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Dear Orly,

We enclose our paper entitled “Pseudogenes in the mouse lineage: transcriptional activity and strain-specific history” which we would like to submit for publication in Nature as part of the ENCODE 3 mouse package, with the manuscript ID ENC122.

Pseudogenes are key markers of genome remodelling processes. In this paper, we report a detailed evolutionary analysis of pseudogenes in 18 mouse strains as well as important updates on the unitary pseudogene dataset in human and mouse reference genome.

The availability of transcriptional time course data during development (just completed in phase 3 of ENCODE) and the sequencing of 18 strains (completed by the Mouse Genome Project), allows us a comprehensive and detailed evolutionary analysis of pseudogenes complements in the mouse lineage. All the data resulted from the annotation and analysis is made available through the online resource [mouse.pseudogene.org](http://mouse.pseudogene.org/). Key-  part of the encode resource , GENCODE genes part of encode , all the data available from [mouse.pseudogene.org](http://mouse.pseudogene.org). and [mouse.gencodegenes.org](http://mouse.gencodegenes.org)

Emphise update human pseudogenes as well as mouse

We highlight that the strains share a number of similarities with respect to pseudogene complement size, biotype distribution, and top family enrichment, similarities that reflect our previous observations in human. However, there are also notable differences. In particular, we observe a that while the majority of the human pseudogenes have been formed through a single retrotranspositional burst, there are multiple burst in the mouse evolutionary history. Moreover, comparative analysis of the strain pseudogene complements suggests a strong strain specific evolution. Finally, we find that ~15% of the pseudogenes are transcribed, and show that processed pseudogenes are commonly associated with highly transcribed genes.

We attach a list of suitable reviewers for the paper. We would prefer it if the paper would not be sent to Peer Bork (EMBL), Christopher Ponting (University of Edinburgh), Henrik Kaessmann (UNIL), Nicolas Vinckenbosch (UC Berkeley) and Tuuli Lappalainen (Columbia University).

Yours sincerely,

Mark B Gerstein

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