

Tumor Metabolism Inhibitors with Radiosensitization Properties

MCW 1788

Description

MCW inventors have developed novel small molecule therapeutics that will help treat pancreatic and other cancers. The new metformin analogs are selectively designed to accumulate in tumor mitochondria and inhibit OXPHOS via mitochondrial complex 1, which affords cytostatic and radiosensitization properties against tumor cells.

Problem Solved

Historically, mitochondria were thought to be dispensable in tumor cells. However, certain cancers are now known to be highly dependent on mitochondrial metabolism, making OXPHOS an emerging druggable target for cancer therapy. The "mito-metformin" compounds described here were designed with tumor-specific OXPHOS inhibition in mind and have shown efficacy towards both *in vitro* and *in vivo* pancreatic cancer models.

Application

These cytostatic compounds have significant potential as therapies in combination with cytotoxic agents and/or radiation therapy for pancreatic or other cancers.

Key Advantages

- Selective to tumor cells with no toxicity to normal cells
- Nanomolar potency
- Sensitizes tumor cells to radiation treatment

Figure: Data from <u>MCW 1788 publication</u>. (A) MiaPaCa-2 cells were treated with metformin analogs for 24hrs. The calculated survival fraction is plotted against compound concentration and IC50 values calculated. (B) MiaPaCa-2 cells were treated with Mito-Met₁₀ for 24hrs before exposure to x-radiation. Clonogenic survival fraction was determined. (C) Pancreatic cancer xenograft mouse model was treated daily for 13 days. Representative bioluminescence images showing significantly decreased tumor growth in mice treated with Mito-Met₁₀.

Stage of Development: In vivo animal model

Intellectual Property Status:

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Lead Inventors



Balaraman Kalyanaraman, PhD

Professor and Chair Department of Biophysics Associate Director of Basic Research, Center for Disease Prevention Research



Jacek Zielonka, PhD, DSc

Assistant Professor Department of Biophysics Director Redox & Bioenergetics Shared Resource Contact Landon Olp 414-955-4884 lolp@mcw.edu