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The androgen receptor mRNA and miRNA dynamics

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Master transcriptional regulator Androgen Receptor (AR) remained as a fascinating and an enigmatic molecule, particularly because of its causative role in Prostate cancer biology. Major impetus in PCa research is currently focused on the development of new generation of therapeutics to target AR expression, in castration-resistant stage of the disease. 920 amino acid coding AR gene encompasses over 180 kilobase (kb) of X-chromosome containing eight exons that produces a nearly 10.7 kb AR mRNA. The fully processed mature AR mRNA account for only 26% of total coding capacity and most of the transcript codes for noncoding regions that includes 5' and 3' UTRs. However, functional roles of UTRs in AR gene expression, principally its regulatory involvement in development of CRPC remained indefinable. Our research is focusing on understanding the functional roles of 6.8 kb long AR 3' UTR in AR gene expression and especially the molecular mechanism that revitalizes AR expression in CRPC. We have shown that a number of regulatory noncoding miRNAs play a critical 3' UTR targeting role in AR gene expression and has potential therapeutic implications. Here we show a synergistic approach of targeting AR expression mediated via its 3' UTR, using a miRNA cocktail combinatorial approach. In addition, we are investigating the potential functional association of 3' UTR in AR gene expression and implication in metastatic CRPC.

Biography

Girish C Shukla is an Associate Professor of Biology. He received his B.S. in Chemistry from Delhi University and PhD in Molecular Biology and Biochemistry from Brunel University, London, in 1997. He has been a faculty member of Cleveland State University since 2006.

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