Selective Photoinduced Eradication of Cancer Cells by DARPin-Gold Nanoparticle Conjugates

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We have demonstrated [1] that the designed ankyril repeat protein (DARPin) _9-29, which specifically target human epidermal growth factor receptor 2 (HER 2) overexpressed in breast cancer cells, binds tightly to gold nanoparticles (GNPs) forming a coating layer around the particle (see Fig. 1). Binding of the protein strongly increase the colloidal stability of the particles. The results of molecular dynamics simulations showed that approximately 35 DARPin _9-29 molecules are bound to the surface of a 5 nm GNP and that the binding does not involve the receptor-binding domain of the protein. The confocal fluorescent microscopy studies showed that the DARPin-coated GNP conjugate specifically interact with the surface of human cancer cells and enter the cells by endocytosis. Illumination of the nanoparticle-treated cells at 633 nm leads to their death, while HER2-negative cell treated and illuminated identically stay alive. We suggest (see Fig. 2) that the DARPin coating layer is removed from the particles by proteolysis in lysosomes and the uncoated particles aggregate into multiparticle structures that efficiently absorb light at wavelengths longer than 600 nm. The results reported here pave the way to developing photodynamic approaches for specific treatment of cancer.

[1] Deyev S., Proshkina G., Ryabova A., Tavanti F., Menziani MC., Eidelshtein G., Avishai G, Kotlyar A. Bioconjug. Chem. 28 (2017), 2569-2574.

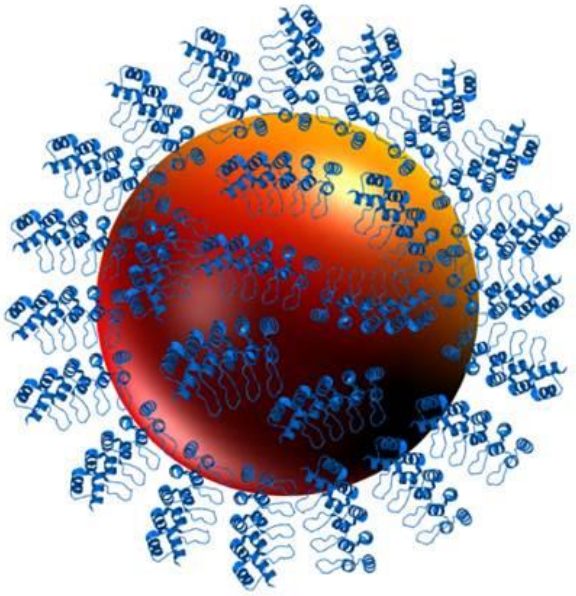

Figure 1: Schematic drawing of a gold nanoparticle (red sphere) DARPin_9-29 (blue spiral-shaped structures) conjugate.

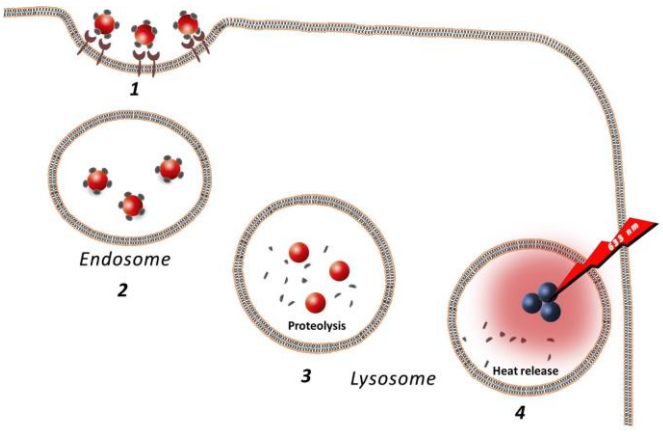

Figure 2: Tentative mechanism of light-induced elimination of HER2-positive SKBR-3 cells. 1 - Binding of DARPin-GNPs through high-affinity interaction of the DARPin molecules on the surface of the conjugate with the receptors on the cell membrane; 2 - internalization of the conjugates by endocytosis; 3 - digestion of the DARPin coating layer by lysosomal proteases; 4 - binding of uncoated nanoparticles and formation of multiparticle structures that can efficiently absorb light at wavelengths above 600 nm. The heat generated upon the illumination severely damages and kills the host cell.