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The role of the long non coding RNA NEAT1 in therapy resistant prostate cancer

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Sequencing of the human genome has revealed a myriad of insights into the complexities of transcriptional program and has shed light on regulatory role of the non-coding transcriptome beyond the speculated "transcriptional noise". Long non coding RNAs (lnc-RNAs) comprise a heterogeneous group of non-coding transcripts (>200nt) that have emerged as key mediators of cellular homeostasis. We recently discovered the lnc-RNA NEAT1 and identified its role in prostate cancer (PCa) progression. NEAT1 expression is low in benign prostate cells but demonstrates a significant increase in expression with PCa progression. We provide experimental evidence to demonstrate that NEAT1 can drive oncogenic cascade via epigenetic modulation of chromatin. By RNA ISH on TMAs we have shown that NEAT1 is up-regulated in both localized as well as metastatic prostate cancer compared to benign. Functionally, NEAT1 is a transcriptional regulator and RNA-seq analysis identified a compendium of genes (NEAT1 signature) that are directly regulated by NEAT1. Analysis of a large clinical cohort suggested that NEAT1 is a novel prognostic biomarker of clinically aggressive disease and a predictive biomarker of patients with advanced prostate cancer. NEAT1 contributes to DNA damage and repair mechanisms and functions as a unique link between oncogenic signaling and DNA damage and response pathway. Biochemical studies reveal that NEAT1 is a histone chaperone and NEAT1 signaling converges at a yet undiscovered DDR pathway. Our studies also support the rationale that NEAT1 modulates large-scale chromatin reorganization for efficient repair of damaged loci. We have discovered a functional feed-back loop between genomic instability and cancer progression pathways that might also explain molecular basis for drug and radiation resistance observed in aggressive cancers. Specific targeting of NEAT1 using si-RNA approach restores sensitivity to radiation in prostate cancer cells. Delineating the role of NEAT1 using a combined molecular-genome wide screen and analysis of NEAT1 in clinical samples will provide rationale for future NEAT1-targeted therapies.

Biography

Dimple Chakravarty completed her Post-graduate from Institute of Medical Education and Research in 2006. She worked as a Post-doctoral researcher UTHSCSA. Currently she is working as an Assistant Professor at Weill Cornell Medical College, USA.

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