Bioinspired thermoresponsive nanovesicles for improved melanoma targeting

Nicola d'Avanzo[1,2]
Antonella Barone[1], Christian Celia[3], Luigi Ciriolo[4] and Donatella Paolino[1]
[1]*Department of Experimental and Clinical Medicine, University "Magna Græcia" of Catanzaro Campus Universitario-Germaneto, Viale Europa, 88100 Catanzaro, Italy;*
[2]*Research Center "ProHealth Translational Hub", Department of Experimental and Clinical Medicine, "Magna Graecia" University of Catanzaro, Campus Universitario "S. Venuta"—Building of BioSciences, Viale S. Venuta, 88100 Catanzaro, Italy*
[3]*Department of Pharmacy, University "G. d'Annunzio" of Chieti-Pescara, Via dei Vestini n.31, 66100 Chieti, Italy;*
[4]*Department of Health Science, University "Magna Græcia" of Catanzaro Campus Universitario-Germaneto, Viale Europa, 88100 Catanzaro, Italy*
nicola.davanzo@unicz.it

The immunosystem plays a crucial role in tumor development and progression. Macrophages associated to the tumor can reach the half mass of solid tumors and play a dual function based on their phenotype and can differentiate into tumor suppressor M1 or pro-oncogenic M2 phenotype. In this context, recently M1-macrophage derived extracellular-vesicles (M1-EVs) attracted the attention of researches thanks to their capability to reach the tumor tissues and deliver bio-derived payloads which induce the in-situ shift of macrophages from M2 to M1, thus providing an anti-cancer effect [1]. To maximize the effectiveness of this nanosystem, the aim of this work is to combine thermoresponsive synthetic liposomes and M1-EVs to realize a hybrid bio-inspired nanovesicles capable of target tumor tissues and release the payloads under the application of external hyperthermia. EVs were isolated from both M0 and M1 murine macrophages and were physicochemically characterized in terms of size distribution, diameter and surface features. After that the hybridization process with thermoresponsive liposomes were carried out by freeze-thaw technique and was validated by FACS analysis. The thermoresponsiveness of resulting hybrid nanovesicles was investigated by using a fluorescent probe through the study of its release at 37°C and 42 °C. Obtained results confirmed a massive and significant higher release during the first 1 h of incubation at 42°C than 37°C. Targeting properties of engineering nanovesicles were in vivo demonstrated in murine melanoma model, showing a higher accumulation of hybrid thermoresponsive M1-EVs/liposomes than conventional liposomes. These results strongly empathize the potential use of engineering bioinspired nanosystem the development of a targeted and stimuli-responsive personalized melanoma therapy.

References

[1] Wang, X., Ding, H., Li, Z., Peng, Y., Tan, H., Wang, C., ... & Wei, W. (2022). Exploration and functionalization of M1-macrophage extracellular vesicles for effective accumulation in glioblastoma and strong synergistic therapeutic effects. *Signal Transduction and Targeted Therapy*, *7*(1), 74.