Faithful transfer of parental histones to newly replicated daughter DNA strands is critical for inheritance of epigenetic states. Although replication proteins that facilitate parental histone transfer have been identified, how intact histone H3-H4 tetramers travel relatively large distances from the front to the back of the replication fork remains unknown. Here, we use AlphaFold-Multimer structural predictions combined with biochemical and genetic approaches to identify the Mrc1/CLASPIN subunit of the replisome as a histone chaperone. Mrc1 contains a conserved histone binding domain that forms a brace around the H3-H4 tetramer mimicking nucleosomal DNA and H2A-H2B histones, is required for heterochromatin inheritance, and promotes parental histone recycling during replication. We further identify binding sites for the FACT histone chaperone in Swi1/TIMELESS and DNA polymerase α that are required for heterochromatin inheritance. We propose that Mrc1, in concert with FACT acting as a mobile co-chaperone, coordinates the distribution of parental histones to newly replicated DNA.

This AlphaFold-Multimer structural prediction dataset is associated with the manuscript “A replisome-associated parental histone H3-H4 tetramer chaperone required for faithful epigenetic inheritance”. All structural predictions were performed using template-free AlphaFold-Multimer through ColabFold. Per-residue confidence score (predicted Local Distance Difference Test, pLDDT), predicted template modeling score (pTM), and interface predicted template modeling score (ipTM) of all five models were used to estimate the confidence of the structural predictions.

This dataset contains 268 structural predictions listed based on the order of their appearances in figures, including:

1) AlphaFold screens between histone H3.1-H4 tetramer, the centromere variant CENP-A-H4 tetramer, or FACT subunits (Spt16/SUPT16 and Pob3/SSRP1) and core replisome components from *Schizosaccharomyces pombe, Drosophila melanogaster,* or *Homo sapiens*

2) AlphaFold predictions of subcomplexes of the replisome, representing several suggested parental histone transfer intermediate states

In this dataset, the predicted structures contain four categories: 1. Known interactions; 2. High confidence interactions (average ipTM ≥ 0.5); 3. Moderate confidence interaction (0.3 ≤ average ipTM < 0.5); 4. Low confidence interaction (average ipTM < 0.3). "Known interaction” refers to experimentally verified or previously described physical interactions. Only the top 3 rank predicted structures are deposited in ModelArchive. All predicted structures are listed in Table S4 in the manuscript.

Here are some highlighted predicted structures in the dataset:

* 181: Predicted interaction between *S. pombe* Mrc1 and histone H3-H4 tetramer.
* 224: **D site-Swi1**, predicted interaction between Spt16 and Swi1.
* 262 (*S. cerevisiae*) and 263 (*S. pombe*): **D site-Mrc1**, predicted interaction between Mrc1-like domain, histone H3-H4 tetramer and Mcm2/Cdc45.
* 258 (*S. pombe*) and 259 (*H. sapiens*): **LD1 site**, predicted interaction between Mcm2, Swi1, histone H3-H4 tetramer and FACT.
* 260 (*S. pombe*) and 261 (*H. sapiens*): **LD2 site**, predicted interaction between Pol1, Mcl1, histone H3-H4 tetramer and FACT.

The image of this entry is the predicted structure of Mrc1-like domain and H3-H4 tetramer on the cryo-EM structure of the replisome (PDB: 8B9C and 7QHS), representing Mrc1 acting as a parental histone distribution site (D site) in the replisome.