Human mitochondrial termination factor mTERF wraps around target DNA through a left-handed helical tandem repeat

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Mitochondria, the organelles that perform essential functions in the cell, contain their own genome, the mtDNA, whose regulation is exerted by dedicated, nuclear-coded proteins imported from the cytosol. Among them is mTERF, a transcription termination factor also implicated in replication pausing, which binds to several strategic mtDNA sites with different affinity. We present the crystal structure of human mTERF in complex with a dsDNA oligonucleotide encompassing its highest-affinity binding sequence from the $tRNA^{Leu(UUR)}$ gene. Nine three-helical repeats generate an unprecedented left-handed superhelical solenoid, the Zurdo motif, which turns opposite to previously described right-handed Armadillo, Pumilio or HEAT repeat domains. Furthermore, this is the first solenoid-DNA complex structure; the protein smoothly wraps around the major groove of its cognate DNA sequence by a right-handed twist of the superhelix. In the structure, the two terminal repeats contact two distinct DNA molecules whose axes form an angle of 36 degrees, agreeing with experiments showing that mTERF bends continuous dsDNA upon binding. We support these results with studies in solution using small angle X-ray scattering. Sequence analyses of mTERF homologues show preservation of residues pivotal for structural integrity of mTERF, indicating this as the structural prototype for a whole family of mitochondrial proteins. The Zurdo motif defines a novel class of proteins thus far unique to eukaryotic organelles.