

Preface

A major portion of the eukaryotic genome is occupied by DNA sequences whose transcripts do not code for proteins. This part of eukaryotic genome is transcribed in a developmentally regulated manner or as a response to external stimuli to produce large numbers of long noncoding RNAs (lncRNAs). Genome-wide studies indicate existence of more than 3,300 lncRNAs. Long ncRNAs are tentatively defined as molecules of ncRNA more than two hundred nucleotides long. Due to the complexity and diversity of their sequences and their mechanisms of action, progress in the field of lncRNAs has been very slow. Nonetheless, lncRNAs have emerged as key molecules involved in the control of transcriptional and posttranscriptional gene regulatory pathways. Although limited numbers of functional lncRNAs have been identified so far, the immense regulatory potential of lncRNAs is already evident, emphasizing that a genome-wide characterization of functional lncRNAs is needed. Here, we review this rapidly advancing field of long ncRNAs, describing their structures, organization, and function in diverse eukaryotic systems.

Although the evidence for diverse biological functions of lncRNAs exists across the wide evolutionary spectrum, the underlying molecular mechanisms are far from clear. In Chap. 1 of this book, Radha Raman Pandey and Chandrasekhar Kanduri discuss the epigenetic and nonepigenetic mechanisms by which lncRNAs regulate various biological functions in model systems, from yeast to mammals. Long ncRNA molecules take part in gene regulation from the single gene level to an entire chromosome via recruitment of chromatin-modifying complexes *in cis* or *trans*. At the posttranscriptional level, lncRNAs regulate the splicing, localization, stability, and translation of the target mRNAs by base-pairing with their target RNAs. Transcriptional repression is mainly done by long noncoding RNAs in contrast to translational repression executed mostly by short noncoding RNA. In Chap. 2, Riki Kurokawa overviews the recent publications regarding the transcription regulation by long ncRNAs. In addition, the relation between a random transcriptional activity of RNA polymerase II and the origin of long ncRNAs is discussed.

In mammalian female somatic cells, one of the two X chromosomes is inactivated, and in the last few decades, several *cis*- and *trans*-acting factors involved in the regulation of the X chromosome inactivation process have been identified. The two main regulatory factors are *Xist* and *Tsix* that both encode functional lncRNAs. In Chap. 3, Joost Gribnau and collaborators describe the current knowledge about the structure and function of *Xist* and discuss the important *cis*- and *trans*-regulatory elements and proteins in the X chromosome inactivation. The authors also highlight new findings with other ncRNAs involved in gene repression and discuss these findings in relation to *Xist*-mediated gene silencing.

Telomeres protect the ends of linear eukaryotic chromosomes from being recognized as DNA double-stranded breaks, thereby maintaining the genome stability. The highly heterochromatic nature of telomeres had, for a long time, reinforced the idea that telomeres were transcriptionally silent. In 2007, the longstanding dogma that telomeres are transcriptionally silent was overturned by the discovery that noncoding RNA molecules, named *TE*lomeric Repeat-containing RNA (TERRA), were found to emanate from and associate with telomeres. In Chap. 4, Claus M. Azzalin and collaborators provide an overview of telomere structure, function, and biology and extensively review the current knowledge about TERRA biogenesis, regulation, and potential functions.

In eukaryotic cells, correct segregation and inheritance of genetic information relies on the activity of specialized chromosomal regions called centromeres. Centromeric and pericentric regions have long been regarded as transcriptionally inert; however, a number of studies in the past 10 years provided convincing evidence that centromeric and pericentric sequences are transcriptionally active. In Chap. 5, Claire Vourc'h and Giuseppe Biamonti review the expression of these sequences in mouse and human cells and discuss the possible functional implications of centromeric and pericentric sequences activation and/or of the resulting noncoding RNAs. An overview of the molecular mechanisms underlying the activation of centromeric and pericentromeric sequences is provided.

Alu elements are the most abundant repetitive elements in the human genome and, recently, it has become evident that they play crucial and diverse roles in regulating gene expression. Audrey Berger and Katharina Strub in Chap. 6 review role of *Alu* and *Alu*-related RNAs in regulation of transcription and translation. Transcription from these elements occurs at low levels under normal conditions but increases transiently after stress, indicating a function of *Alu* RNA in cellular stress response. *Alu* elements provide a source for the biogenesis of miRNAs and, when embedded into mRNAs, can be targeted by miRNAs. Certain *Alu* elements evolved into unique transcription units with specific expression profiles producing RNAs with highly specific cellular functions.

The large noncoding *roX* RNAs have a central role in sex chromosome dosage compensation in flies, where they fulfill a role with similarities to that of *Xist* during mammalian dosage compensation. In Chap. 7, S. Kiran Koya and Victoria H. Meller summarize the current knowledge of the function of the noncoding *roX* genes in the process of dosage compensation in *Drosophila*. The unexpected discovery of a role for *roX* in the expression of heterochromatic genes is discussed.

Satellite DNAs are major heterochromatin constituents in many insect species found to be transcribed during all developmental stages. Transcripts play a role in heterochromatin establishment and regulation, although the detailed molecular mechanism and proteins involved are not elucidated yet. The satellite DNA transcription is associated with development and differentiation and is actively regulated by environmental factors such as temperature. In Chap. 8, Đurđica Ugarković and collaborators review the transcription of satellite DNAs in different insects. They also discuss the role of satellite DNA transcripts in regulation of heterochromatic genes as well as genes located in the vicinity of satellite DNA elements within euchromatin.

In contrast to small RNAs, much less is known about the large and diverse population of long noncoding RNAs in plants, and only few have been implicated in diverse functions such as abiotic stress responses, nodulation and flower development, and sex chromosome-specific expression. Moreover, many long noncoding RNAs act as antisense transcripts or are substrates of the small RNA pathways interfering with a variety of RNA-related metabolisms. As plants show a remarkable developmental plasticity to adapt their growth to changing environmental conditions, understanding how ncRNAs work may reveal novel mechanisms involved in growth control and differentiation. In Chap. 9, Virginie Jouannet and Martin Crespi discuss a major class of long noncoding RNAs and antisense transcripts in plants. They also introduce long noncoding RNAs interacting with specific RNA-binding proteins to modulate their action or localization.

Zagreb, Croatia

Đurđica Ugarković



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