Reviewer Report

Title: A genome alignment of 120 mammals highlights ultraconserved element variability and placenta associated enhancers

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Reviewer name: Quan Nguyen

Reviewer Comments to Author:

The authors present a valuable resource for comparative genomics analysis and demonstrate important insights into the sequences of ultraconserved elements and conserved enhancers.
My minor comments and suggestions are below:
The definition of conserved placental mammal specific enhancers is based on the presence of at least one shared 10-mer across all placental mammal clades, assumming that the 10-mer represents the typical size for transcription factor (TF) binding sites. It would be interesting to predict which TF binding sites are enriched in all of those 10-mers identified for 1820 enhancers and if these TFs are related to placenta-related genes. Results from this analysis would serve as orthogonal validation of the GREAT enrichment analysis.
Among the FANTOM conserved enhancers, are there enhancers with experimental validation to be active enhancers for human and mouse as reported in other databases such as the VISTA database?
What improvements or new features does the Human120Way alignment have compared to other publicly available enhancers, for example in comparison with the multiple alignment of 144 vertebrate genomes, which were also contains the mapping of human genes to other 133 species using CESAR (Sharma and Hiller, 2017)?
Regarding Supplementary Table S2, it appears the variability measured by lower bounds and the upper bounds is inversely proportional to the length, i.e. longer regions have lower values. It will be useful to describe in more details, how the UCEs were determined and explain why their lengths are different. To make the bounds comparable between regions, the authors may consider weighting the variability by length for each region.
Very minor: Use a full name for CESAR (Coding exon-structure aware realigner) when it is first mentioned

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