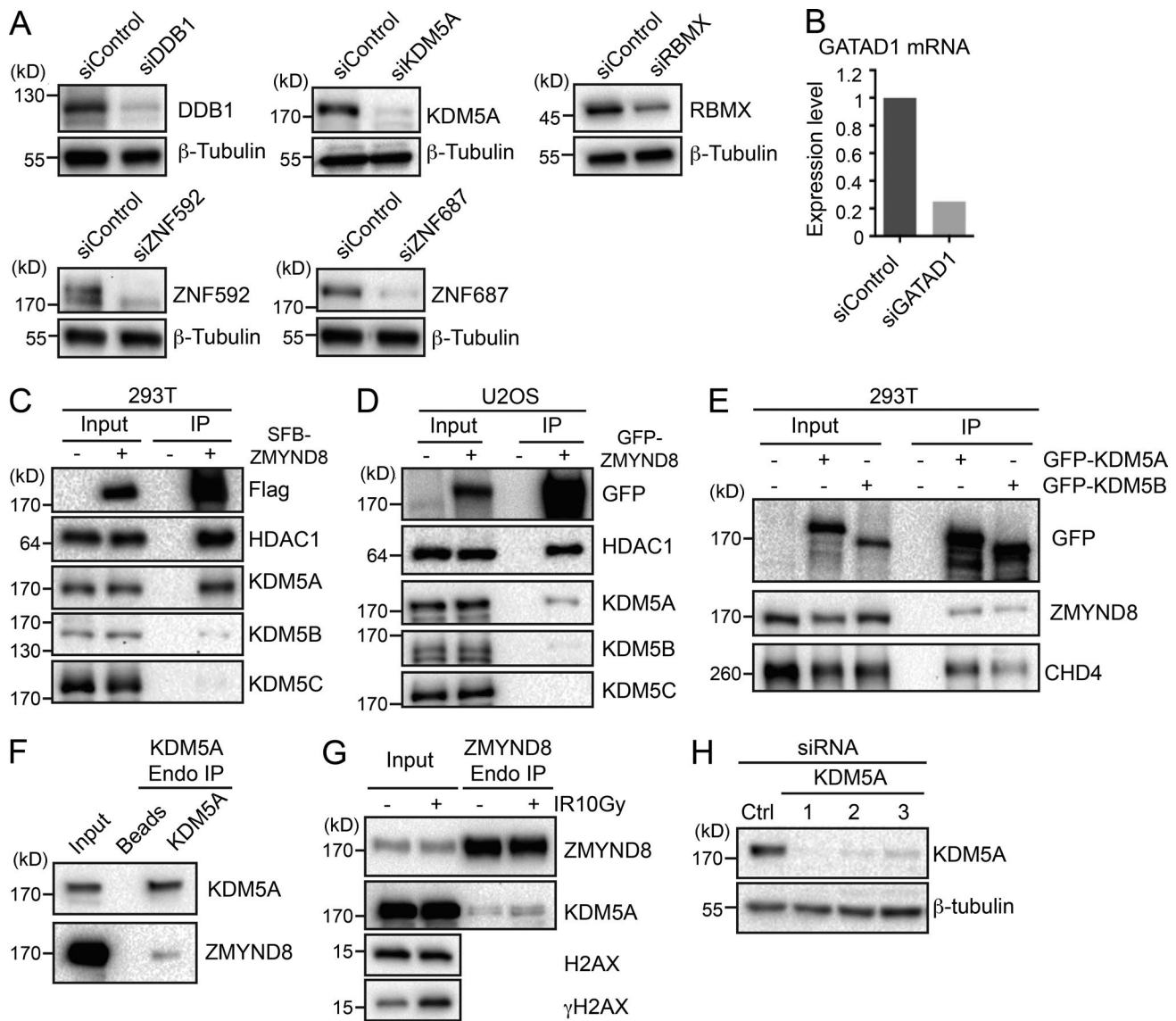Figure S1. **KDM5A interacts with ZMYND8–NuRD and promotes its damage recruitment.** (A) Western blot analysis of siRNA knockdown efficiency. (B) Representative GATAD1 knockdown efficiency analyzed by quantitative RT-PCR. (C) SFB-tagged ZMYND8 was expressed in HEK293T cells, purified with Streptavidin beads, and analyzed by WB. (D) Experiment was performed as in Fig. 1 E with GFP-tagged ZMYND8 purified from U2OS cells stably expressing GFP-ZMYND8. (E) The experiment was performed as in Fig. 1 E, with GFP-tagged KDM5A or KDM5B expressed in HEK293T cells. (F) Immunoprecipitation (IP) analysis of endogenous KDM5A and ZMYND8 interactions. The experiments were performed as in Fig. 1 F using a KDM5A-specific antibody. (G) Coimmunoprecipitation analysis of endogenous KDM5A and ZMYND8 proteins in control and 10 Gy IR–treated conditions. The experiments were performed as in Fig. 1 F. (H) Confirmation of knockdown efficiency of KDM5A siRNAs by WB.
