



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-Goutières Syndrome, Schizophrenia, Amyotrophic Lateral Sclerosis (ALS), and normal aging (reviewed

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THE GLASS MENAGERIE, [MUSIC: 'THE GLASS MENAGERIE' UNDER FAINTLY. Lightly.] Not one gentleman ... [MUSIC: 'THE GLASS MENAGERIE'. He stretches out his hand.] Oh, be careful - if ... The Glass Menagerie book script of the play. [SCREEN LEGEND: 'OÙ SONT LES NEIGES.'] There was young Champ Laughlin who later became vice-president of the Delta Planters. Bank. The Glass Menagerie - Tennessee Williams (AMANDA exits through living-room curtains. TOM is left

with LAURA. He stares at her stupidly for a moment. Then he crosses to shelf holding glass menagerie. The Glass Menagerie Amanda Wingfield is a faded, tragic remnant of Southern gentility who lives in poverty in a dingy St. Louis apartment with her son, Tom, and her daughter, ... The Glass Menagerie When Amanda convinces Tom to bring home from his workplace a "gentleman caller" for Laura, the illusions that Tom, Amanda, and Laura have each created in order ... The Glass Menagerie Text Scene 1: The Wingfield apartment is in the rear of the building, one of those vast hive-like conglomerations of cellular living-units that flower as. Tennessee Williams - The Glass Menagerie (Scene 3) LEGEND ON SCREEN: 'AFTER THE FIASCO' [TOM speaks from the fire-escape landing.] TOM: After the fiasco at Rubicam's Business College, the idea of getting a ... "The Glass Menagerie," Scene One and Scene Two, by ... 41 Scene 1. 352 The Wingfield apartment is in the rear of the building, one of those vast hive-like conglomerations of cellular living-units that flower as ... Tennessee Williams - The Glass Menagerie (Scene 7) A moment after the curtain rises, the lights in both rooms flicker and go out.] JIM: Hey, there, Mr Light Bulb ! [AMANDA laughs nervously. LEGEND: 'SUSPENSION ... The Glass Menagerie: Acting Edition: Tennessee Williams A new introduction by the editor of The Tennessee Williams Annual Review, Robert Bray, reappraises the play more than half a century after it won the New York ... New Link for 2004 Shadow VT750 Aero Repair Manual Mar 29, 2021 — Hi, New member here! Does anyone here has a new download link for one of the repair manuals for a 2004 Honda Shadow VT750 Aero Model? Manuals VT750DC.com OEM PDF Factory Service and Owners Manuals and related links for several Honda Shadow 750 motorcycle models. Honda Shadow Aero VT750 Workshop Manual 2005-2007 Honda Shadow Aero VT750 Workshop Manual 2005-2007 - Free ebook download as PDF File (.pdf), Text File (.txt) or read book online for free. Honda Shadow 750 Service Manual VT750DC Spirit 2001 ... Service your motorcycle with a Cyclepedia Honda Shadow 750 Service Manual. Color photographs, wiring diagrams, specifications and step-by-step procedures. HONDA VT750C OWNER'S MANUAL Pdf Download View and Download Honda VT750C owner's manual online. VT750C motorcycle pdf manual download ... Motorcycle Honda Shadow Aero VT750C 2018 Owner's Manual. (141 ... Honda service manuals for download, free! Honda motorcycle workshop service manuals to download for free! 2005_yt750c.pdf Always follow the inspection and maintenance recommendations and schedules in this owner's manual. 52. The Importance of Maintenance. Servicing Your Honda. Honda VT750C2 Shadow Spirit Service Manual View and Download Honda VT750C2 Shadow Spirit service manual online. 2007-2009 Motorcycle. VT750C2 Shadow Spirit motorcycle pdf manual download. Honda 2004 VT750CA Shadow Aero Service Manual Fully bookmarked and searchable digital download of the above listed service manual. All of our manuals come as easy-to-use PDF files. Our downloads are FAST ... Service Manuals Service manuals available for free download, please feel free to help out ... Honda Shadow Aero VT750 Service Manual 05-07 · Honda VF750C Magna 1994 Service ... Correctional Officer Test This practice test is divided into three (3) areas: General Knowledge; Basic Skills; and Career-Specific Aptitude on professional standards, facility operations ... Louisiana Correctional Officer Test | Online 2023 ...

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