

## The Modeling and Analysis of Mechanisms for lncRNA Regulation

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### Modeling and Analysis of lncRNA

Long non-coding RNA- lncRNA is a class of RNA molecule that is found in eukaryotes with a length between 200-100000 nt and no long reading frame, but its structural features are similar to mRNA [1,2]. The achievements in the genomic research project show that in the human genome sequence only 1.5% of nucleic acid sequences are used for protein coding (Data from ENCODE research published in 2012 [3]), 98.5% of DNA sequence in human genome belongs to non-coding sequence, most of the non-coding sequence are transcribed into RNA which length is more than 200 bases so-called “long noncoding RNA”.

The concept of lncRNA was first proposed by biologist Okazaki in 2002. His research group identified a lot of long noncoding RNA transcripts in large-scale sequencing of full-length cDNA Library in mice [4]. However, due to no functional annotation, these lncRNA transcripts were considered to be the by-products of RNA polymerase II transcripts in the following period of time, and they were thought to be “noise” and had no biological functions. Until 2007 the Stanford University Rinn et al. [5] study found a length of about 2.2Kb lncRNA gene HOTAIR plays an important role in regulating the growth and development of organisms (such as HOTAIR RNA can modify chromatin and inhibit the transcription of *HOX* gene by regulating the interaction with protein complex Polycomb, thereby regulating the growth and development of organism.), the researches of lncRNAs have aroused people’s attention, and becoming a hot and frontier of international research. In recent years, with the wide application of the two generation sequencing technology, the mysterious veil of lncRNA was gradually uncovered, the accumulated research data show that lncRNA is involved in the regulation of cell differentiation and ontogeny and other important life processes in many aspects such as: lncRNA participates in the process of X chromosome silencing [6], chromosome modified [7], genome modified [8], transcriptional activation [9], transcriptional interference [10], and nuclear transport [11], etc. lncRNA is also closely related to major human diseases [12-15]. Examples include: (1) in some cases, the overexpression of lncRNA is associated with certain cancers, including breast cancer, prostate cancer and leukemia et al. [12-14]; (2) lncRNA also plays an important role in the immune system [15], for instance the research team led by Katherine A. Fitzgerald of the University of Massachusetts medical school confirmed that a lncRNA (lincRNA-EPS) can play a transcriptional brakes and play a role in restricting inflammation. In addition, lncRNA can also regulate the differentiation of stem cells [16], such as Pnky is a newly discovered lncRNA that exists in the neural stem cells of the mouse and the human brain. The study found that knocking out Pnky from stem cells can increase the output of neurons by three to four times, which implies that Pnky and other lncRNA will eventually play an important role in regenerative medicine and cancer treatment. More studies have focused on the lncRNA regulation of gene transcription [17,18], recent studies have shown that a new mechanism of lncRNA-Cox2 can regulate Il12B transcription, supporting lncRNA to play an important role in regulating the inflammatory response of intestinal epithelial cells [17], and lncRNA-Cox2 can mediate the activation and inhibition of different immune genes in innate immune cells [18]. In a word, the regulation of long noncoding RNA is being paid more and more attention.

About 16000 lncRNAs have been identified in human beings [12], but most of the biological functions are unexplained and need to be studied in depth. Mathematical modeling and analysis provide a new perspective for understanding various possible mechanisms of lncRNA, especially providing a feasible way to solve the lncRNA mechanism hypothesis proposed by biologists. In fact, the use of mathematical modeling and theoretical analysis to study the biological functions of small RNA molecules has been recognized by many biologists. For example, Siciliano etc. through modeling analysis, this dissertation gets the conclusion that microRNA can achieve the effect of phenotypic stability by suppressing noise [19]. Martirosyan through modeling analysis how RNA affects each other’s level by competing with limited microRNA, thereby affecting gene expression [20]. Relatively, because the research of lncRNA has only recently started, so we haven’t seen the mathematical model of lncRNA regulation mechanism, let alone use the model to analyze the dynamic mechanism of the system.

In recent years, although there are a lot of experimental research articles on the lncRNA, but the function of lncRNA identification, especially on the effect mechanism is still in the initial stage, there is an urgent need for both experimental and theoretical researchers together to tackle the conundrum of lncRNA regulation mechanism. This approach is becoming the mainstream of the research of system biology, which has been proven effective and is expected to make breakthrough progress. Application of systematic biological methods to study the transcriptional regulation mechanism of lncRNA which will provide a new perspective to reveal the biological function of lncRNA, the related research work combined with the experimental data will help biologists to correctly understand the principle of lncRNA regulation mechanism and its biological function.

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