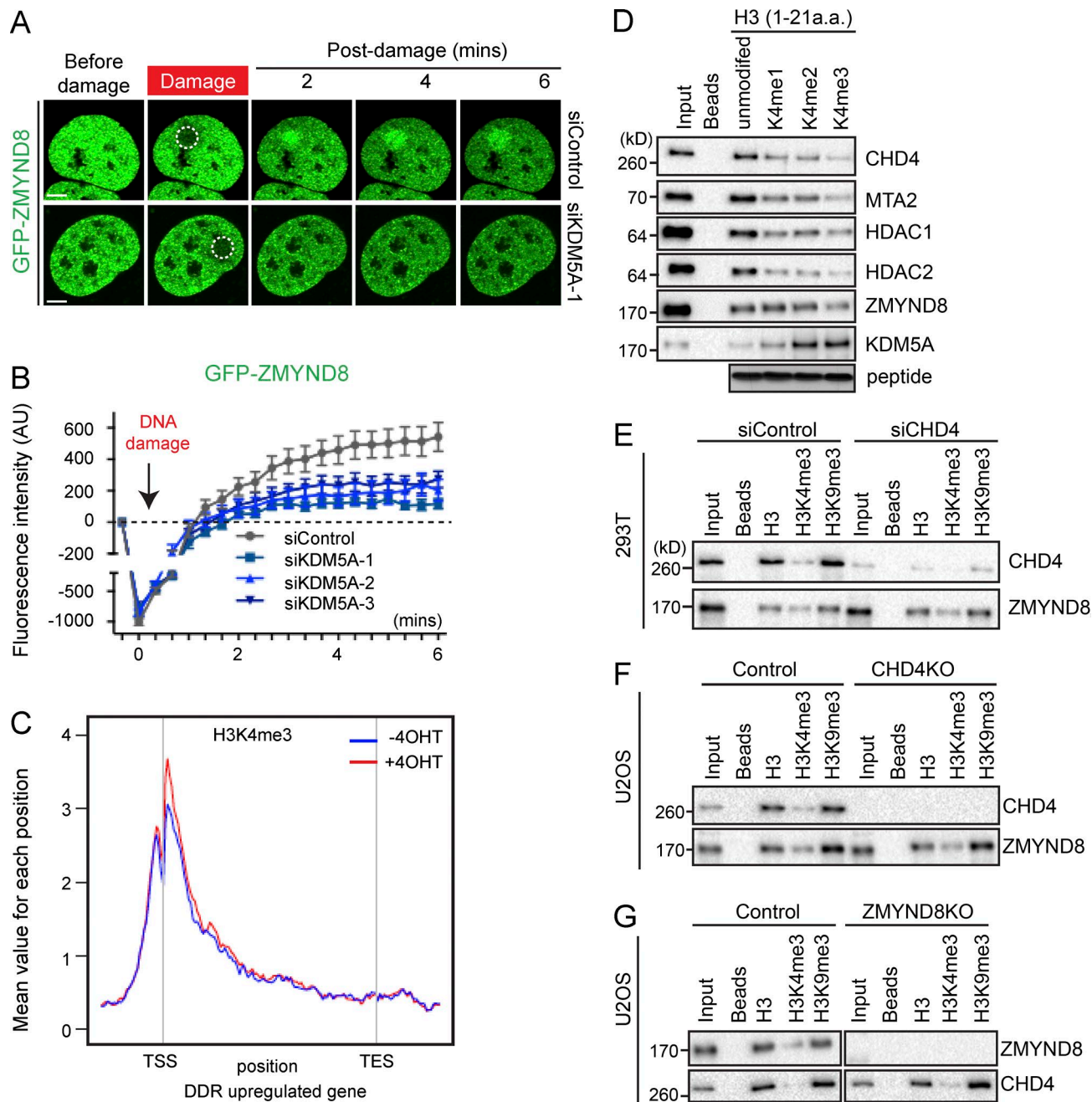
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Figure S2. **Influence of DNA damage on H3K4me3, ZMYND8–NuRD, and KDM5A.** (A) Damage recruitment of ZMYND8 was examined in siControl and siKDM5A U2OS cells. Experiments were performed as in Fig. 1 C. Regions of laser damage are indicated by dotted white circles. Bars, 5 μm. (B) Quantifications of GFP-KDM5A damage recruitment in siControl and siKDM5A (three independent siRNAs) in U2OS cells. Plotted values are fluorescence intensity of damaged versus undamaged region at each time point. One representative experiment out of three is shown (error bars represent SEM; n > 10 cells per condition; AU, arbitrary units). (C) Analysis of H3K4me3 levels ±4-OHT on the promoter regions of IR-induced 296 genes identified previously (Rashi-Elkeles et al., 2014). The experiments were performed as in Fig. 2 (B and C). (D) Peptide pull-down assays followed by WB analysis were performed as in Fig. 3 A. Unmodified and methylated H3 peptides were used as indicated. (E–G) Peptide pull-down assays as in Fig. 3 A were performed in 293T (E) and U2OS (F and G) cell extracts with the indicated genotypes or siRNA treatments.
