Award ID:
RP170152

Project Title:
Targeting the HNF4A and WNT/Beta-catenin pathways in childhood malignant yolk sac tumors.

Award Mechanism:
Individual Investigator Research Awards for Cancer in Children and Adolescents

Principal Investigator:
Amatruda, James F

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

The long-term goal of our work is to improve the treatment of children with malignant yolk sac tumor. Yolk sac tumor (YST) is a cancer of the germ cells, the cells that give rise to the ovary and testis. YST is the most common type of germ cell cancer in children. While most children with YST are thankfully cured, there are still about 10% who will die of their disease. It is also troubling that the chemotherapy agents we use for treating YST can cause a host of long-term adverse health effects. Our work is aimed at developing new types of treatments that would target the tumors more effectively and specifically, sparing the normal tissue of the body.

Recently, we studied the DNA genome of YSTs and discovered that the tumors commonly have alterations in two cellular growth-promoting pathways, called HNF4A and WNT. Both of these pathways are well-known to be essential for development of the liver, gut and other organs, but they have not been studied in YSTs. We believe that inappropriate activity of these pathways reprograms a normal developing germ cell into a cancer cell. Our goal is to interfere with this process to prevent YST tumor growth.

To achieve this goal, we need to intensively study just how HNF4A and WNT act, alone or in concert, to drive tumor growth. We will study cells growing in the lab, as well as making innovative mouse models of YST, in which we can study the development of tumors in a living organism. Excitingly, our discovery of the role of HNF4A and WNT in these tumors suggests that several drugs that are approved for use in humans, or currently being tested in clinical trials, might be effective new agents for YST. We will test those drugs in the course of this proposal.

Success in these aims will shed light on the causes of YST and may lead directly to new treatments that are more effective and less toxic than current approaches.