Noncoding RNAs: The Fourth Dimension of the Human Genome

Editorial

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Ramaswamy Narayanan*
Department of Biological Sciences, Charles E. Schmidt College of Science, Florida Atlantic University, USA

***Corresponding author:** Ramaswamy Narayanan, Department of Biological Sciences, Charles E. Schmidt College of Science, Florida Atlantic University, Boca Raton, FL33431, USA, Tel: 5612972247; Fax: 5612973859; E-Mail: rnarayan@fau.edu

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Abbreviations: lncRNA: Long non-coding RNA; lincRNA: Long intergenic RNA; miR: Micro RNA; SNP: Single Nucleotide Polymorphism

Editorial

The human genome encoding the three billion letters of DNA alphabet continues to deliver surprises and raise new questions [1,2]. The initial focus of the genome project was on the discovery of gene targets for diagnosis and therapy [3]. Until recently, the knowledge base of the genome largely revolved around three dimensions: DNA, RNA and protein. A vast amount of the human genome once considered Dark Matter or junk DNA has become an area of intense research [4-9]. It is estimated that over 93% of the human genome is transcribed [10]. The role of this huge amount of the transcriptome in biology is however, unclear. This part of the genome, the noncoding RNAs (ncRNAs) can be rightly be considered the fourth dimension of the genome.

The ncRNAs comprise the long non-coding RNAs (lncRNAs), the long intergenic RNAs (lincRNAs), endogenous antisense RNAs, the microRNAs (miRs) and pseudogenes-derived lncRNAs [7]. The current version of the GENCODE database (v 22) estimates there to be 25,794 ncRNAs in humans [11,12]. The ncRNAs are crucial in gene regulation exerting their regulatory role at the chromatin, transcriptome and proteome level [13]. The regulation of the target genes by the ncRNAs occurs at the level of RNA and protein stabilization, protein binding and protein translocation or processing [9].

Originally thought to be non-protein coding transcripts, at least some of the ncRNAs now seem to be capable of coding for Open Reading Frames [14,15]. Thus, eventually the terminology non-coding will have to evolve to accurately reflect the differences between the coding and the non-coding nature of the transcriptome. Increasing evidence in the ncRNA field of research is beginning to challenge our current understanding of the human genome. Pseudogene-derived lncRNAs are emerging as key regulators of gene expression and as a reservoir for miRs and endogenous antisense transcripts [16]. In addition, various Genome Wide Association Studies (GWAS) have identified a vast majority of disease-associated Single Nucleotide Polymorphisms (SNPs) which are present at the non-coding intronic or intergenic regions of the genes [17,18]. These regions were neglected in the past because of the focus on the protein coding regions. However, the attention is beginning to shift to this unexplored region of the human genome. Understanding the impact of these SNPs is going to allow us to develop a better understanding of diverse disease-associated phenotypes in the future.

The ncRNAs including the miRs are of major interest for novel therapeutics as well as diagnostic biomarker development [4,19,20]. Numerous tools are becoming available to study the ncRNAs [21-26]. A microRNAs miR 222, is being developed as a therapeutic for hepatocellular carcinoma [27]. The Federal Drug Agency (FDA) approved its first lncRNA, the Prostate cancer antigen 3 (PCA3) as a urinary biomarker for prostate cancer diagnosis [28]. The miRs because of the stability in body fluids due to the secretome nature involving the exosomes, offer tremendous opportunities for biomarker potential for diagnosis and prognosis for cancer and other diseases [19,29-31].

The ncRNAs are the next frontier in molecular biology. The fruits of research in the ncRNA arena in the next decade are likely to challenge the current dogma in molecular biology. As we begin to understand more about the role of the entire transcriptome in gene regulation, our understanding of biology and function of a gene will achieve greater clarity. This is likely to lead into novel therapy and diagnosis for diverse diseases.

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