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Noncoding RNAs in control of gene expression[★]

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Noncoding RNAs (ncRNAs) constitute the vast majority of the human transcriptome. They have various lengths and shapes including small (microRNAs), long (lncRNAs), and circular (circRNAs). Due to the large diversity of these RNA molecules, they are found to regulate gene expression both at the transcriptional and posttranscriptional levels. They are involved in almost all cellular processes including proliferation, differentiation, survival, apoptosis, etc. Thus, they are associated with human diseases such as cancer, neurologic and metabolic disorders, and cardiovascular diseases, and in several cases, ncRNAs may serve as disease biomarkers. In this issue “ncRNAs in control of gene expression”, authors have summarized and discussed the roles of ncRNAs in cellular processes including metabolic and immune activities, myogenesis, and formation of ribonucleoprotein complexes with adaptor proteins.

Due to the recent advances in RNA sequencing technology and computational analyses, numerous ncRNA have been identified and annotated. In chapter one Szczepaniak et al., discuss and describe more in depth annotation of novel long noncoding RNAs. They utilized available transcriptomic and genomic data to provide characteristics such as tissue specificity, abundance, polyA status, localization, stability, and conservation facilitating the road towards understanding their biological significance.

lncRNAs vary in length from 200 to several thousands of nucleotides. These transcripts are expressed in all cells and usually lack open reading frames for protein-coding. They are a heterogeneous class of ncRNAs and function via diverse mechanisms. In chapter two Dangelmaier et al., discuss an important mechanism of action through the interaction of lncRNAs with RNA binding proteins. Thus, acting as adaptor proteins to form large ribonucleoprotein complexes by recruiting other proteins that indirectly associate with the lncRNA. This chapter also discusses the roles of adaptor proteins in lncRNA functions and proposes mechanistic scenarios for their actions.

Recent studies have indicated that lncRNAs are involved in the control of metabolic homeostasis. Chapter three by Ji et al., summarizes and discusses various lncRNAs implicated in metabolic disorders with the focus on chronic inflammation, insulin resistance, and lipid homeostasis. They also discuss lncRNAs as diagnostic and therapeutic targets to improve metabolic homeostasis. In chapter four by Hamilton et al., the maternally expressed gene 3 (MEG3) is discussed, particularly for its role in metabolic programming. They

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discuss how nutritional status alters MEG3 expression to influence cancer and metabolic dysfunctions. Furthermore, the mammalian Target of Rapamycin (mTOR) is known as a master regulator of cell growth and metabolism and its dysregulation is associated with several diseases. In chapter five, Aboudehen summarized and discussed the regulation of mTOR signaling by lncRNAs.

LncRNAs are important regulators of immune response and initial defense against infection. In chapter six, Robinson et al., utilized the biological model system of macrophage activation as a framework to provide an approach to study the role of lncRNAs in the regulation of immune responses. They also discuss the challenges, therapeutic intervention, and the new technologies available to study lncRNAs in the immune system.

Since ncRNAs, including microRNAs, are involved in several diseases including cancer, they can be employed to explore and develop therapeutic strategies. In chapter seven, Bofill-De Ros et al., discuss the canonical and non-canonical (microRNA isoforms or isomiRs) target site recognition beyond the seed region. With a focus on isomiRs, they discuss the current knowledge of miRNA-target recognition and the process through which microRNA isoforms achieve functional diversification. In chapter eight, Tomar et al., provide a comprehensive understanding of functions and mechanisms of ncRNAs, including microRNAs, which are crucial in breast cancer progression such as cell proliferation, angiogenesis, EMT, CSCs, drug resistance, and metastasis. They also discuss ncRNAs, including microRNAs, as potential therapeutic targets in breast cancer.

Circular RNAs (circRNAs) are formed through non-linear back splicing, during which the 5' and 3' ends are covalently joined. This class of ncRNAs regulates gene expression through their interactions with RNA binding proteins, microRNAs, and other transacting factors. Thus, they are involved in several cellular processes including proliferation and differentiation. In chapter nine, Das et al., discuss circRNAs in differentiation of muscle cells to myotubes in the process of myogenesis. They also discuss circRNAs involved in muscle diseases.

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