CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100146

Project Title:
Imaging cancerous tissues with liposomal MRI contrast agents that utilize bioengineered nanovalves

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Early detection of aggressive malignancies such as pancreatic cancer is critically important for successful treatment outcomes. While several imaging modalities have advanced the field there is still a great need for improved sensitivity and accurate early detection of pancreatic cancer and other aggressive malignancies. The fundamental goal of this proposal is to design and construct responsive or “smart” magnetic resonance imaging (MRI) nanoprobes for high resolution in vivo cancer imaging and early detection. Normally MRI contrast agents work by modifying the water exchange rate, which can vary in different parts of the body. We propose to use a biological pore, which we will engineer to open preferentially at or near cancerous tissues by opening only in low-pH environments, to change the water exchange rate of encapsulated MRI contrast reagents. If successful, this will lead to an increased sensitivity of MRI for cancerous tumors.the effect of the MRI contrast agent to the bulk water pool is compromised within the vesicles thus severely compromising the effectiveness of the contrast enhancement. Hence, it would be advantageous to increase the water exchange rate, especially if this could be performed within the cancerous tissue environment. Since inflamed and cancerous tissues often have lower extracellular pH, we will concentrate on generating a system in which the water exchange process is drastically increased by low pH. This will be performed by incorporating a pH-responsive nanopore, based on a modified bacterial mechanosensitive channel, MscL, within the vesicular membrane; previous studies have already demonstrated the feasibility of such bio-engineering and changing the modality of this sensor. The resulting nanodevice will thus selectively and greatly enhance the image contrast of low-pH cancerous tissues.