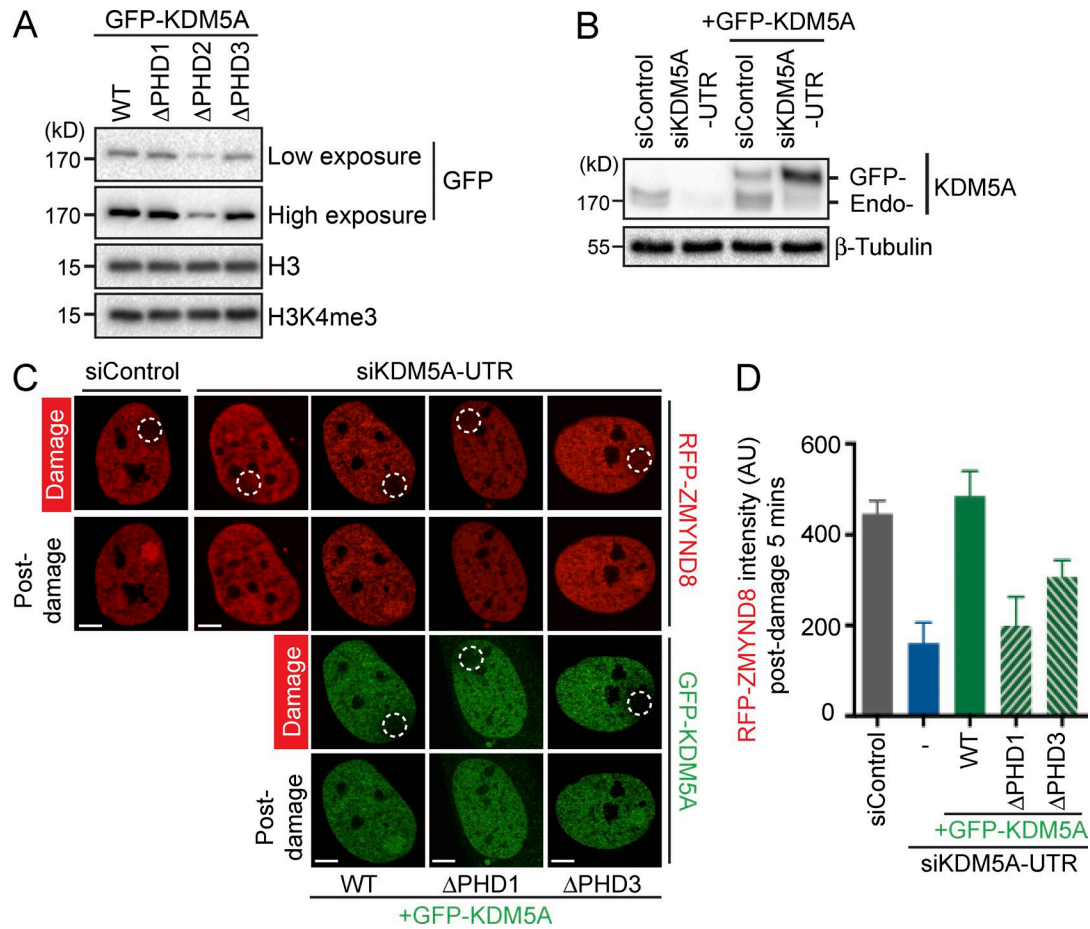
Figure S3.   **Regulation of damage recruitment of KDM5A.** (A) Protein expression levels of GFP-tagged WT and KDM5A derivatives were analyzed by WB. (B) Validation by WB of depletion of endogenous, but not ectopically expressed, KDM5A by siKDM5A-UTR. (C) Complementation assays in U2OS cells depleted of endogenous KDM5A. U2OS Flp-In cells harboring WT or indicated mutant GFP-KDM5A were treated with siKDM5A-UTR after induction of various GFP-KDM5A derivatives by doxycycline (Dox) and transient expression of RFP-ZMYND8. RFP-ZMYND8 laser recruitment data were collected from GFP-positive cells. Regions of laser damage are indicated by dotted white circle. (D) Quantification of C from one representative experiment out of two as in Fig. 3 F (error bars represent SEM; *n* > 10 cells; AU, arbitrary units). Bars, 5 µm.
