

Preface

Retrotransposons are highly repetitive and dispersed sequences. These transposable elements have the ability to proliferate via an RNA-mediated copy-and-paste mechanism, called retrotransposition, and belong to several distant subclasses in humans.

The Long INterspersed Element-1 (L1 or LINE-1) is the only autonomous transposable element able to generate new copies in the modern human genome. The role of this process as a source of genetic diversity and diseases in humans has been recognized since the late 1980s. However, the advances of deep-sequencing technologies have recently shed new light on the extent of L1-mediated genome variations. They have also led to the discovery that L1 is not only able to mobilize in the germline—resulting in inheritable genetic variations—but can also jump in somatic tissues, such as embryonic stem cells, neuronal progenitor cells, and in many cancers. L1 is also able to mobilize *in trans* other sequences, leading to the expansion of Alu elements, which belong to another class of repeats, the Short INterspersed Elements (SINEs); or to the formation of processed pseudogenes, which also contribute to genome plasticity. Understanding the link between retrotransposon-mediated structural genomic variation and human phenotypes or diseases has become an intense field of research.

Although insertional mutagenesis is one of the mechanisms by which retrotransposons reshape our genome, retrotransposition-independent mechanisms also impact genome stability and cellular physiology (e.g., recombination, exaptation, creation of novel or alternative transcripts or proteins, DNA damage). These processes implicate a much broader set of retrotransposon sequences, some being very ancient and totally unable to mobilize, at least in humans. For example, the remodeling of the epigenetic landscape during early embryonic development activates the transcription of defective retrotransposons. The latter are unable to jump, but their transcription allows the synthesis of long noncoding RNA (lncRNA) with essential roles in stemness.

One of the originalities of this book is to explore not only insertion-based effects and their related consequences on germline and somatic genome dynamics but also the role and impact of retrotransposon sequences in a broader context, including a

number of novel topics that emerged recently (lncRNA, neuronal disorders, exaptation, aging). We hope that it will illustrate how much retrotransposon biology is tightly connected to a myriad of cellular or physiological processes and will stimulate the next generation of young scientists to join a fascinating field and a highly dynamic research community.

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