New Jersey State Commission on Cancer Research
LAY ABSTRACT OF RESEARCH PROJECT

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Project Title: **Control of TACE-mediated TGF-α Release in Cancer**

Description: **We study the mechansim for controlling the release of a growth factor named TGF-α that is important for cancer formation and metastasis, which will aid the development of therapies to block TGF-α release in cancer without affecting the normal function of other proteins that are released similarly to TGF-α.**

We plan to study how a protein called transforming growth factor-α (TGF-α) contributes to cancer development. TGF-α is present in both normal and cancer cells, and can stimulate cell growth. However, there is a difference in the way how much TGF-α is produced in normal and cancer cells. The human body is an efficient system, in which every part is built according to its needs. Therefore, only a limited degree of growth occurs for most of the cells in the body. Accordingly, normal cells are allowed to produce only a small amount of TGF-α. When cells in the body have lost their ability to control their growth they may develop cancer. Many cancer cells produce much more TGF-α than normal cells. Not only do normal and cancer cells produce different amounts of TGF-α, they also handle it differently. In normal tissues, TGF-α is largely retained by the producer cells; therefore, it stimulates only the producer cells themselves or the neighboring cells in direct contact with the producers. However, cancer cells release TGF-α into the surrounding tissue fluid. As a result, the freely diffusible TGF-α can stimulate the growth of cells at appreciable distances from the producer cells. Overproduction of TGF-α by cancer cells helps cancer grow and spread from their original site to other organs. Disseminated cancer cells form secondary tumors which eventually cause dysfunction of multiple organs at the late stage of disease and are the major cause of death of cancer patients. Increasing TGF-α release is an important strategy that cancer cells use to gain growth advantage over normal cells. Therefore, strategies to inhibit TGF-α release have been sought after for cancer treatment and prevention. Nevertheless, this issue is complicated by the fact that present strategies to inhibit TGF-α release also affect the generation of proteins that are required for normal physiological functions such as immune reactions. In order to specifically block TGF-α release with no or minimal effects on normal physiology, we study how TGF-α release is specifically controlled. Thus, our work is important and significant not only because it will help us understand how cancer occurs and progresses, but also helps develop new strategies for prevention and treatment of cancer.