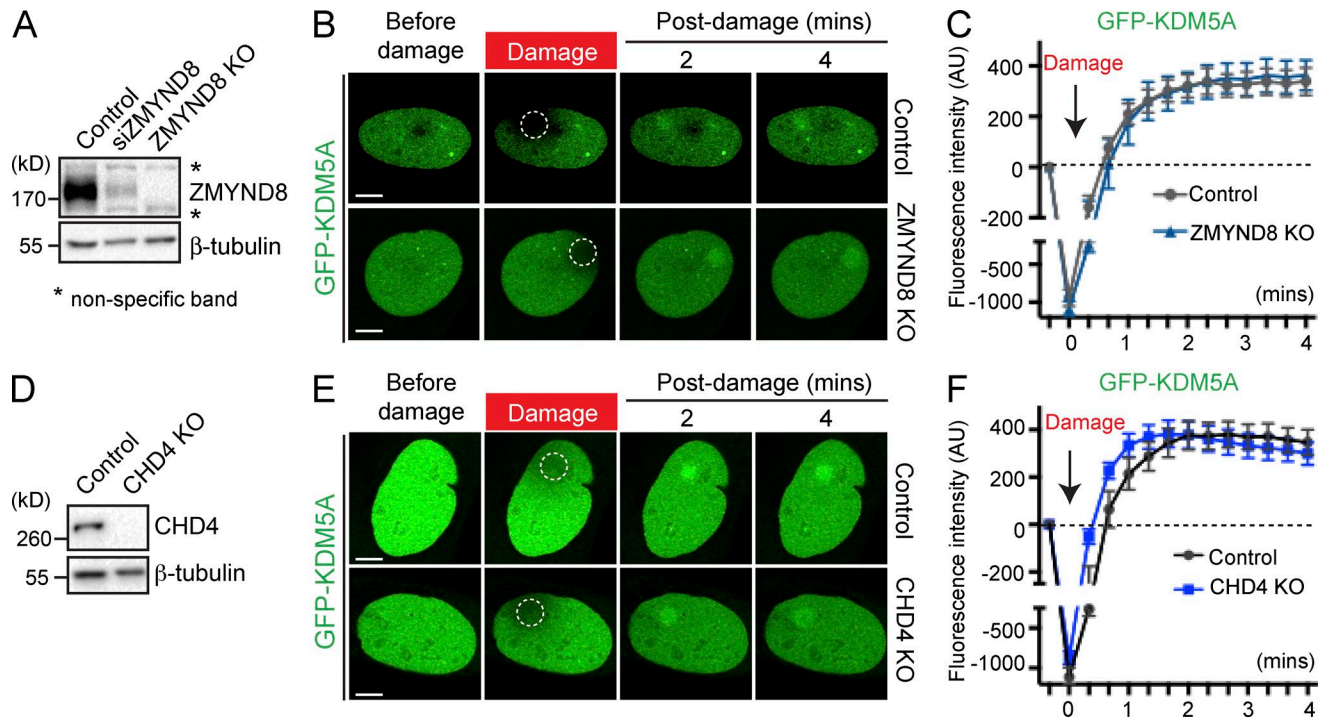
Figure S4. **KDM5A recruitment to DNA damage is independent of ZMYND8–NuRD.** (A–F) GFP-KDM5A damage recruitment was analyzed in ZMYND8 and CHD4 KO cells. Western blots in A and D validate ZMYND8 and CHD4 KO in U2OS cells. Experiments were performed (B and E) as Fig. S2 A and quantified (C and F) as in Fig. S2 B. Quantification plots (C and F) in this figure are shown as one representative experiment out of two (error bars represent SEM; *n* > 10 cells). Regions of laser damage are indicated by dotted white circle. AU, arbitrary units. Bars, 5 µm.
