Satellite RNAs, Heterochromatin and Cancer: A Novel Mechanism of Induction of Breast Cancer by Loss of BRCA1?

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3pm, Clifford Allbutt Lecture Theatre, Clifford Allbutt Building, Cambridge Biomedical Campus.

Heterochromatic repetitive satellite RNAs are extensively transcribed in a variety of human cancers, including BRCA1-mutant breast cancer. Aberrant expression of satellite RNAs in cultured cells induces the DNA damage response, activates cell cycle checkpoints, and causes defects in chromosome segregation. However, the mechanism by which satellite RNA expression leads to genomic instability is not well understood. We have demonstrated that increased levels of satellite RNAs in mammary glands induce tumor formation in mice. Using mass spectrometry, one can further show that genomic instability induced by satellite RNAs occurs through interactions with BRCA1-associated protein networks required for the stabilization of DNA replication forks. Additionally, formation of RNA-DNA hybrid contributes to DNA replication defects in cells expressing satellite RNAs. These studies lay the foundation for developing novel therapeutic strategies that block the effects of non-coding satellite RNAs in cancer.

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