

## Mtor mm10 – a simple regulatory model

Paul Shannon for Noa Rappaport  
3 nov 2021

The goal here is to illustrate the use of ENCODE mm10 annotations, FIMO motif finding, trena, and rna-seq from Gladyshev 2019 can be combined to produce a low-res regulatory model of Mtor

> [Cell Metab.](#) 2019 Sep 3;30(3):573-593.e8. doi: 10.1016/j.cmet.2019.06.018. Epub 2019 Jul 25.

## Identification and Application of Gene Expression Signatures Associated with Lifespan Extension

Alexander Tyshkovskiy <sup>1</sup>, Perinur Bozaykut <sup>2</sup>, Anastasia A Borodina <sup>3</sup>,  
Maxim V Gerashchenko <sup>2</sup>, Gene P Ables <sup>4</sup>, Michael Garratt <sup>5</sup>, Philipp Khaitovich <sup>6</sup>,  
Clary B Clish <sup>7</sup>, Richard A Miller <sup>5</sup>, Vadim N Gladyshev <sup>8</sup>

Regulatory elements from ENCODE cCRE Registry via UCSC Table Browser

Select dataset

clade: Mammal

genome: Mouse

group: Expression and Regulation

track: ENCODE cCREs

table: encodeCcreCombined

describe table schema

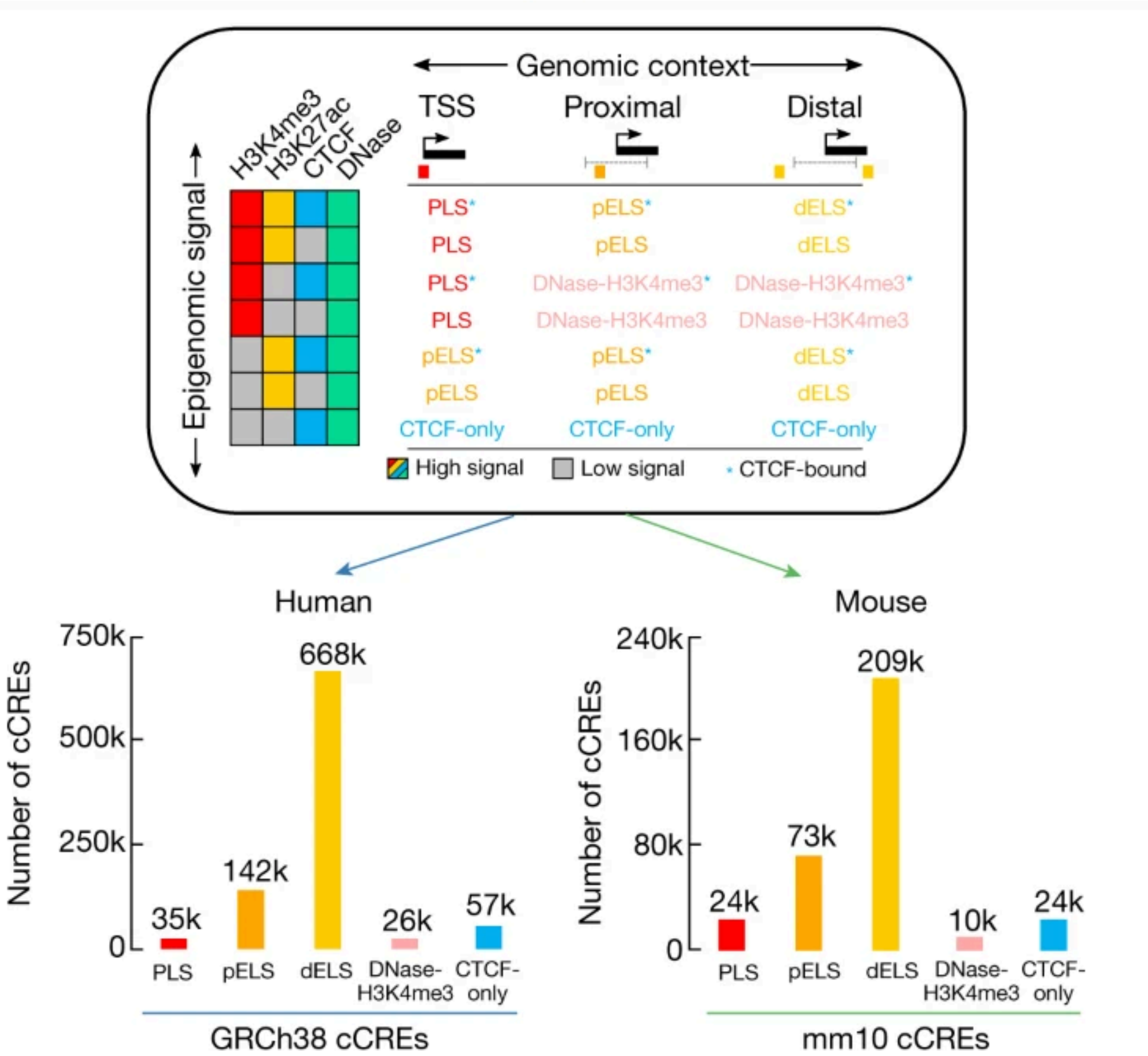
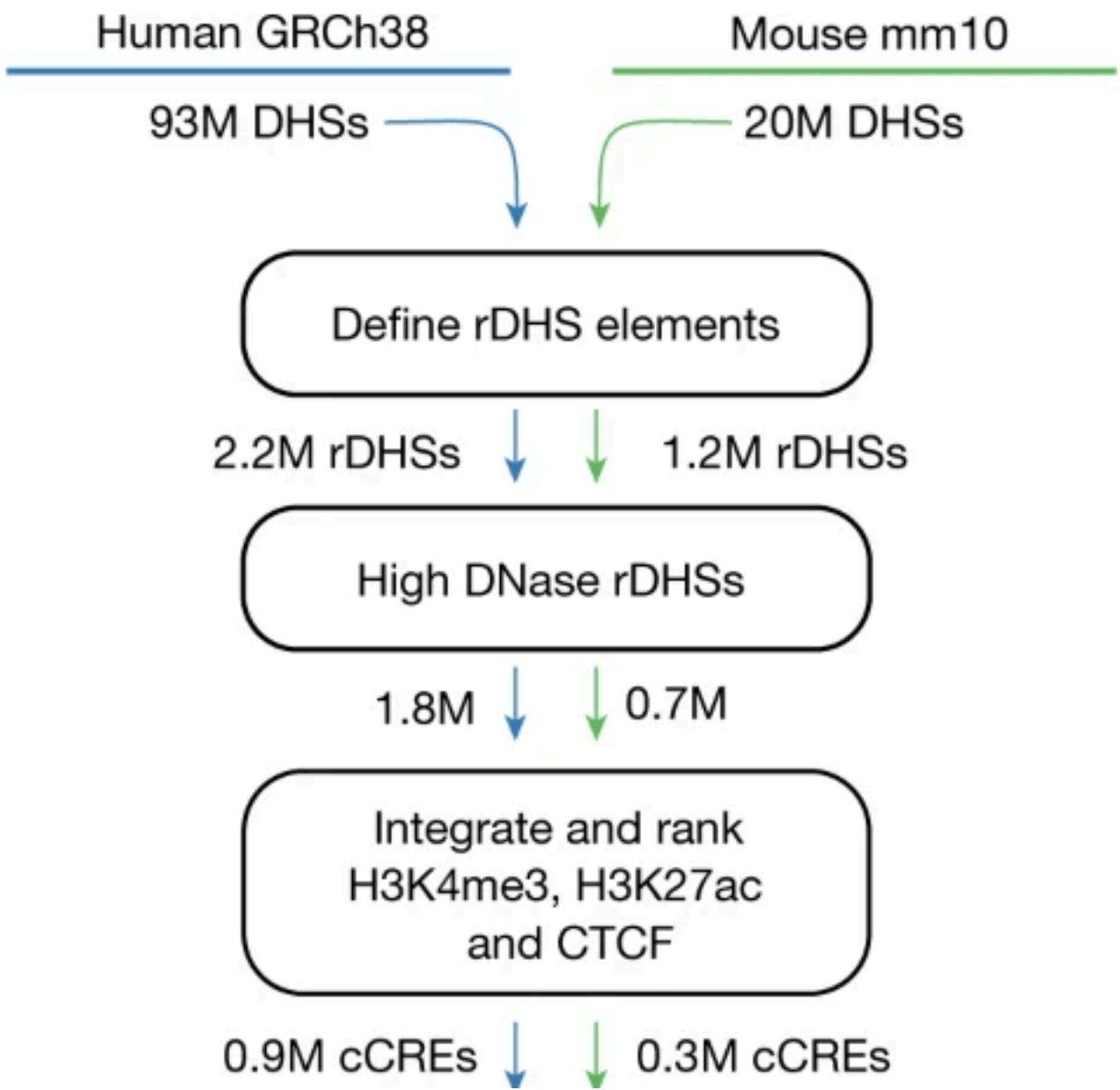
Article | [Open Access](#) | [Published: 29 July 2020](#)

