

### **Description of Additional Supplementary Files**

File Name: Supplementary Data 1

Description: All protein groups identified in Tier1 and Tier2 by RDPprox in HEK293T cells with indicated mean log<sub>2</sub> fold changes and FDR.

File Name: Supplementary Data 2

Description: Annotated CUT&RUN peaks indicative of GFP-DDX41 binding in U2OS cells. Only peaks present in both biological replicate experiments are included in the table.

File Name: Supplementary Data 3

Description: Annotated MapR peaks with a FC > 2 (R-loop gain and loss) in U2OS cells. Distal intergenic peaks are not included in the table.

File Name: Supplementary Data 4

Description: Gene list from RNA-sequencing analysis in U2OS cells with indicated log<sub>2</sub> fold change and FDR derived using a Wald test and Benjamini-Hochberg correction for multiple testing.

File Name: Supplementary Data 5

Description: Annotated sBLISS peaks used for the fold change analysis in HCT116 cells

File Name: Supplementary Data 6

Description: Annotated MapR peaks with a FC > 1.5 (R-loop gain and loss) in HCT116 cells. Distal intergenic peaks are not included in the table.