Award ID:
RP160775

Project Title:
Becoming fatter to survive: cancer cells increase lipid storage to counter metabolic stress

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
The University of Texas Health Science Center at Houston

Lay Summary:

The primary challenge in cancer therapy is how to kill cancer cells without harming normal cells. To solve this, we propose exploiting the fact that cancer cells require more lipids than normal cells, due in part to their increased proliferation. Supporting this dependency, our lab and others have recently found that cancer cells store more lipids in the form of triglycerides, possibly due to the overexpression of enzymes that synthesize triglycerides in many cancers. One such enzyme is DGAT1, and we have seen in preliminary studies that inhibiting DGAT1 promotes cancer cell death. These data suggest that lipid storage is critical for cancer progression and maintenance, and that targeting enzymes involved in triglyceride synthesis would be an efficient strategy for cancer therapy. In this proposal, we will investigate whether increased lipid storage is a general mechanism that cancer cells use to counter metabolic stress. To design better therapy, we will also determine whether DGAT1 is critical for tumor growth and whether its inhibition can be used alone or in combination with current cancer therapies. Because there already exists drugs that target triglyceride synthesis, such as DGAT1 inhibitors, and they show little or no toxicity in previously preclinical and clinical studies, the success of this proposal could quickly lead to a new type of cancer therapy.