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Review Article

New Developments In The Photodynamic Therapy For Hypoxia Tumor By Using Oxphos-Targeted Nanoparticles

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ABSTRACT

Hypoxia, a hallmark of solid tumours, poses a substantial task to conventional cancer therapies due to its role in tumor progression, metastasis, and resistance to treatment. Photodynamic therapy (PDT) has appeared as a promising modality for cancer treatment, leveraging the cytotoxic effects of light-activated photosensitizers to selectively destroy tumor cells. Still, the efficacy of PDT in hypoxic tumor microenvironments remains restricted due to reduced oxygen availability, leading to decreased generation of reactive oxygen species (ROS) essential for therapeutic efficacy. In recent times, innovative strategies have been developed to overcome this difficulty, with a focus on targeting the Oxidative Phosphorylation (OXPHOS) pathway within mitochondria, the cellular powerhouses crucial for energy metabolism. OXPHOS-targeted nanoparticles represent a new approach to develop PDT outcomes in hypoxia tumors by delivering photosensitizers directly to mitochondria, thus circumventing the need for molecular oxygen. This review highlights the current developments in PDT for hypoxia tumor treatment, with a importance of OXPHOS-targeted nanoparticles.

INTRODUCTION

Hypoxia is a representative of most cancers.[1] Hypoxia tumor consequences from ingesting of huge quantities of oxygen by cancer cells for quick formation, though the tumor vasculature is misshapen and irregular, off-putting the acceptable oxygen distribution.[2] Distribution of oxygenated blood is strictly fraught because of uninhibited creation of cancer cells and chaotic evolution of vasculature. oxygen diffusion like this restriction results into the hypoxic tumor microenvironment (TME). Nearly entirely hard tumours are introduced by hypoxia, whose oxygen limited pressure is under 10 mm Hg.[3] The TME is somewhat acidic below hypoxia. while, glucose transporters and glycolysis-related genes are both

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up-controlled when it is facilitated by HIF-1, resulting into an boosted anaerobic glycolysis in cancer cells and more infuriating the acidic environment.[4] \In summary, TME is strictly linked to quick evolution and underprivileged clinical projection, which can be observed as per a substantial goal for clinical cancer treatment.[5] As eagerly seen, hypoxia rises through an disproportion among delicate oxygen ingesting and inadequate oxygen distribution. Different than policies which mostly emphasis on recompense meant for inadequate supply of oxygen and simply gain short-acting effects.[6] Over the decade nanoparticles have developed rapidly, creating up novel ranges in biomedical and biochemical applications including bioimaging, tumor therapy and targeted drug delivery. [20-23] Hence, because outcome of the enhanced permeation and retention (EPR) effect, nanoparticles have former accretion in cancer tissues.[24] Use of nanoparticles as drug delivery systems have various advantages: (I) nanoparticles are advantageous to pharmacokinetics modification of drugs and increase delivery effectiveness.[25] (II) nanoparticles have manageable drug transport in the circulation activity to escape drug outflow and huge drug encapsulation capacity.[26] (III) nanoparticles also be improved simply and furthermore boost solubility, multifunctionality and stability of nanomedicine, to elect it beneficial for in vivo administration.[27]

PHOTODYNAMIC THERAPY (PDT):

Photodynamic therapy (PDT) is a fresh beneficial method which integrates 3 fundamentals—a photosensitizer (PS), light and oxygen.[7] Photosensitizers (PSs) are stereotypically classified as first-, second-, and third-generation on the word of the time of discovery and their exclusive features.[8] First-generation PSs, for instance hematoporphyrin derivative (HpD) and photofrin, were the first PSs to be revealed in Photodynamic therapy applications.[9] PSs of second generation comprise hematoporphyrin-derived and synthetic PSs such as chlorin, thiopurine derivatives, 5-aminolevulinic acid, benzoporphyrin derivatives, along with phthalocyanines and bacteriochlorin analogues [10] While PSs of third generation are similar to second-generation PSs improved with directing moieties, such as peptides, antibodies, and carbohydrates, or fused with biological conjugates such as nanoparticles, micelles and antibodies, to boost their physical and chemical properties and their accretion at aimed tumor areas.[7, 11, 12] Photodynamic Therapy (PDT) depend on the maintenance of Photosensitizers in tumors after that their light initiation to activate photooxidative reactions that destruct and abolish tumors.[13]

Oxygen is the most vital constituent of PDT. Still, the unrestrained creation of cancer cells excites a hypoxic tumor microenvironment. [14,15] for lighten hypoxia, various chemical and engineering aimed tissues and expand the therapeutic index of PDT in cancer treatment.[16] In this research, an oxidative phosphorylation (OXPHOS) targeting nanoparticles invented to lighten hypoxia and boost the action of PDT by encapsulating IR780 and OXPHOS inhibitor atovaquone (ATO) in triphenylphosphine (TPP) modified poly(ethylene glycol) methyl ether-block-poly(L-lactide-co-glycolide) (mPEG-PLGA) nanocarriers (TNPs/IA).Advancing from the mitochondrial targeting function of TPP, ATO was straight a way delivered to its targeted site to get emphasized effect at a lower dosage.In General, TNPs/IA was a probable strategy in photodynamic extermination of tumors.[17]

MECHANISM OF PHOTODYNAMIC THERAPY:

Photodynamic therapy (PDT) is based upon the excitement of Photosensitizers (PS) with light at definite wavelengths, concluding in type I and type II photochemical reactions.[18] Upon radiance of a PS with a wavelength of light equivalent to its

absorption spectrum, the PS molecules convert from a ground state into a singlet excited state.[9] Nevertheless, the excited singlet PS might undertake intersystem system crossing, a process where the rotation of its excited electrons reverses to form a more stable excited triplet state.[18]

Photodynamic Therapy can similarly provoke inflammatory reactions, which cause leukocyte growth and the initiation of pro-inflammatory factors and cytokines at the location of cancer.[19] Additionally, antigen-presenting cells (APCs), mostly dendritic cells, can identify DAMPs single or composed with tumor antigens, triggering T and B-cells, which fallouts in long-standing adaptive antitumor immunity.[8]

CONCLUSION:

Photodynamic therapy is the most used type of treatment in the hypoxia cancer or tumors. hence, to improve this therapy various methods or mechanism also used with photodynamic therapy in hypoxia tumor. Oxidative phosphorylation (OXPHOS) is a type of metabolic pathway occur in mitochondria. OXPHOS targeted nanoparticles are premeditated to selectively deliver therapeutic agents to components involved in oxidative phosphorylation within cells, mainly mitochondria. By targeting OXPHOS, researcher's purpose to interrupt the energy production processes within cancer cells, thus potentially improving the effectiveness of photodynamic therapy against hypoxic tumors.

This helps to new development in the photodynamic therapy in hypoxia tumors which are more efficient and effective.

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