Award ID: RP130639

Project Title:

A role for non-coding RNA in the regulation of telomerase in breast cancer

Award Mechanism: High Impact/High Risk

Principal Investigator: Shippen, Dorothy E

Entity: Texas Agrilife Research

Lay Summary:

Telomerase is an enzyme expressed in cells with unlimited mitotic potential (e.g. germinal and stem cells), but its expression is blocked in specialized (differentiated) cells that have limited growth potential. On the other hand, telomerase is aberrantly expressed in neoplastic cells and plays a critical role in cancer development. Thus, precise regulation of telomerase is essential for maintaining normal tissue homeostasis and blocking carcinogenesis. In this study, we will investigate a new regulatory mechanism for telomerase involving one or more RNA molecules that control enzyme activity in response to DNA damage. This mechanism was recently discovered in plants but has not been studied in human or other mammalian systems. We hypothesize that this regulatory mechanism is operational in normal human cells, but is abrogated in premalignant and malignant cells, increasing their genomic instability. Here we seek to identify the non-coding RNA molecules that are responsible for telomerase regulation, and to determine whether this RNA-mediated mode of regulation is lost when mammary cells progress to premalignant or malignant cells. The results of our study may have important implications for understanding how telomerase regulation is hijacked in cancer cells, and how proper control can be re-established.