profile of CM-NEsoSOme intensities by STED analysis: the black dots depicted in the panel show the intensities of the corresponding pixel values in the image, blue line is the Gaussian fit of the values, nano-carrier size was extracted from image **C. C)** STED image of CM-NEsoSOme (Scale bar 1μm). Confocal images of CM-NEsoSOmes: **D)** green channel related to FITC signal of Ct-NEs, **E)** red channel signal of cell membrane **F)** overlay (Scale bar 5 μm).

### *In vitro* validation

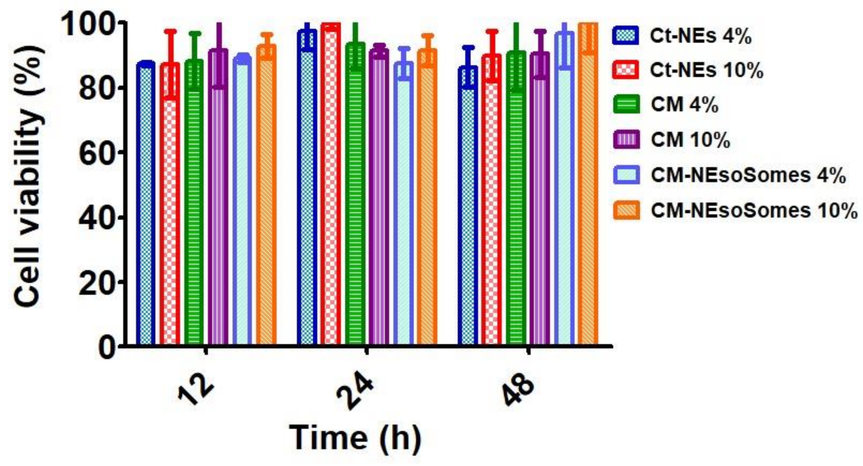


**Fig 4** Cell Viability Assessment obtained by Alamar Blue Assay.

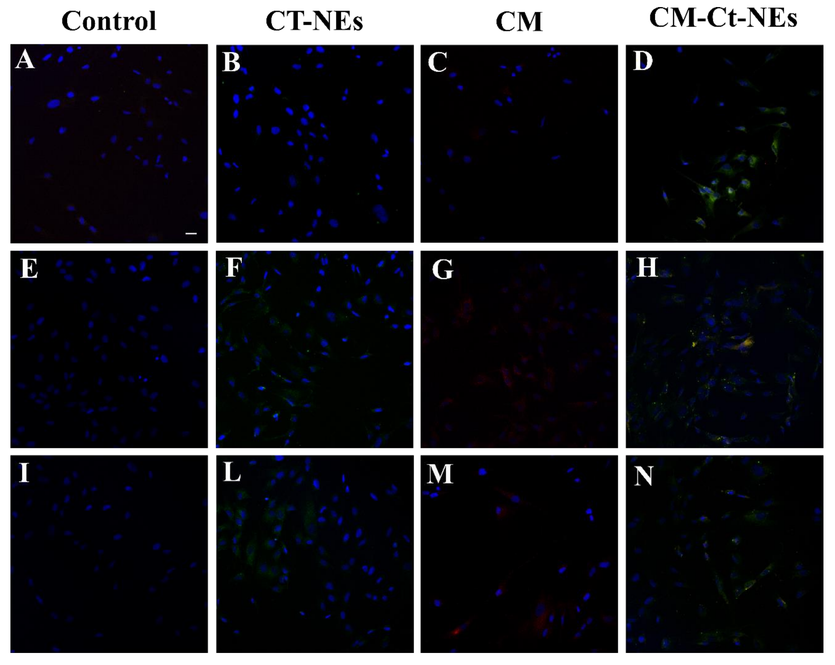


**Fig 5** Confocal images of HDF uptake of cell medium alone (**A, E, I**); CM as is **(C,G,M)** and CM-NEsoSOme **(D,H,N)** after 12, 24, 48 h of incubation (Scale bar 30 μm).

## Conclusion

In this scenario, thanks to the Ct-NE versatility and the biomimetic feature provided by the cell membrane coating, a novel delivery systems with increased bioavailability and stability of the carried drugs has been developed.

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## References

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