

Nanoparticle Delivery of 3-Bromopyruvate to Treat Cancer

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Technology description

Technology Summary

A key hallmark of many aggressive cancers is accelerated glucose metabolism. The enzymes that catalyze the first step of glucose metabolism are hexokinases. Hexokinase 2 (HK2) is expressed at high levels in cancer cells, but only in a limited number of normal adult tissues. Cancer cell mitochondrial alterations and metabolic reprogramming using the energy blocker, 3-bromopyruvate (3-BP) that inhibits HK could be used in the development of tumor-specific anticancer agents. However, the unique structural and functional characteristics of mitochondria prohibit selective subcellular targeting of 3-BP to modulate the function of this organelle for therapeutic gain.

To help to address this problem, Dr. Shanta Dhar developed a mitochondria-targeted gold nanoparticle (T-3-BP-AuNP) decorated with 3-BP and delocalized lipophilic triphenylphosphonium (TPP) cations to target the mitochondrial membrane potential for delivery of 3-BP to cancer cell mitochondria by taking advantage of higher membrane potential in cancer cells compared to normal cells. The construct demonstrated remarkable anticancer activity as well as a markedly enhanced ability to alter cancer cell metabolism by inhibiting glycolysis as well as demolishing mitochondrial oxidative phosphorylation in prostate cancer cells. Further, this anticancer activity was enhanced upon laser irradiation by exciting the surface plasmon resonance band of AuNP, thereby utilizing a combination of 3-BP chemotherapeutic and AuNP photothermal effects.

Application area

- Cancer treatment
- Demonstrated in vitro efficacy in prostate cancer cells

Advantages

- Can deliver agents to a variety of mitochondrial compartments (outer mitochondrial membrane, inner mitochondrial membrane, inter membrane space)
- Targeted delivery of HK2 inhibitors such as 3-BP to mitochondria using a gold nanoparticle delivery system, coupled with subsequent laser irradiation further enhances the therapeutic efficacy of the composition

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