

Use of Cell-Penetrating Peptides and/or Antibody Drug Conjugates for Tumor Radiosensitization

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BACKGROUND

Tumor resistance to radiotherapy can be an obstacle to patient therapy. One way to overcome radioresistance is via the use of drugs to sensitize cells to ionizing radiation (IR). Although many radiosensitizers have been developed, their clinical benefit is hampered by a failure to improve the therapeutic ratio due to a lack of tumor specific delivery over normal tissue. To overcome this obstacle, activatable cell penetrating peptides (ACPPs) target various cargoes to sites of protease activity in vivo. ACPPs consist of a polycationic cell penetrating peptide attached to a cargo and a polyanionic inhibitory domain with a protease cleavable linker. Probe activation and cargo uptake depends on localized proteolysis of the linker sequence that connects the polyanionic and polycationic domains, which converts the probe to an adherent form. This method provides detection of spatially localized enzymatic activity in living tissues via accumulation of cleaved probe. Recently, the use of anti-tumor drugs conjugated to antibodies has been introduced as a way to increase tumor kill and improve patient outcomes.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have demonstrated the therapeutic potential of utilizing cell penetrating peptides and antibody drug conjugates (ADC) to deliver radiosensitizers. Moreover, pretargeted ACPP technology allows for selective delivery of radiosensitizing agents to tumor as opposed to normal tissue and improvement in the therapeutic index of radiation therapy for non-resectable, locally aggressive tumors. Once cleaved, they release drug-conjugated polycation cell penetrating peptides that are taken up by tumor cells. Alternatively, ADC consist of a drug that is covalently attached to an antibody recognizing a specific cell surface receptor. The ADC binds to the specific receptor and undergoes receptor-mediated endocytosis whereby the drug is released from the antibody via endolysosomal proteases.

APPLICATIONS

The invention is purposed for use in personalized medicine for the radiosensitization of tumors utilizing drug conjugated activatable cell penetrating peptides (ACPP) or ADC as tumor selective delivery vehicles for potent radiosensitizers

ADVANTAGES

The current invention and method demonstrate the use of ADC to radiosensitize tumors, provide a decrease in toxicity and improvement in efficacy as measured in tumor models. The use of ADC with IR offers several advantages that can result in improved patient outcomes, specifically the reduction of risk in developing tumor resistance as well as other advantages.

STATE OF DEVELOPMENT

Antibody drug conjugates (ADC) were synthesized and the conjugated antibodies were validated in vitro on tumor xenographs which radiosensitized tumor cells.

INTELLECTUAL PROPERTY INFO

A provisional patent has been submitted and the technology is available for licensing.

RELATED MATERIALS

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OTHER INFORMATION

KEYWORDS

radiotherapy, radiosensitization,
antibody drug conjugates, activatable
cell penetrating peptides, cancer
therapy, ionizing radiation

CATEGORIZED AS

- **Medical**
- **Disease: Cancer**
- **Therapeutics**

RELATED CASES

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PATENT STATUS

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United States Of America	Published Application	20180140703	05/24/2018	2017-022

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