PHYSICAL PROPERTIES OF PARTICLES CAN CONTROL CELL SPECIFICITY

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Abstract

Growing evidence shows correlation between cancer aggressiveness and the mechanical properties of tumor cells. For many cancer diseases it was found that the deformability of the cells is higher in cancer compared to normal cells, and further raises with the degree of cell malignancy.

The goal of our multidisciplinary research is to investigate how physical properties of particles affect their internalization into non-cancer and cancer cells of varying malignancy potential, from the same origin. Such insight can promote specificity in uptake of drug delivery systems and can potentially be applied in diagnostic schemes. For that aim we used inert rigid colloids of different sizes, as well as nano particles of varying rigidity. Uptake of these particles was tested in non-cancer and cancer cells, including cells of increasing malignant potential. A wide range of biological and physical schemes was used and mechanistic insights were provided by a physical model.

A microfluidic based methodology to produce highly controlled nanoparticles was developed (1) followed by cell assays. We found that flexible particles are less internalized into the cells due to increased contact area that requires massive cell deformation in their engulfment (2).

A non-monotonic dependence on colloid size was found, explained by the energetic interplay between adhesion and cancer cell deformation. Importantly, uptake capacity of colloids was significantly higher in cancer compared to non-cancer originated cell lines, and also higher the more invasive the cancer cells were. The phagocytic capability of cells was found to correlate with the malignancy potential as well as with the mechanical deformability of the cells. Our study provides new mechanistic insights related to cancer progression that can potentially be applied in the rational design of drug delivery systems.

References

[1] Amoyav, B. & Benny, O. Appl Nanosci, , Issue 4, pp 905–914

[2] Stern T*, Kaner I*, Laser Zer N, Shoval H, Dror D, Manevitch Z, Chai L, Brill-Karniely Y, Benny O. Rigidity of polymer micelles affects interactions with tumor cells. J Control Release. pii: S0168-3659(16)30783-0. 2016

Figures

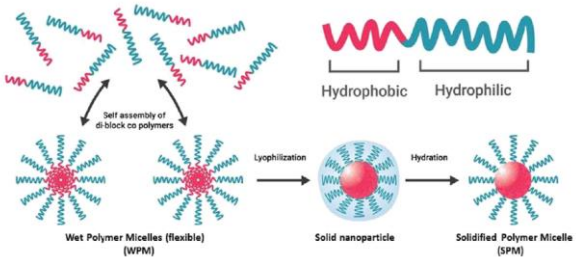

Fig. 1. Example of mechanical tuned particulate system, Illustration of soft (“wet”) polymeric micelles compared to semi-solid stiffer ones.

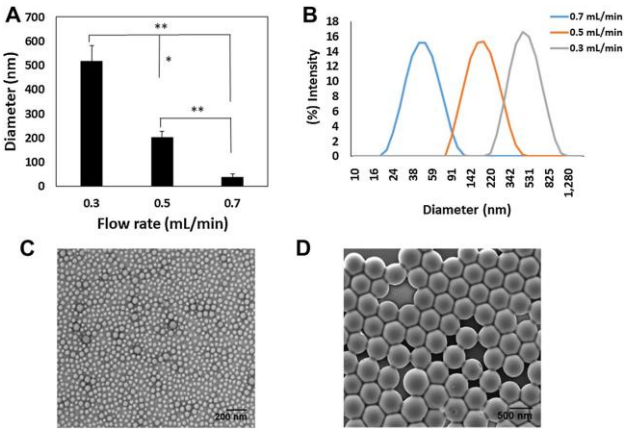

Fig. 2. An example of highly tunbnable polymer particles produced by a microfluidic device. A single chip can produce nano to micro range particles.

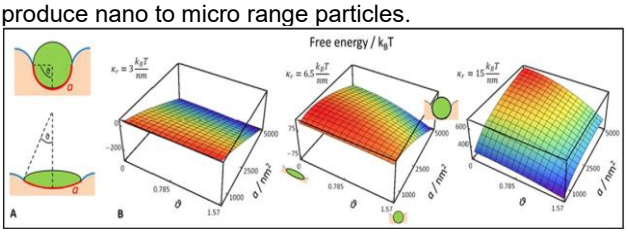

Fig. 3. Physicalmodel. **A**. A scheme of the model geometry, with definition of the flattening state,ϑ, and the contact area, a. **B.** Free energy plots as a function of ϑ and a for different values of the rim constants, κr, with ε ¼ 0:1 kBT. nm2 and c=20kBT.