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Dear Editor [\[\[FN: Any specific editor?\]\]](#),

Please find enclosed our manuscript entitled “Comprehensive survey of LINE-1 transcriptional activity in human cell-lines, healthy somatic tissue and tumors”, which we hope will be considered for publication in Science. We are particularly interested in Science because we had a very good experience in the review and revision of our recent paper related [\[\[FN: Any paper we should mention here?\]\]](#). We hope that this new manuscript regarding the landscape of LINE-1 activity elements in a vast number of human samples will be considered for publication.

Transposable elements are one of the most important sources of variation in the genome but, until this moment, we couldn't assess their activity comprehensively. Due to their repetitive nature, we have been only able to assess small number of samples at a time. One way of solving this problem is by leveraging the multitude of available RNA-Seq experiments. The transcriptome from different tissues and diseases can help us uncovering the biology and implications of LINE-1 activity. We present a method able to analyze regular RNA-seq and gauge LINE-1 autonomous transcription. Using this uniform and unbiased method, we characterized the thousands of RNA-seq experiments and describe the landscape if LINE-1 activity in normal tissue. We also present a model that suggests that LINE-1 activity is entangled with genome instability in tumors by creating double strand breaks and small insertions and deletions. Thus, we do not only present a totally new solution to tackle the problem but also perform the biggest and most comprehensive assessment of LINE-1 activity in human cells.

[\[\[FN: Are we submitting it as part of the ENCODE? Could we maybe try it as PCAWG?\]\]](#).

We are submitting our paper as a companion to the other manuscripts written in the ENCODE Consortium's 3rd phase, i.e., ENCODE3. Our paper does not depend heavily on the other ENCODE3 manuscripts. Nevertheless, it is very important because it is the only study that uses ENCODE data to analyze the activity of LINE-1.

We believe that our efforts provide resources and methods that are useful for the genomic community. An important manuscript from ENCODE3 paper rollout is the paper on Encyclopedia of elements. As we mentioned earlier, our manuscript does not directly relate to it. If needed, the encyclopedia manuscript can be obtained from Orli Bahcall.

We list a number of suitable reviewers

Yours sincerely,

Mark Gerstein  
Albert L. Williams Professor  
of Biomedical Informatics