Submitter Name: Sarven Sabunciyan Submitted email: ssabunc1@jhmi.edu

Repetitive Element Expression is Altered in the Brain Following Glucocorticoid Exposure

Richard Lee¹ and Sarven Sabunciyan²

¹Department of Psychiatry and ²Department of Pediatrics, Johns Hopkins University

Repetitive elements (RE) constitute nearly half of the human genome. Certain RE loci regulate gene expression or take part in other cellular functions. In contrast, the inflammatory potential of specific RE loci have been implicated in ALS, multiple sclerosis, age related macular degeneration and Aicardi-Goutières syndrome. Additionally, RE activity has been associated with addiction, schizophrenia and the stress response. To investigate the role of RE in the stress response we characterized RE expression following glucocorticoid treatment in the HT22 mouse hippocampus cell line. We found extensive changes to RE expression, both down and upregulation, across the genome. We were able to validate the differentially expressed RE loci identified by our analysis via quantitative PCR. More importantly, we were able to replicate the identified RE expression changes in the hippocampus of mice treated with corticosterone. Further analysis revealed that 10 intergenic regions had multiple differentially expressed RE loci near each other. The syntenic regions for these loci in the human genome are within two schizophrenia susceptibility loci, smoking as a guantitative trait locus, syndromic X-linked mental retardation locus and a locus associated with early improvement and early partial response to citalopram/escitalopram treatment. Our results suggest that RE contribute to the stress response. As stress is associated with various psychiatric disorders including addiction, the characterization of RE expression has the potential to provide insights into pathology and novel opportunities for biomarker and drug development.