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Introductory Chapter: Noncoding RNAs—A Brief Overview

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1. Introduction

Noncoding RNAs (ncRNAs) are an attractive research field to prompt extensive genome-wide transcriptional efforts by different international initiatives such as the Encyclopedia of DNA Elements (ENCODEs) [1] and the Functional Annotation of the Mammalian Genome (FANTOM) [2]. Existence of ncRNAs is ubiquitous to all three domains of life, but they play different roles according to type of its RNA family [3, 4]. Dysfunction of ncRNAs may lead to various human diseases from tumorigenesis to neurological, cardiovascular, and developmental disorders [5]. Hence, ncRNAs have become a hot topic in molecular genetic and epigenetic research.

Findings of Human Genome Project have disclosed that approximately 1.5% of human genome is comprised of protein encoding genes. On the other hand, the majority of the human genome is transcribed and yields ncRNAs. Noncoding RNAs, which are not translated as peptides or proteins, may be categorized as housekeeping noncoding RNAs and regulatory noncoding RNAs. Noncoding RNAs may be grouped into two major classes based on their size: small noncoding RNAs (sncRNAs) are shorter than 200 nucleotides (nts) in length and long noncoding RNAs (lncRNAs) are longer than 200 nts. Albeit these RNAs are named as noncoding, some lncRNAs code for small bioactive peptides [6, 7].

SncRNAs accorporate functional RNAs including r-RNAs, snRNAs, and t-RNAs, which play important roles in transcriptional and translational regulations. Furthermore, sncRNAs also contain regulatory RNAs, which play roles in gene expression such as P-element-induced wimpy testis (PIWI) interacting RNAs (piRNAs), small interfering RNAs (siRNAs), and microRNAs (miRNAs). Per contra, lncRNAs represent a large group of noncoding regulatory RNAs. The lncRNAs are divided according to their mode of action, such as natural antisense transcripts (NATs), intergenic (lincRNAs), intronic lncRNAs, circular RNAs (circRNAs), promoter-associated long RNAs (pRNAs), and enhancer RNAs (eRNAs).

2. miRNAs and siRNAs

siRNAs and miRNAs are 19–24 nts in size and silent transcription of genes via inducing mRNA degradation or translational repression. Generally, protein-coding genes are negatively regulated by a single miRNA or multiple miRNAs [8]. While miRNAs originated from pri-miRNAs, source of siRNAs is double-stranded RNAs. Moreover, miRNAs potentially play important roles in biological processes in a cell such as cell differentiation, cell proliferation, cell death, and development by inducing mRNA degradation or translational repression. Dysregulation of miRNAs leads to several human diseases including cancer, cardiovascular, and neurodegenerative diseases [9].

3. piRNAs

piRNAs are 21–35 nts long and originated from long single-chain precursor transcripts. Their main functions are transposon repression, DNA methylation, silencing transposable elements, regulating gene expression, and fighting with viral infections. PIWI proteins are guided by piRNAs to cleave target RNA, promote heterochromatin assembly, and methylate DNA [10]. Up- and downregulated expressions of piRNAs in several cancer types and Alzheimer's disease suggest that piRNAs take part in several human diseases [11].

4. lncRNAs

lncRNAs are more than 200 nts long and originated in multiple ways and may be transcribed from both noncoding DNA by RNA polymerase II and protein coding (e.g., H19 and TUG1). lncRNA genes are more abundant than short ncRNAs and outnumber protein-coding genes. They mainly function in genomic imprinting and X-chromosome inactivation. Furthermore, they take roles in gene regulation, chromatin remodeling, cancer cell invasion, and metastasis and cell differentiation by acting as *cis*- or *trans*-regulators in biological processes [12]. Moreover, function of lncRNAs linked to some human diseases including hepatocellular carcinoma, Alzheimer's disease, and diabetes [13].

5. Future perspectives

Mounting evidence and recent discoveries of novel short and long regulatory noncoding RNA classes revealed remarkable complexity of RNA-guided regulation on biological processes in a cell. There is a complex problem between RNA regulatory network and protein-based regulatory mechanisms. Noncoding RNA regulatory network is a challenging process to analyze and untwist. For example, notwithstanding their size, both lncRNAs and miRNAs play regulatory roles on protein-coding genes at post-transcriptional repression, but also lncRNAs may act as miRNA sponges and may degrade regulatory effect on mRNA [14]. It is known that dysregulation of ncRNAs may stir up several diseases including cancer and neurodegenerative diseases. Hence, further development of bioinformatics, genome scanning, and biochemical techniques is required to illuminate detailed functions and interactions of ncRNAs. It is clear that further research on ncRNAs will change our understanding about the nature of genome composition by rummaging previous dogmas.

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