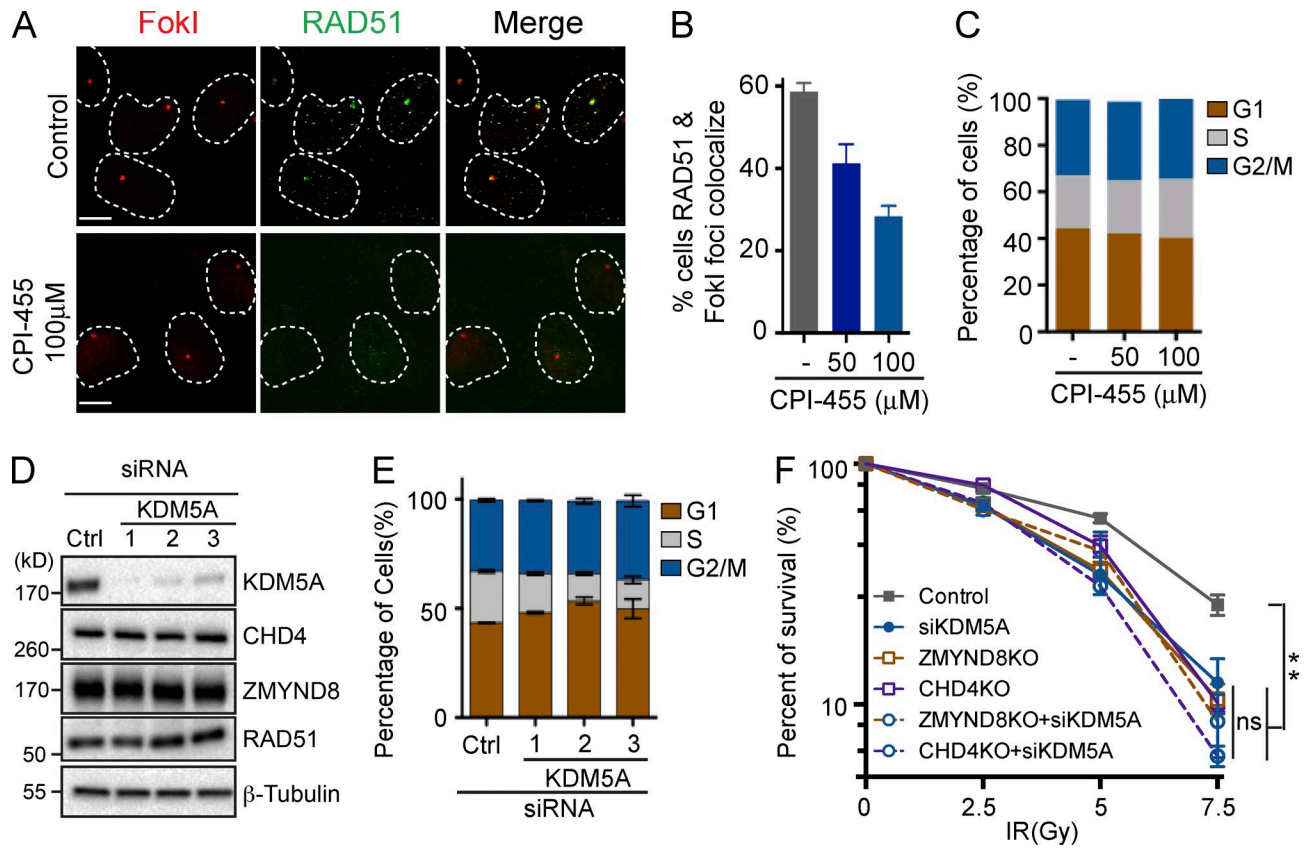
Figure S5.   **Interplay between KDM5 and ZMYND8–NuRD in the DDR.** (A) RAD51 loading at FokI-induced DSBs was analyzed as in Fig. 6 D in ±CPI-455–treated U2OS cells (dotted white circles indicate nuclei; bars, 10 µm). (B) Quantification of A (error bars represent SEM; n = 3). (C) Cell cycle distribution by FACS of U2OS cells from A. (D) WB analysis of ZMYND8, CHD4 (i.e., NuRD) and RAD51 protein levels in KDM5A-depleted cells. (E) Cell cycle distributions for siControl and siKDM5A performed as in C (error bars represent SEM; n = 2). (F) Epistasis analysis of IR sensitivity for KDM5A-, ZMYND8-, and NuRD-deficient cells by clonogenic survival assays. Graphs are means ± SEM; n = 2. P value was determined by Student's t test (**, P < 0.01; ns, not significant). Supplemental .txt file provides source code for computational methods used to draw Figs. 2 D and S2 C (see Materials and methods).

A supplemental .txt file provides source code for computational methods used to draw Fig. 2 D and Fig. S2 C (see Materials and methods).