Expanded encyclopaedias of DNA elements in the human and mouse genomes

[The ENCODE Project Consortium](#), [Jill E. Moore](#), [...] [Zhiping Weng](#)

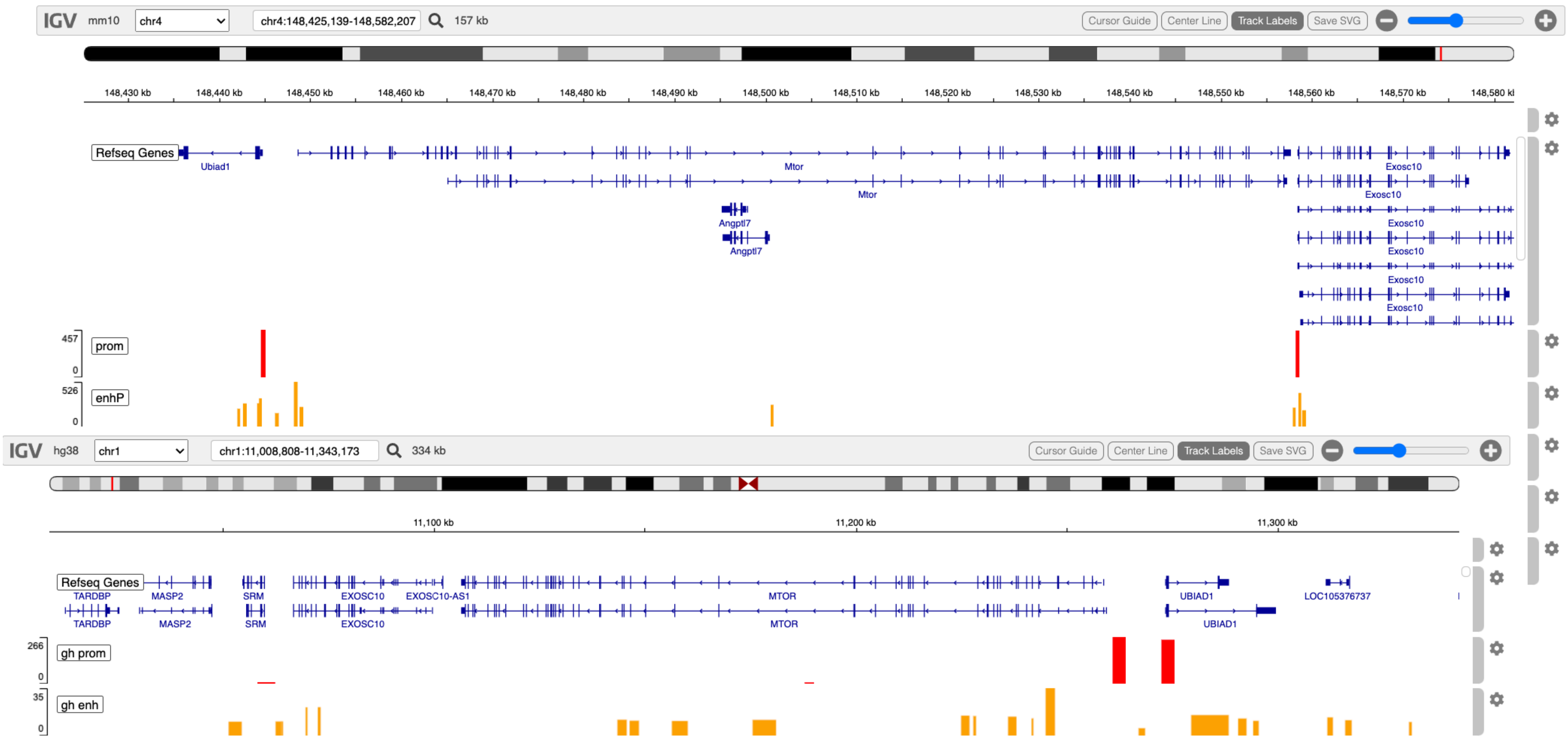
[Nature](#) **583**, 699–710 (2020) | [Cite this article](#)

Fig. 3: Selection and classification of cCREs to build the registry of candidate cis-regulatory elements.



