Full Project B: *In Vivo* Assessment of Localized Magnetic Fluid Hyperthermia for Ovarian Cancer Treatment
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The overall goal of this proposal is to pursue the optimization of the spatial and temporal behavior of Magnetic Nanoparticle Heaters (MNH) and perform an in vivo efficacy assessment of targeted or "intelligent" (iMNHs) developed in our laboratories for cancer treatment applications.

Inputs

- UPR Comprehensive Cancer Center
- MD Anderson Cancer Center
- University of Florida at Gainsville
- UPR-Medical Sciences Campus (UPR-MSC)
- UPR Mayaguez (UPR-M)
- Administrative Core (PIs)
- BEBiC
- Faculty
- Students (3)
- Mentors
- Internal Advisory Committee (IAC)
- Program Steering Committee (PSC) members
- Other funds:
  - NSF CREST
  - NSF IFN
  - NIH RISE

Aims

1. To optimize magnetic nanoparticles for the targeted selective destruction of ovarian cancer cells through magnetic fluid hyperthermia
2. To determine the in vivo safety, pharmacokinetics and biodistribution of targeted and non-targeted MNHs in orthotopic ovarian cancer models.
3. Determine the in vitro and in vivo efficacy of targeted and non-targeted MNHs using ovarian orthotopic cancer models.

Activities

Research Design Aim 1

1. Preparation of iron oxide nanoparticles with maximized energy dissipation rates.
2. Coating of MNPs with covalently-grafted poly(ethylene glycol).
3. Conjugation of targeting peptides and aptamers
4. Magnetic nanoparticle characterization

Research Design Aim 2

1. Assess the in vivo toxicity of the iMNHs, NCr in nude mice
2. Pharmacokinetics of targeted and non targeted nanoparticles
3. Establishment of orthotopic ovarian cancer tumors (applicable to both SA#2 and SA#3).
4. In vivo biodistribution of targeted and non-targeted magnetic nanoparticles.

Research Design Aim #3

1. In vitro Magnetic Fluid Hyperthermia
2. In vitro uptake
3. In vivo Application of MFH

Outcomes -- Impact

Short-term

A. *Aim1*. Obtain gram quantities of iron oxide magnetic nanoparticles with maximized energy dissipation rates (e.g., SAR values above 500 W/g), coated with PEG with long circulation time (determined using the methods of Specific Aim 2), and functionalized with labeling molecules (e.g., fluorophores and radiolabels) and targeting agents (e.g., RGD peptide or thio-aptamers).

B. *Aim 2*. These research tasks will provide evidence to demonstrate that nanoparticles with optimized surface properties can overcome challenges regarding limiting accumulations in target areas such as ovarian cancer tumors

C. *Aim 3.* In vitro experiments are intended to provide us with fundamental information regarding the sensitivity of the selected cell lines to heat as well as the effects of targeting ligands in the improved efficacy of the aforementioned treatment.

D. *Aim 3.* In vivo experiments will provide the means to establish the relationship between particle properties and in vivo efficacy.

Intermediate

E. Demonstrate the innovation that by manipulating nanoparticle's physical properties and by attaching specific targeting ligands, these innovative "intelligent" nanoparticles will recognize tumor cells resulting in the delivery of sufficient amounts of particles to cancer cells using an in vivo orthotopic ovarian cancer model.

Long-term

F. As a consequence of the proposed research, new approaches to the application of magnetic nanoparticles in AMFs in the treatment of cancer are expected.

G. The long-term goal of this project is to develop MNPs as a clinically feasible tool by providing a comprehensive understanding from fundamental particle design to clinical application.

Process Evaluation

Outcome Evaluation

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