

DESCRIPTION OF ADDITIONAL SUPPLEMENTARY FILES

File: **Supplementary Data 1**

Description: Overview of FOXG1 syndrome-like cases harbouring non-coding structural variants (SVs) overlapping the FOXG1 topologically associating domain (not affecting FOXG1).

File: **Supplementary Data 2**

Description: Results of POSTRE in silico analysis of structural variants (SVs).

File: **Supplementary Data 3**

Description: Coordinates of cCREs tested in in vivo enhancer assays.

File: **Supplementary Data 4**

Description: Results of zebrafish enhancer assays for candidate cis-regulatory elements (cCREs).

File: **Supplementary Data 5**

Description: CRISPR editing efficiencies for all target deletions.

File: **Supplementary Data 6**

Description: Local genomic constraint scores of the kb bins harboring the HS, PE and EC (after QC filtering).

File: **Supplementary Data 7**

Description: Primer design for UMI-4C.

File: **Supplementary Data 8**

Description: Paired CRISPR/Cas9 sgRNA design for engineering enhancer cluster (EC) and TAD boundary (TAD) deletions.

File: **Supplementary Data 9**

Description: Primer design for PCR screening of CRISPR/Cas9 edited clones.

File: **Supplementary Data 10**

Description: Antibodies/stains used in this study.