We began by filtering and clustering DNase peaks to create representative DHSs (rDHSs). We then selected those rDHSs with high DNase signal (maximal Z-score or max-Z across all biosamples with data; see [Methods](#)) and high signal for at least one other assay (H3K4me3, H3K27ac or CTCF) to be cCREs. In total, we defined 926,535 cCREs in human and 339,815 cCREs in mouse. On the basis of combinations of signal and genomic context, we classified cCREs into one of these groups: PLS, pELS, dELS, DNase-H3K4me3, or CTCF-only, and their counts are indicated (k, thousand; M, million). Human and mouse silhouettes were adapted under Public Domain Mark 1.0 and Public Domain Dedication 1.0 licenses, respectively.

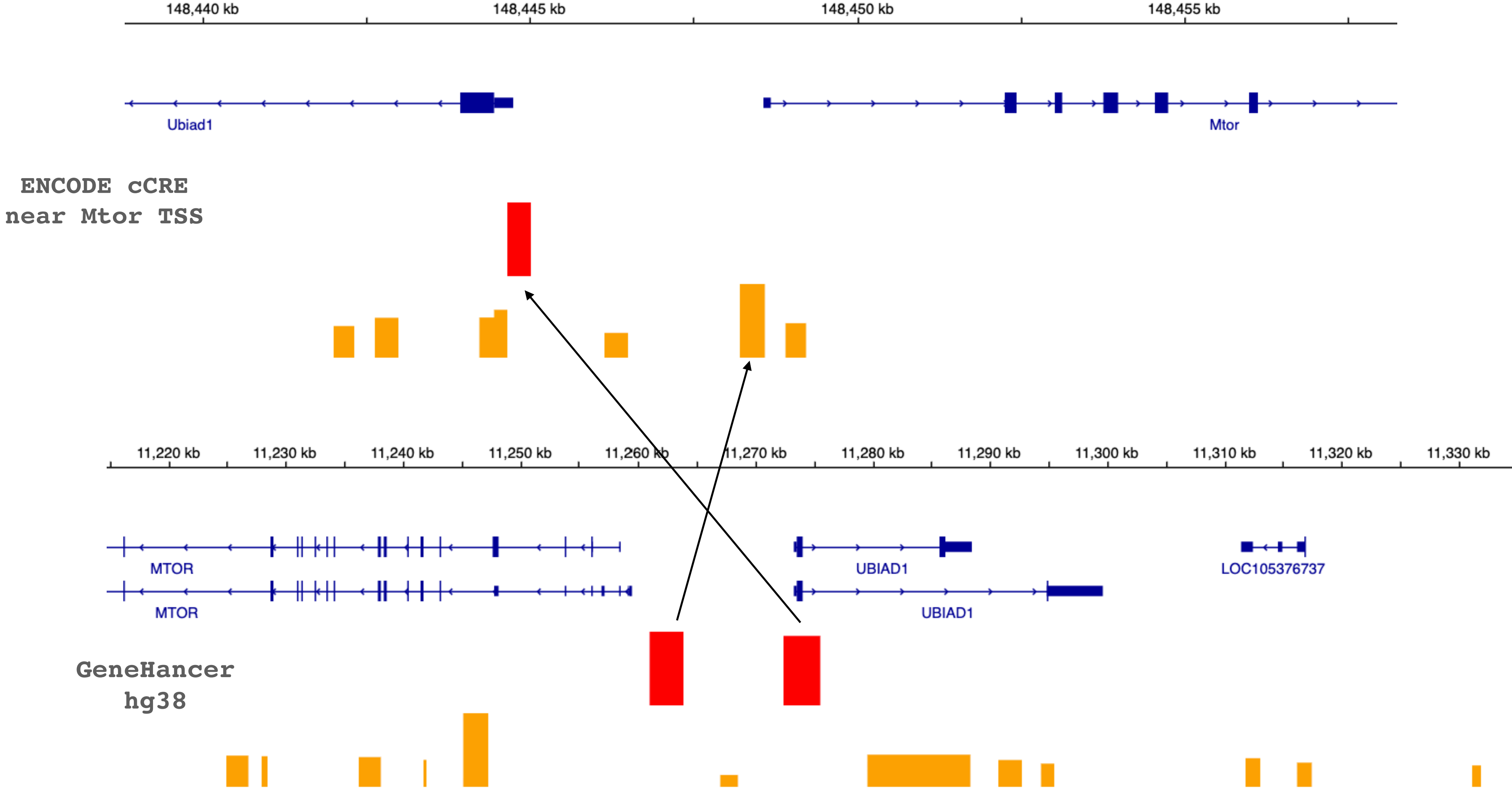
Candidate cis-regulatory elements (cCREs) in the vicinity of mm10 Mtor  
hg38 GeneHancer shown below (note that direction is reversed)  
zoomed in on next slide



