
Contents

Foreword	ix
Preface	xvii
Chapter 1. Non-coding RNA, Its History and Discovery Timeline	1
1.1. The biology of RNA, a century of history	3
1.1.1. From nuclein to the double helix.	3
1.1.2. The “RNA world” concept.	4
1.1.3. Small bacterial RNA: pioneers of non-coding RNA.	7
1.1.4. Micro-RNA and RNA interference.	9
1.2. The discovery of long non-coding RNA in the pre-genomic era	12
1.2.1. H19: the first in the history of long non-coding RNA.	12
1.2.2. Inactivation of X, the eXISTence of XIST	14
1.3. From the non-coding genome to the non-coding transcriptome, the advent of the genomic era.	18
1.3.1. The human genome project: genomic DNA is essentially non-coding.	18
1.3.2. Permissive transcription and the hidden face of the genome	20

Chapter 2. Definition and Families of Long Non-coding RNA	25
2.1. The portrait of an ideal suspect in terms of long non-coding RNA	25
2.1.1. The coding potential of non-coding RNA	25
2.1.2. lncRNA transcription and the organization of their transcripts	27
2.1.3. The chromatin signatures of lncRNA genes	29
2.1.4. lncRNA expression: their stability, specificity and abundance	30
2.1.5. The cellular distribution of lncRNA	31
2.1.6. The structure of lncRNA	32
2.2. Classification of lncRNA	33
2.2.1. Based on size	33
2.2.2. Based on position relative to gene promoters	34
2.2.3. Based on their position relative to DNA regulator elements	40
2.2.4. Based on their biogenesis and degradation	43
2.2.5. Based on their distribution in the cell	45
2.2.6. The labeling of lncRNA: facing the challenge	46
Chapter 3. Biological Functions of Long Non-coding RNA	55
3.1. Non-coding RNA: rejects or functional elements of genomes?	55
3.1.1. Where do non-coding RNA come from?	56
3.1.2. Conservation and evolution of lncRNA	58
3.2. Functions of lncRNA in biological diversity	59
3.3. The classified functions of lncRNA	61
3.2.1. “Scaffold” lncRNA	62
3.2.2. Architect lncRNA (arcRNA)	63
3.2.3. “Guide” lncRNA	64
3.2.4. “Decoy” lncRNA	64
3.2.5. Competitive endogenous lncRNA (ceRNA)	65
3.2.6. miRNA precursor lncRNA	65
3.3. Classification based on association with biological processes	66

Chapter 4. Non-coding RNA in Development	69
4.1. Inactivation of the X chromosome	69
4.1.1. Identification and expression of XIST	69
4.1.2. The mechanism of XIST regulation	70
4.2. Genomic imprinting.	71
4.3. Regulation of HOX genes	72
4.3.1. lncRNA that act in <i>cis</i>	72
4.3.2. lncRNA that act in <i>trans</i>	74
4.4. Pluripotency by preventing the initiation of cell differentiation	75
4.5. Brain and central nervous system (CNS) development	77
4.5.1. The abundance of lncRNA in the nervous system	77
4.5.2. lncRNA associated with the expression of neuronal development proteins.	77
4.5.3. lncRNA of the retina.	78
4.5.4. The circRNA of the brain.	79
4.6. Development of other organs.	79
4.6.1. The heart	79
4.6.2. The muscles of the skeleton	80
4.7. Development of skin, blood and adipose cells	82
Chapter 5. Long Non-coding RNA and Cancer	85
5.1. Identifying the lncRNA signals in cancer transcriptomes	88
5.2. lncRNA, “drivers” of the cancer phenotype.	90
5.2.1. LncRNA, new tumor suppressors?	91
5.2.2. Proliferation circuits.	93
5.2.3. Cell longevity circuits	96
5.2.4. Cell motility circuits	98
5.3. lncRNA as diagnostic and prognostic tools and as therapeutic targets	100
5.3.1. Diagnostics and prognostics	100
5.3.2. Therapeutic targets	101

Concluding Perspectives	103
Bibliography	105
Glossary	151
List of Acronyms	157
Index	171