

My research project focuses on how drug-loaded nanoparticles can be shuttled directly to the cancer cell nucleus and that these nanoconstructs then induce severe changes in nuclear phenotype. We found that the number and depth of the nuclear envelope (NE) deformations could be directly correlated to increased apoptosis and decreased cell viability. The nanoconstruct is composed of gold nanostars synthesized based on a procedure that did not rely on surfactants or incompatible reducing agents. Next, we attached aptamers, synthetic strands of DNA or RNA that are emerging as attractive anti-cancer agents, onto gold nanostars. Although therapeutic efficacy of the free aptamer is attributed to disrupting processes mediated by nucleolin there has been no characterization of nuclear phenotype—which is surprising since nucleolin is shuttling bio-components such as proteins between the cytoplasm and the nucleus . As a side result of this work, we found that therapeutic concentrations of the free aptamer also produced deep invaginations in the nuclear envelopes (NE). The innovative result was for us to exploit this active shuttling mechanism to traffic a localized, high concentration of aptamer near the nucleus. Near-infrared light irradiation of gold NPs has been used for cancer treatment because of its minimal damage to human tissues. In our case, we used femtosecond, pulsed NIR light to release the AS-1411 intact from the gold nanostar surface. Ultra-fast light sources have only become available in the last several years, and this advanced spectroscopic tool enables us to control the release of the aptamer and to use short irradiation times (seconds). Released aptamers affect a greater population of cancer cells and cell function. After AS-1411 was released from the gold nanostar surface, changes in the NE were exacerbated. The NE invaginations increased in number, became deeper, and showed larger changes in overall structure. Moreover, although 60% of cells showed NE folding in the presence of the nanoconstruct, when the aptamer was released from the gold nanostar by fs-pulses, over 95% of the cells showed changes in nuclear phenotype. By carrying out the appropriate biological assays, we found that increased changes in nuclear phenotype were directly correlated with increased apoptosis and decreased cell viability. Therefore, this newly discovered correlation should transform how the community thinks about intentionally inducing changes in organelle phenotype to boost efficacy in cancer treatment.