Overview/Abstract: In spite of the recent progress in cancer diagnosis and treatment, many of the available treatment methodologies are invasive and harmful to patients.[1] The most common treatment options involve (a) surgical removal, (b) chemotherapy, and (c) radiation therapy.[2] While they all represent viable options for the treatment of various types of cancers, each option possesses disadvantages.[3] For instance, highly invasive surgical methods can place patients at risk for complications and infections. The delivery of anticancer drugs can be a non-invasive procedure, but it is associated with its own intrinsic toxicity and is highly non-specific in terms of the cells that are targeted, thereby resulting in damage to normal, healthy cells as well as to malignant cells. Similarly, radiation therapy, while more localized than chemotherapy, is also non-specific. In addition to traditional chemotherapy and radiation, other treatment options, ranging from photodynamic therapy, radio-frequency, microwave, hyperthermia, drug delivery, and gene therapy,[2] have been combined with conventionally available imaging techniques. Therefore, to provide for less invasive and safer, alternative cancer treatments, focus has centered on an intimate combination of treatment and imaging, namely "theranostics". [4-5]

Hence, in this context, a goal we seek to achieve has been to create a single platform with which reliable, real-time monitoring can be coupled with the capacity to diagnose and locate malignancy as well as to simultaneously deliver an effective, localized dose of therapy to eradicate cancer. Specifically, the theranostic material should be easily tailored from a chemical and biological perspective to ensure the best treatment possible. In doing so, we propose to demonstrate the potential of nanoscale particle (NP) systems for incorporating targeting ligands and/or imaging modes, which have been previously used for cancer cell targeting and Positron Emission Tomography (PET) imaging, respectively. Hence, we will be able to effectively deduce robust biomedically relevant structure-property correlations in these oxide NPs.

Specifically, our objective is to gain fundamental insights into and to correlate the effects of surface chemistry with the latent potential of these multi-functional NPs for (1) computed tomography (CT) imaging, (2) magnetic resonance (MR) imaging, (3) biocompatibility, (4) cancer cell targeting, and (5) effective hyperthermia treatment. These data will allow us to create a truly innovative, reliable platform technology, which can be purposely and specifically targeted for well-defined medicinal applications. The expectation is that by understanding how to 'pack' various biologically relevant and biocompatible surface ligands in a quantitative and geometrically consistent manner, the pronounced effects of additional product variables, such as but not limited to morphology and particle size, can be weaved into the development of novel oxide-based model systems that are inexpensive, flexible, earth-abundant, and biocompatible.

Specific Aims (SA)

(1). To introduce and model relevant biomedical modalities by functionalizing (e.g. modifying) the surfaces of these NPs with distinctive examples of capping agents to investigate their biocompatibility, and to demonstrate their ability to incorporate other complementary PET imaging and/or targeting ligands within a metal oxide system. We will select TiO_2 as our model test platform, but expect to be able to generalize these results to analogous metal oxides.

(2). To assess various chemical compositions, particle sizes, and morphologies to maximize sensitivity and selectivity for combined MRI/CT/PET imaging & hyperthermia treatment for cancer theranostics. For example, we can vary the dimensions (i.e., sizes from 1 to 100 nm) and morphological type (i.e., 0D nanoparticles versus 1D nanowires versus 3-D motifs) of TiO_2. We can tune the external surface chemistry of these materials to evince specific functionality.

(3). To develop a reliable synthesis of a unique family of novel theranostic nanomaterials.

Broader Impacts: Our proposed work will be impactful and far-reaching in that it should yield valuable insights into the rational design of relatively "less-studied" nanomaterials for theranostics. With the emphasis on synergy between theory and experiments in this proposal, participating graduate students in PI/co-PI-led teams will develop an intimate understanding of how close interactions between theory and experiments can best achieve the desired outcomes. To increase the participation of under-represented and minority groups in our research, we plan to partner with the Center for Inclusive Education (CIE) at Stony Brook University.