MECHANICAL CUES AFFECTING INTERACTIONS OF NANOPARTICLES WITH TUMOR CELLS

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Abstract

Drugs delivery into tumor tissue is one of the central challenges in cancer therapy. The ability to cross biological barriers is a critical parameter for success of treatment. Nanoparticles are being extensively studied as drug carriers which potentially can improve efficacy and selectivity of anti-cancer treatments. Polymer micelles composed of di-block polymers are a promising drug delivery system with markedly benefits including small dimension, ease of preparation, controlled drug release, drug targeting and reduction of side effects (1). However, as many other nanoparticle forms, the ability of polymer micelles to penetrate the core of solid tumor tissues is relatively low especially in poorly-vascularized tumors, such as pancreatic adenocarcinomas.
We addressed that issue and developed a novel form of highly penetrating particles which are based on Solidified Polymer Micelle (SPM). We showed that solely by changing the mechanical properties of the drug-carrier, without modifying its composition, the interactions with tumor cells is improved (2). Biodegradable polymer micelles composed of poly-ethylene glycol poly lactic acid (PEG-PLA) were tested in their solidified form vs. their "wet" elastic form. It has been shown that solid particles have better internalization into tumor cells, in addition to their ability to perform exocytosis, and they could penetrate into multi-layer cellular 3D culture which mimic the tumor microenvironment (3). This study suggests that transcytosis nanoparticle transport can provide an important mechanism for drug penetration into tumors, even when their stroma is dense and enhancing the exposure of the core to the chemotherapy. This work lay the ground for future rationale design of drug delivery systems, in respect to the vascular state of the tumor tissue.

References

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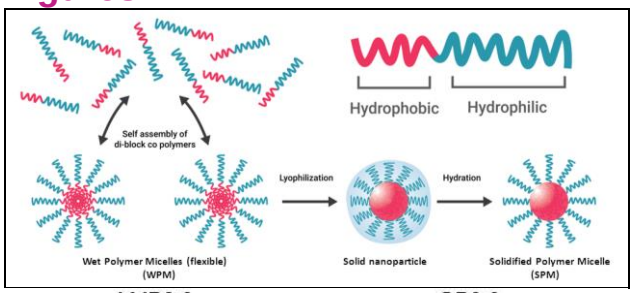
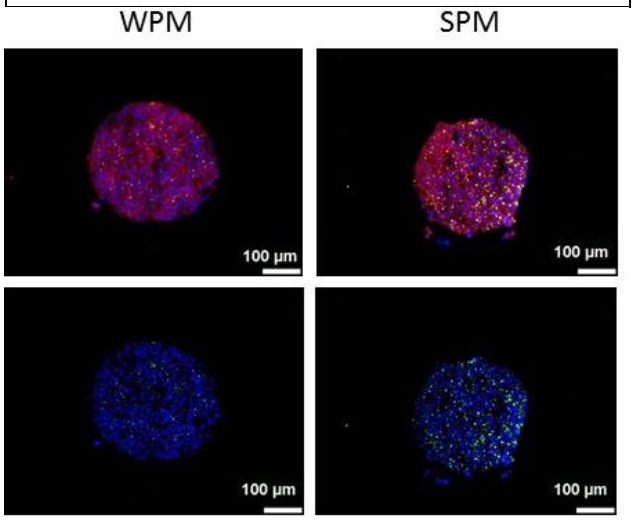
Figures



A

B



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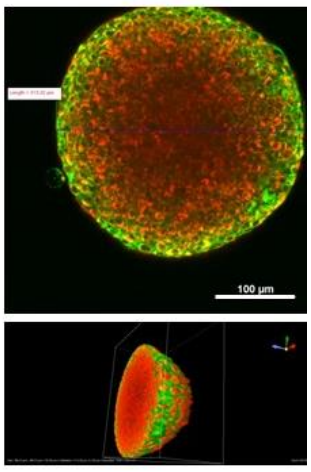

Figure 1. Solidified Polymer micelles show higher penetration to 3D tissue-like multi cell culture (A) Schematic diagram of solidified polymer micelles (B) penetration of flexible" vs. rigid SPMs in tumor multicellular spheroids (red-cell cytoplasm, green-particles, blue- cell nuclei). (C) Two photon image of particles penetrating tumor 3D spheroid.