

Review

# Emerging Opportunities to Study Mobile Element Insertions and Their Source Elements in an Expanding Universe of Sequenced Human Genomes

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**Abstract:** Three mobile element classes, namely *Alu*, LINE-1 (L1), and SVA elements, remain actively mobile in human genomes and continue to produce new mobile element insertions (MEIs). Historically, MEIs have been discovered and studied using several methods, including: (1) Southern blots, (2) PCR (including PCR display), and (3) the detection of MEI copies from young subfamilies. We are now entering a new phase of MEI discovery where these methods are being replaced by whole genome sequencing and bioinformatics analysis to discover novel MEIs. We expect that the universe of sequenced human genomes will continue to expand rapidly over the next several years, both with short-read and long-read technologies. These resources will provide unprecedented opportunities to discover MEIs and study their impact on human traits and diseases. They also will allow the MEI community to discover and study the source elements that produce these new MEIs, which will facilitate our ability to study source element regulation in various tissue contexts and disease states. This, in turn, will allow us to better understand MEI mutagenesis in humans and the impact of this mutagenesis on human biology.

**Keywords:** *Alu*; LINE-1; L1; SVA; mobile element insertions; human genomes



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## 1. Introduction

Mobile genetic elements occupy approximately half of the human genome [1]. However, only three element classes, i.e., *Alu*, LINE-1 (L1), and SVA elements, remain actively mobile and continue to mutagenize human genomes today [2–15]. All three of these element classes are non-LTR retrotransposons that are mobilized through RNA intermediates using the protein machinery that is encoded by the L1 retrotransposon. Specifically, the L1-encoded proteins ORF1p and ORF2p generate new *Alu*, L1, and SVA “offspring” mobile element insertions (MEIs) through a mechanism that is termed target primed reverse transcription (TPRT) [16] (Figure 1). ORF1p encodes a nucleic acid chaperone [17,18], whereas ORF2p encodes an endonuclease (EN) [17,19] and a reverse transcriptase (RT) [17,20]. Since the L1 machinery mobilizes all three of these element classes [17,21–23], new *Alu*, L1, and SVA MEIs share characteristic features of L1 elements, including L1-like target site duplications (TSDs), poly (A) tails, and interior mutations that may be created by the error-prone L1 reverse transcriptase.

New MEIs are generated both in the germline [6–15] and in at least some somatic human tissues (i.e., epithelial cancers [6,24–30], reviewed in [31,32] and neuronal tissues [33–38], reviewed in [39]). Germline MEIs have been implicated in several dozen human diseases, including hemophilia [40], neurofibromatosis [41], and Duchenne muscular dystrophy [42] (reviewed in [43,44]). Somatic MEIs have been implicated in a wide range of epithelial cancers, including colon, lung, liver, esophageal, and pancreatic cancer (reviewed in [31,32]) and in several neurological diseases, including Rett Syndrome, Aicardi-Goutieres Syndrome, Schizophrenia, Amyotrophic Lateral Sclerosis (ALS), and normal aging (reviewed

# Opportunities Read Text Audcass Element

**Camilla Rothe**



**Opportunities Read Text Audcass Element:**

The book delves into Opportunities Read Text Audcass Element. Opportunities Read Text Audcass Element is an essential topic that must be grasped by everyone, from students and scholars to the general public. This book will furnish comprehensive and in-depth insights into Opportunities Read Text Audcass Element, encompassing both the fundamentals and more intricate discussions.

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    - Chapter 1: Introduction to Opportunities Read Text Audcass Element
    - Chapter 2: Essential Elements of Opportunities Read Text Audcass Element
    - Chapter 3: Opportunities Read Text Audcass Element in Everyday Life
    - Chapter 4: Opportunities Read Text Audcass Element in Specific Contexts
    - Chapter 5: Conclusion
  2. In chapter 1, this book will provide an overview of Opportunities Read Text Audcass Element. This chapter will explore what Opportunities Read Text Audcass Element is, why Opportunities Read Text Audcass Element is vital, and how to effectively learn about Opportunities Read Text Audcass Element.
  3. In chapter 2, the author will delve into the foundational concepts of Opportunities Read Text Audcass Element. The second chapter will elucidate the essential principles that must be understood to grasp Opportunities Read Text Audcass Element in its entirety.
  4. In chapter 3, this book will examine the practical applications of Opportunities Read Text Audcass Element in daily life. The third chapter will showcase real-world examples of how Opportunities Read Text Audcass Element can be effectively utilized in everyday scenarios.
  5. In chapter 4, this book will scrutinize the relevance of Opportunities Read Text Audcass Element in specific contexts. This chapter will explore how Opportunities Read Text Audcass Element is applied in specialized fields, such as education, business, and technology.
  6. In chapter 5, this book will draw a conclusion about Opportunities Read Text Audcass Element. This chapter will summarize the key points that have been discussed throughout the book.
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