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Non-coding Pri-miRNA-encoded novel peptides/proteins regulate migration of cancer cells

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Only two percent of the Human genome was shown to code for proteins and the rest of the 80-90 percent was shown to transcribe into non-coding RNAs such as pri-miRNAs, lncRNAs and CircRNAs. Mature miRNAs are known to be processed from large primary transcript (pri-miRNAs) in two stages. First stage involves processing of pri-miRNA into shorter pre-miRNA followed by second stage, where pre-miRNA will be processed to mature miRNAs. Earlier studies suggested that deregulation or aberrant expression of miRNAs can lead to several human diseases and cancers (including gynaecological cancers). Recently, it was shown that pri-miRNA codes for peptides (miPEPs) that regulate the expression of active mature miRNAs in plant cells. Since miRNAs are well conserved in humans, animals and plants, it is important to study whether pri-miRNAs code for such peptides/proteins in mammalian cells. In addition, it will be highly significant and remarkable, if one can prove the presence/absence of pri-miRNA encoded peptides in normal and cancer cells and their metastatic cells and show that they function as tumor suppressors and/or oncogenes like in the case of miRNAs. Here, we demonstrate for the first time, the presence of an ORF in pri-miRNA which codes for - peptides or small proteins that show novel biological properties in human cells. We show these pri-miRNA (miR-200a and miR-200b)-encoded peptides/proteins (miPEP-200a and miPEP-200b) to inhibit the migration of cancer cells by regulating epithelial to mesenchymal transition of these cells. These miPEPs have the potential to serve as diagnostic markers for metastasis and can also be used as therapeutic agents to many cancers (including gynecological cancers). We will also discuss how these novel peptides/proteins encoded by pri-miRNAs are evolved in nature and their potential role in cancer and other human diseases. These results may revolutionize our present understanding of the functional role of the so called junk DNA (non-coding DNA) and its noncoding RNAs in the biology of humans and animals.

Biography

E Shyam P Reddy is a Professor and Director, Cancer Biology Program, Department of OB/GYN, Morehouse School of Medicine, Georgia Cancer center for excellence, Grady Memorial Hospital, Atlanta, Ga. He carried out his Ph.D. work at the Center for Cellular and Molecular Biology, Hyderabad, India and at Max Planck Institute for Biophysical Chemistry, Gottingen, West Germany. His Ph.D. work was published as two papers (back to back) in the prestigious Nature journal for which he was awarded National Young Scientist award by the Prime minister of India. He obtained postdoctoral training in molecular biology at Yale University, CT (Dr Weissman, PNAS member). Dr Reddy discovered and cloned several cancer genes/oncogenes (close to 20 genes) and studied their functions. The most notable genes discovered by Dr Reddy include ERG-1, ERG-2, ERG-3 and human FLI-1genes. Drs Reddy and Rao named the gene as ERG (ETS Related Gene, Science and PNAS). ERG is a transcriptional factor, endothelial permeability factor and also a stem cell factor and is involved in 50-80% of Prostate cancers, Ewing sarcoma and also leukemias (AML). Dr Reddy also discovered human Fli-1, EWS-Fli-1, EWS-erg, TLS-erg, EWS, TLS/FUS and ELK-1. Dr Reddy and his group have also discovered novel post-translational mechanism mediated by BRCA2 in Breast Cancer. Recently, Dr Reddy's group decoded non-coding DNA and it's non-coding RNA, which will revolutionize the landscape of cancer biology, future diagnosis and therapy of cancers including Breast cancer, Ovarian cancer, Prostate cancer, Lung cancer etc. (2017).

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