JOURNAL OF RNA and Genomics ISSN: 2591-7781

ISSN: 2591-7781 J RNA Genomics, 2018, Vol 14, 608-609

EDITORIAL

LncRNA, a Noisy or Real Transcriptional Entity?

Quamarul Hassan*

School of Dentistry, Institute of Oral Health Research, Department of Oral & Maxillofacial Surgery, RNA Biology and Epigenetics Lab, University of Alabama at Birmingham, Birmingham, AL

*Correspondence to: Quamarul Hassan, E-mail: hassank@uab.edu , Tel: + 205 975 3020

Received Date: 7 February 2018; Accepted Date: 7 February 2018; Published Date: 14 February 2018

Editorial

Surprisingly, only 2% of the mammalian genome encodes proteins, whereas an estimated 98% accounts for non-coding RNA that includes anywhere from 20,000 to 100,000 long non-coding RNA (lncRNA) transcripts. It is now clear that many lncRNA are indeed functional and regulate bi-directional gene transcription. Hence, understanding the function of lncRNA transcripts from a massive transcriptome is an utmost priority and challenge. In a recent Leading Edge review published in Cell (Cell 172, January 25, 2018), Joshua T. Mendall (HHMI) and Florian Kopp from University of Texas South-western Medical Centre, provide a conceptual and rational experimental framework for mechanistic classification and function of lncRNA. They categorized lncRNA based on genomic location and mode of regulatory function (*cis vs. trans*).

Mechanisms of LncRNA Regulation

Regarding the *cis* acting mechanism of lncRNA function, the authors discuss three mechanisms through which lncRNAs can influence the chromatin state of nearby genes. The first *cis* mechanism, sequence-dependent lncRNA regulation, is modelled by one of the best studied mechanisms of lncRNA regulation, Xist-mediated silencing of one X chromosome in females, known as X chromosome inactivation (Xi). Mechanistically, the lncRNA Xist recruits regulatory factors to the promoters of neighboring genes and thereby regulates promoter function. The sequence-specific requirements have been well studied, yet some of the mechanisms involved in this process remain debated.

In the second *cis* mechanism discussed, the transcription and/or splicing of the lncRNA locus controls the transcription of the neigh boring gene in a manner independent of the lncRNA transcript or product. In these cases, silencing by the lncRNA appears to be mediated by transcriptional overlap, such that transcription of the lncRNA prevents RNA polymerase II (Pol II) recruitment to the promoter of the neighboring gene, even in the presence of active chromatin. Furthermore, evidence suggests that transcription or splicing of some lncRNAs alters the chromatin state of neighboring gene promoters, thereby regulating the expression of those genes.

Lastly, DNA elements present within an lncRNA promoter or gene locus may function in cis, independently of the lncRNA product, to regulate neighboring genes. Indeed, recent studies suggest that the regulation of gene expression by enhancer-like elements that reside within the lncRNA locus but function independently of the lncRNA may be relatively common.

Kopp and Men dell note that lncRNAs that function in *trans* can also be grouped into three categories: those that regulate chromatin and gene expression at distant sites, those that alter nuclear structure and organization, and those that interact with and regulate the behavior of other proteins or RNA that regulate transcription. These latter interactions may occur in the nucleus or the cytoplasm.

Discerning Chaos from Function

Despite the recent attention to lncRNAs and advances in the experimental procedures available to study these ubiquitous RNAs, numerous confounding factors have complicated efforts to define the functions of individual lncRNAs. For example, the human transcripts of some lncRNAs display limited to no sequence similarity to the respective mouse transcripts. This raises concern about whether the associated gene-regulatory mechanisms are the same in rodent cells and in human cells. Moreover, lncRNAs that function in *trans* through direct binding mechanisms may require stoichiometric interaction for observable effects, thus experimental conditions must be rigorously evaluated. Methods for reliably inhibiting lncRNAs, especially those in the nucleus, are also needed.

Over the last decade, the regulatory functions of numerous lncRNAs, including Xist, HOTAIR, and MALAT1, have been well studied. On the other hand, many studies of lncRNA have encouraged spirited debate over whether noncoding RNAs represent “non-coding transcriptional chaos” or serve as truly functional regulatory RNAs. Undoubtedly, there is no definitive answer. Rigorous approaches can persuasively identify and characterize functional lncRNAs linked to biology.

Hence, I am very hopeful that persistent research on lncRNA epitranscriptome will keep due promise to uncover new and unanticipated regulation to impact our fundamental basis for normal physiology and disease.