NATIONAL CANCER INSTITUTE
Technology Transfer Center

Radioprotectants and Tumor Radiosensitizers Targeting Thrombospondin-1 and CD47

NIH Reference Number
E-153-2008

Keywords
- Radioprotective Agents
- Tumor Sensitizers
- Thrombospondin-1 (TSP1)
- CD47
- Morpholinos
- Cancer
- Radiotherapeutics

Collaboration Opportunity
This invention is available for licensing.

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Description of Technology

The National Cancer Institute''s Laboratory of Pathology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize CD47-targeting agents as radioprotectants and tumor sensitizers.

Radiation therapy not only damages cancer cells, but it also damages healthy cells and can cause serious side effects for patients. One effort to enhance the therapeutic potential of radiotherapy, while reducing its detrimental effects on normal tissue and maintaining tumor sensitivity, is centered upon the development of radioprotective agents.

NIH inventors previously discovered that when the secreted protein, thrombospondin-1 (TSP1) binds to its receptor CD47, this signaling pathway prevents nitric oxide from dilating blood vessels and increasing blood flow to organs and tissues. They found that blocking TSP1-CD47 interaction through the use of antisense morpholino oligonucleotides,

peptides or antibodies has several therapeutic benefits; one of them being increased blood flow to ischemic tissues.

In the present technology, the inventors discovered that hindlimb irradiated TSP1 and CD47 null mice have less hair loss, and decreased cell death in muscle and bone marrow than untreated TSP1 and CD47 null mice. They also discovered that when irradiated human vascular cells are treated with antibodies towards TSP1 or CD47, viability and proliferative capacity are preserved. Furthermore, the inventors determined that irradiation of wild type mice following treatment with CD47 antisense morpholino resulted in decreased apoptosis in irradiated tissues at 24 hours, preservation of hematopoietic stem cell proliferative capacity in irradiated bone marrow, and less alopecia, ulceration, and desquamation at the end of eight weeks. These results led the inventors to propose that antagonists of TSP1 and/or CD47 preserve cell viability and tissue function following radiation treatment, and these antagonists may be useful as radioprotective agents to reduce side effects associated with radiation therapy. Remarkably, the same treatment dramatically enhanced the delay in melanoma and squamous carcinoma tumor regrowth following irradiation. Thus, these agents are radioprotective agents for normal tissue but radiosensitizers for tumor tissue.

The present technology describes the use of morpholinos, peptides and antibodies that block the TSP1/CD47 signaling pathway as radioprotectants for normal tissue, radioenhancers for tumor tissue, and methods of selectively protecting normal tissue from damage caused by radiation exposure by contacting the tissue with these agents.

Development Status:
Mouse data available. In vitro data available in mouse, bovine, porcine, and human cells.

Potential Commercial Applications

- Protect normal tissue from damage following radiation therapy.
- Enhance tumor responses to radiotherapy.
- Enable use of higher therapeutic doses for radiotherapy of cancer.
- Protect personnel from radiation injuries resulting from occupational exposure to ionizing radiation, military exposure, or terrorist acts.

Patent Status

- **Foreign Filed:** Foreign Filed - Patent Application PCT/US2009/52902, Filed 05 Aug 2009

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