

Faculty of Pharmaceutical Sciences

Cancer targeted phototherapy, based on photo-chemical reaction

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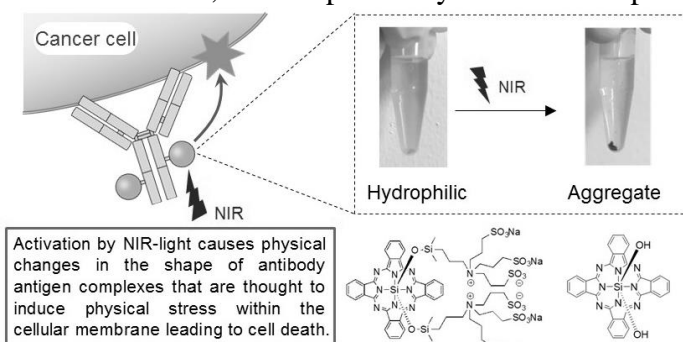
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Photoimmuno therapy (PIT) is a new molecular-targeted phototherapy in which an antibody (Ab) conjugated with IR700, a hydrophilic silicon phthalocyanine derivative, is administered followed by irradiation with near-infrared light (690 nm) ¹.

When antibody-IR700 conjugates are bound to their target cells and are exposed to NIR-light, target cells rapidly undergo necrotic/immunogenic cell death in a highly selective manner. Real time microscopy demonstrates swelling, blebbing and bursting of the target cell membrane within minutes of light exposure with minimal damage to adjacent non-target cells.

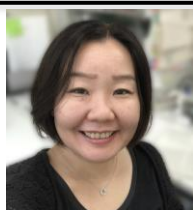
When exposing NIR light, physical stress was thought to be induced within the cellular membrane leading to increases in transmembrane water flow that eventually lead to cell bursting and immunogenic cell death (ICD). ICD induced by NIR-PIT rapidly matures immature dendritic cells adjacent to dying cancer cells initiating a host anti-cancer immune response. Major cytotoxic mechanism of PIT is different from conventional photo-therapies which require singlet oxygen.

One of the characteristics of PIT is that the antibody-IR700 complex only needs to bind to the surface of cancer cells, and the drug does not need to be internalized into the cells ². In other words, the cell plasma membrane is the starting point for cell injury. The formation of aggregates of IR700 on the cell membrane by photochemical reaction is an important mechanism of cell killing. That is, water-soluble axial ligands of IR700 is cleaved by the photochemical reaction, and the phthalocyanine stacks up due to the π - π interaction, resulting in the formation of aggregates. In addition, it was recently found that the formation of radical anions of IR700 and their protonation are essential for the progress of this photochemical reaction ³. The elucidation of these mechanisms may lead to the development of more effective compounds.



Reference

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