Categories of genes based on inferred cis-regulatory structure

GROUP 1) Housekeeping gene constitutively-expressed in all tissues

GROUP 2) Developmentally-regulated gene expressed in multiple tissues

GROUP 3) Developmentally-regulated gene expressed in one tissue (i.e. tissue-specific)

Effect of cis-regulatory mutation & pleiotropic consequences

Alter expression in ALL tissues
HIGH PLEIOTROPY

Alter expression in ONE, SOME, or ALL tissues
INTERMEDIATE PLEIOTROPY

Alter expression in ONE tissue
LOW PLEIOTROPY

Expectated contribution of cis changes to gene expression differences assuming high pleiotropy = more likely deleterious

Less cis

More cis

Pipeline to categorize genes based on inferred cis-regulatory structure

DATA: expression level data for all genes across many tissues

Housekeeping/constitutively-active? (group 1 or 2/3)
- Expressed above given threshold (X) in ALL tissues.
- Use X that gives around previously estimated number of housekeeping genes.

Of non-housekeeping, tissue-specific or not? (group 2 or 3)
- Calculate tissue-specificity metric (Tau).
- Use median across all genes = 0.61 as cutoff for tissue-specific vs non-tissue-specific.
  --> Cutoff used in Kondo et al. 2017

QUALITY CHECK
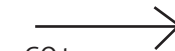
- GO terms
- Check known genes

MERGE WITH DATA FOR EXPRESSION DIVERGENCE DUE TO CIS CHANGES (Coolon et al. 2014) & CONTRAST ACROSS GENE GROUPS