# Bioinspired nanoparticles for glioblastoma treatment

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Nanotechnology has enabled many improvements in cancer therapy, in terms of increased efficacy in selective drug delivery, allowing to limit systemic toxicity. In particular, extracellular vesicles (EVs) have attracted great deal of interest as theranostic tools, presenting features that make them feasible drug delivery systems. However, the application of EVs in drug delivery is hampered by several issues like the high heterogeneity and batch-to-batch variation caused by the lack of efficient GMP protocols, possible contamination from residual genetic material, difficulty in drug loading, low production and isolation yield hindering scalability [1,2].
Recently, cell membrane-derived nanoparticles have emerged as innovative theranostic tools which allow to retain the complexity and versatility of the cell membrane, overcoming the limits of the traditional surface modification approach. Therefore, the purpose of our project is to develop a safe biomimetic nanosystem able to target parent malignant tumor cells, exploiting its cancer-mimetic characteristics. To this aim, primary glioblastoma cell homogenates underwent sequential centrifugations leading to the isolation of cell membrane fragments, which were extruded through polycarbonate filters. The obtained nanovesicles were characterized for their chemical-physical properties by photon-correlation spectroscopy; the protein content was evaluated by proteomic analysis, and the presence of detrimental residual genetic material was ruled out by gel electrophoresis. Then, the selective internalization in cancer cells was studied through confocal microscopy (Figure 1) and fluorescence activated cell sorting analysis.
To further improve the production yield, ongoing studies are dedicated to the preparation of hybrid vesicles, obtained by the fusion of the cell-membrane derived vesicles with biocompatible synthetic lipids. Future studies will involve the loading of the nanosystem with an active anticancer compound, and the preparation of analogous cell derived nanosystems from different types of cancer cells.

## References

[1] Lu M., Huang Y., Biomaterials, 242 (2020) 119925
[2] Ailuno G., Baldassari S., Lai F., Florio T., Caviglioli G, Cells, 9 (2020) 2569

## Figures

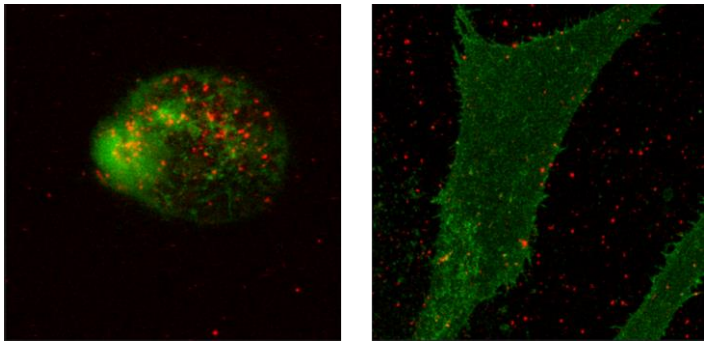

**Figure 1:** On the left, internalization of the cell-derived vesicles in the parent glioblastoma cells, after 30 min incubation; on the right, scarce internalization of the nanovesicles in healthy oligodendrocytes after 30 min incubation.