Promoters in **red**, proximal enhancers in **gold**  
GeneHancer regions come with evidence for target gene association  
ENCODE cCREs are selected only by proximity



Zoomed in. MM10 predictions and GeneHancer have some agreement, but mm10 proximal enhancer appears where TSS-intersection hg38 promoter is found



trena model with fimo threshold 1e-5, putative promoter & proximal enhancers

|   | tf    | betaLasso | betaRidge | spearmanCoeff | pearsonCoeff | rfScore | xgboost | tfbs |
|---|-------|-----------|-----------|---------------|--------------|---------|---------|------|
| 1 | Klf12 | 0.278     | 0.136     | 0.845         | 0.876        | 5.016   | 0.414   | 3    |
| 2 | Tcf12 | 0.243     | 0.364     | 0.752         | 0.770        | 2.861   | 0.166   | 1    |
| 3 | Tcf3  | 0.481     | 0.349     | 0.733         | 0.733        | 3.734   | 0.204   | 1    |
| 4 | Nr2f6 | 0.000     | 0.180     | 0.528         | 0.497        | 1.527   | 0.055   | 1    |
| 5 | Zfx   | 0.000     | 0.096     | 0.250         | 0.231        | 0.546   | 0.026   | 1    |
| 6 | Nr5a2 | 0.000     | 0.055     | 0.146         | 0.174        | 0.936   | 0.052   | 1    |
| 7 | Klf1  | 0.000     | -0.037    | -0.084        | -0.063       | 0.528   | 0.083   | 1    |



trena model with fimo threshold 1e-4, putative promoter & proximal enhancers

|    | tf      | betaLasso | betaRidge | spearmanCoeff | pearsonCoeff | rfScore | xgboost | tfbs |
|----|---------|-----------|-----------|---------------|--------------|---------|---------|------|
| 1  | Klf12   | 0.196     | 0.067     | 0.845         | 0.876        | 4.998   | 0.361   | 5    |
| 2  | Rxra    | 0.428     | 0.221     | 0.808         | 0.841        | 2.684   | 0.084   | 2    |
| 3  | Tcf12   | 0.153     | 0.182     | 0.752         | 0.770        | 1.064   | 0.112   | 3    |
| 4  | Tcf3    | 0.232     | 0.177     | 0.733         | 0.733        | 1.356   | 0.164   | 3    |
| 5  | Hnf4a   | 0.024     | 0.105     | 0.717         | 0.750        | 1.613   | 0.031   | 1    |
| 6  | Mlxip   | 0.000     | 0.072     | 0.626         | 0.649        | 0.640   | 0.004   | 1    |
| 7  | Nr2f6   | 0.000     | 0.075     | 0.528         | 0.497        | 0.205   | 0.010   | 3    |
| 8  | Rfx1    | 0.000     | 0.058     | 0.498         | 0.489        | 0.328   | 0.005   | 2    |
| 9  | Creb3l2 | 0.016     | 0.082     | 0.492         | 0.475        | 0.261   | 0.042   | 1    |
| 10 | Bhlhe40 | 0.000     | -0.040    | -0.489        | -0.419       | 0.231   | 0.018   | 2    |























