# **Supplementary Information Guide**

### **Supplementary Note 1: Outline of the SLICE model**

This document provides the mathematical derivation of the SLICE model, and outlines how it is applied to the mESC-400 GAM dataset.

# Supplementary Note 2: Detection of the most prominently interacting loci with the SLICE model

This documents shows how the SLICE model can be used as the basis for a statistical test, and how that test is applied to obtain the most prominently interacting pairs of loci.

#### **Supplementary Note 3: Mathematical equations**

Mathematical equations used to estimate sequencing saturation, estimate non-interacting distances between FISH probes and to calculate linkage disequilibrium.

## **Supplementary Table 1: Details of sequencing datasets**

Details of sequencing datasets generated for this study (NPs, negative and positive control), including experimental batch, sequencing depth, and all metrics used to judge the quality of each NP.

#### **Supplementary Table 2: Top 2% most interacting TAD triplets**

List of TADs forming the top 2% most interacting TAD triplets, including their transcriptional/se class.

#### **Supplementary Table 3: Details of published datasets**

Details of published genome-wide datasets used in this study, including accession numbers.

#### **Supplementary Table 4: Details of FISH probes**

Details of FISH probes used for validating long-range interactions.

## **Supplementary Table 5: FISH edge-to-edge distances**

Measurements of distances between the edges of two FISH probe signals.