CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160520

Project Title:
Effect of Chest Radiation Therapy on Cardiomyocyte Turnover

Award Mechanism:
Individual Investigator Research Awards for Prevention and Early Detection

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

Lay Summary:

There are currently over 270,000 survivors of childhood and adolescent cancers in the United States. Chest radiotherapy is an effective treatment modality for numerous types of these cancers, including Hodgkin lymphoma and bone cancers among others. Unfortunately, radiotherapy has significant deleterious effects on the heart that are far more pronounced in patients receiving the therapy at younger age. One of the most serious, and poorly understood side effects is the delayed effect of radiotherapy on the heart muscle. Epidemiological studies indicate that the majority of patients undergoing chest radiotherapy during adolescence and young adulthood develop fibrosis in the cardiac muscle and are 6 times more likely to develop heart failure (Mulrooney et al, British Medical Journal, 2009). Unfortunately, precisely how radiation therapy affects the heart muscle, and whether this injury can be prevented remain unknown. Radiotherapy results in damage to the DNA of cancer cells which results in slowing the rate of cancer growth, and because the heart muscle cells generally divides very slowly, the effect of chest radiotherapy on heart muscle renewal has generally been underappreciated. Our group was the first to describe the effect of DNA damage on heart muscle renewal. We showed that exposure to high levels of oxygen after birth stops heart muscle growth by inducing oxidative DNA damage, while a rare group of heart muscle cells are protected from this oxidation, and are able to divide throughout life. We also generated a transgenic mouse line where this rare population of dividing heart muscle cell can be visualized and studied. Our preliminary results show that these cells are exquisitely sensitive to chest radiation, which stops them from dividing. Therefore, we propose to study the effect of radiotherapy on the growth and renewal of the heart muscle and to investigate how preventing DNA damage in the heart can protect against the deleterious effects of radiotherapy.