

SUPPLEMENTARY NOTE

WES- and WGS-unique *de novo* variant calls

5 A further 69 coding DNVs were called only by WES, of which 38 were observed to be possible DNVs by IGV visualization of the WGS reads. One of the 38 candidate DNVs exclusive to WES was not included in the WGS VCF, while 29 of the 37 that were included in the WGS VCF but removed during quality filtering due to not-PASS filter (5), AC >2 (4), ExAC AF > 1e-04 (2), low proband alternate allele depth (AAD) and/or parental read depth (3), or multiple nucleotide polymorphisms were present at that allele in the cohort (15). Eight other DNVs appeared true by IGV (11% of WES-unique DNVs), were present in the WGS VCF and passed GATK DNV filtering criteria but were removed in subsequent FB or IGV-bot filtering. Five did not have IGV plots available. The remaining 28 coding DNVs identified by WES were not confirmed by WGS IGV, 8 being inherited and 20 removed due to quality filtering.

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HeartENN model architecture

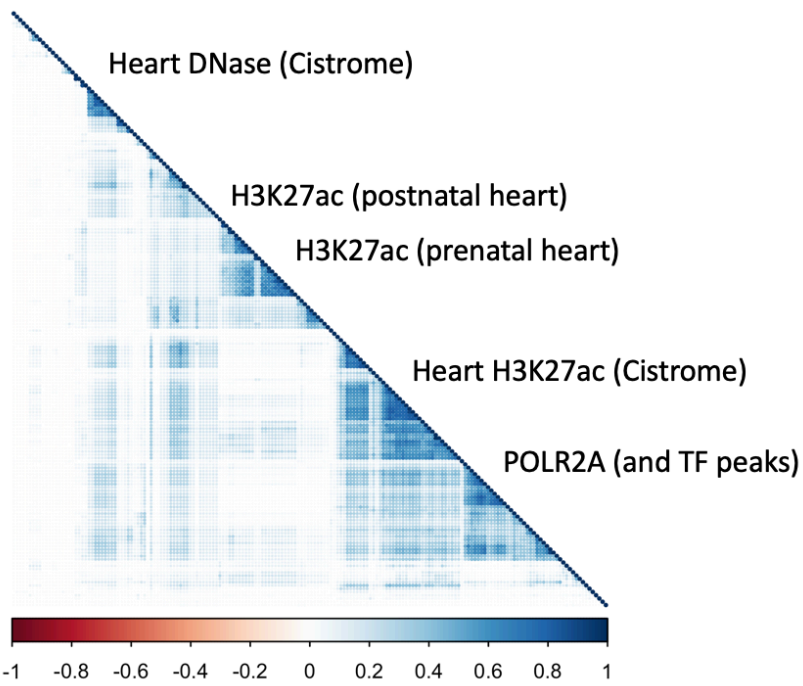
1. Convolution layer: 60 kernels, window size: 8, step size: 1
2. Convolution layer: 60 kernels, window size: 8, step size: 1
- 20 3. Pooling layer: window size: 4, step size: 4
4. Convolution layer: 80 kernels, window size: 8, step size: 1
5. Convolution layer: 80 kernels, window size: 8, step size: 1
6. Pooling layer: window size: 4, step size: 4
7. Convolution layer: 240 kernels, window size: 8, step size: 1
- 25 8. Convolution layer: 240 kernels, window size 8, step size: 1
9. Fully connected layer: human model 90 epigenomic features, mouse model 94 epigenomic features
10. Sigmoid output layer

Parameters:

- 30 • Dropout proportion:
 - Layer 6: 40%
 - Layer 8: 50%
 - All other layers: 0%
- Batch normalization is applied after layers 3, 6, and 8, before applying dropout (when applicable).
- 35 • Both models use the binary cross-entropy loss function and the stochastic gradient descent optimizer (momentum: 0.9, weight decay: 10^{-6}).

ADDITIONAL SUPPLEMENTARY FIGURES

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Supplementary Figure 1. Correlations between 184 noncoding annotations with major categories enumerated along the diagonal.

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