Radiation-Activated Release of Active Drug from Nontoxic Nanoparticle Prodrugs

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BACKGROUND

The concept of restricting toxic chemotherapeutics to tumor tissue is not new. In a contemporary version of the approach, a nontoxic, inactive caged drug is selectively delivered to a tumor and low dose radiation is delivered to convert prodrug to active, toxic drug. In 2008, UC inventors attempted to improve on the approach by using nanoparticles. However, technical limitations severely compromised absorption of the excitation radiation and radiation was also quenched by tissue oxygen. Both of these problems have been solved by developing unique compositions, which pave the way for finely localized delivery of therapeutics, in terms of anatomy and timing, that might otherwise be "undruggable".

TECHNOLOGY DESCRIPTION

UC inventors have developed compositions and methods for targeting tumors with very high doses of nanoparticle-caged prodrug, which is locally released as active drug by either localized or wide field/total body, low dose radiation. The prodrug is comprised of a nanoparticle and drug (e.g. Doxorubicin) and is nontoxic until activated by radiation. The inclusion of ligands can facilitate crossing the blood-brain-barrier.

APPLICATIONS

For the treatment of cancer, a radiation activated prodrug may significantly improve the management of solid, invasive tumors with a minimum of side effects. The 100 nm size of the nano-prodrugs enables them to exit from leaky tumor vessels. However, normal tissues are protected from damage by the nontoxic nature of the prodrug and by localized activation. The prodrug is otherwise cleared by the liver and kidneys. In addition, because the radiation dose is low, patients can be treated every few days and there is an increased probability that small metastatic sites, which might escape conventional therapies, will be treated by the radiation activated drug.

ADVANTAGES

Problem	Solution
Because radiation is quenched by electrons in tissue oxygen, radiation could only release active drug in an anoxic environment	Drug is linked to a nanoparticle which bypasses oxygen quenching
Photodynamic therapy is safe but does not penetrate deeply into tissues so limited to such uses as dermatology. Radiation penetrates deeply but is toxic at high doses.	Low-dose (0.1-2Gγ), deeply-penetrating radiation is used to excite the nanoparticle.
Many nanoparticles and drugs are not activated by low doses of radiation.	Numerous compositions (some novel) have been shown to be activated by low dose, low energy radiation.
Many elements used in nanoparticles may be toxic.	Elements comprising the tested compositions are nontoxic. Some have FDA approval for other uses.

STATE OF DEVELOPMENT

- Core/shell structures have been synthesized and demonstrate robust efficiency.

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OTHER INFORMATION

KEYWORDS
nano-particle, nanoparticles, pro-drugs, nontoxic, oncology, cancer, light-activate, tumor, low dose radiation, prodrug, compositions, platform

CATEGORIZED AS
- Biotechnology
  - Health
- Medical
  - Delivery Systems
  - Disease: Cancer
- Nanotechnology
  - NanoBio

RELATED CASES
2013-199-0

- Animal models and the design of the radiation activated nanoparticle-prodrug platform have been developed.

- Fifty two compositions, which have been developed, are activated by low dose, low energy radiation.

INTELLECTUAL PROPERTY INFO

Worldwide rights available; pending patents available under confidentiality.

RELATED MATERIALS

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PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20160250330	09/01/2016	2013-199

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