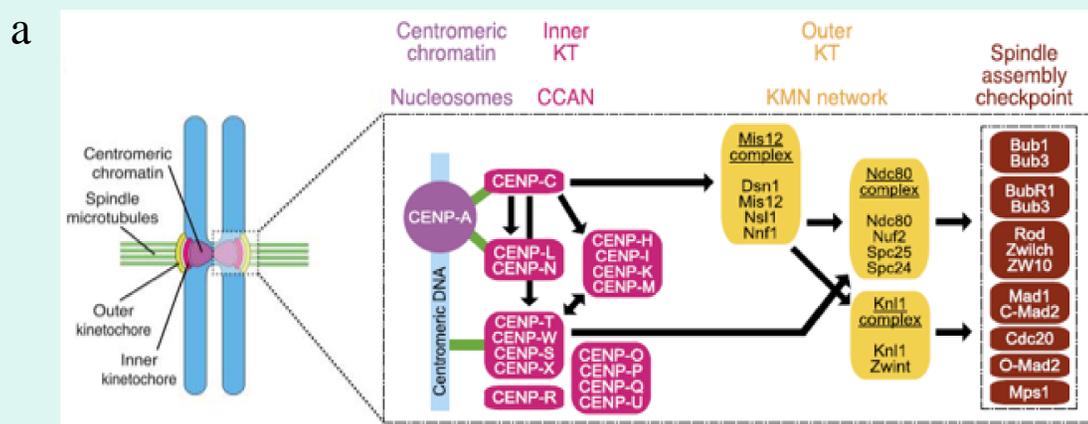


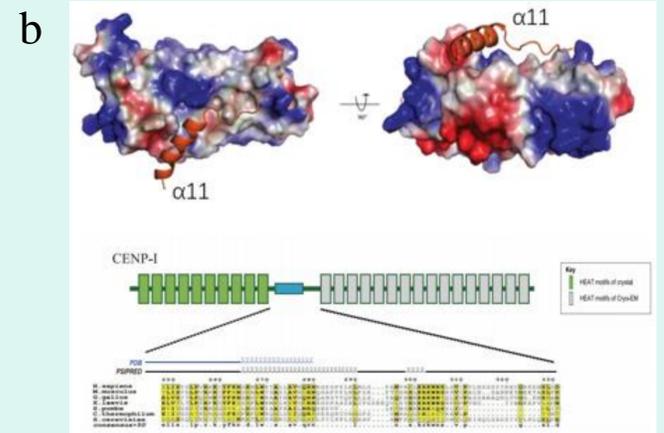
# Structural insights into the intramolecular interactions of centromere protein CENP-I

Yu Zhang, Congcong Zhao, Beibei Cao, Jingjing Ye, Hao Huang, Liqiao Hu, Wei Tian, Xiaojing He

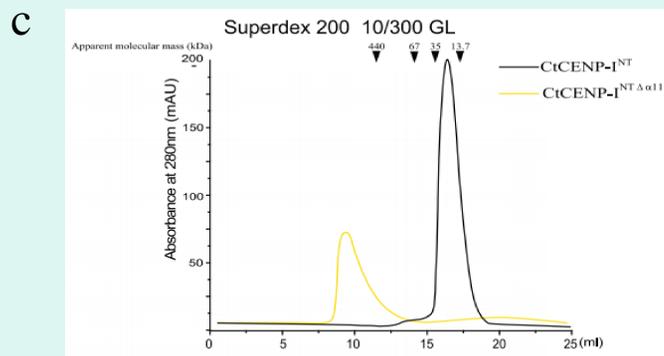
During mitosis of eukaryote cells, the faithful separation of sister chromatids depends on kinetochore which located at the centromere. At the inner layer of kinetochore, as an important component of CENP-H/I/K/M, CENP-I plays an important role in mitosis. We previously reported the N-terminal half structure of fungal CENP-I that forms a ternary complex with C-terminal heterodimer of fungal CENP-H/K. However, the intramolecular interactions of CENP-I and the interaction mechanism between CENP-I and CENP-M remains unknown. In this study, we verified a unique helix  $\alpha 11$ , which interacts with the N-terminal HEAT domain and participates in maintaining the stability of the CENP-I N-terminal structure, is highly conserved in human CENP-I. Deletion of the corresponding helix in human CENP-I dramatically reduced the functional activity to interact with CENP-H and CENP-M. Mutations of the conserved residues on the helix in human CENP-I significantly weakened the binding to CENP-M, but not CENP-H, and influenced the centromeric localization of CENP-I/M during cell cycle in HeLa cells. Thus, for the first time, we identified a conserved helix of CENP-I that is important for intramolecular interaction and function, and may providing a structural basis for exploring the role of CENP-I in kinetochore assembly during cell cycle.



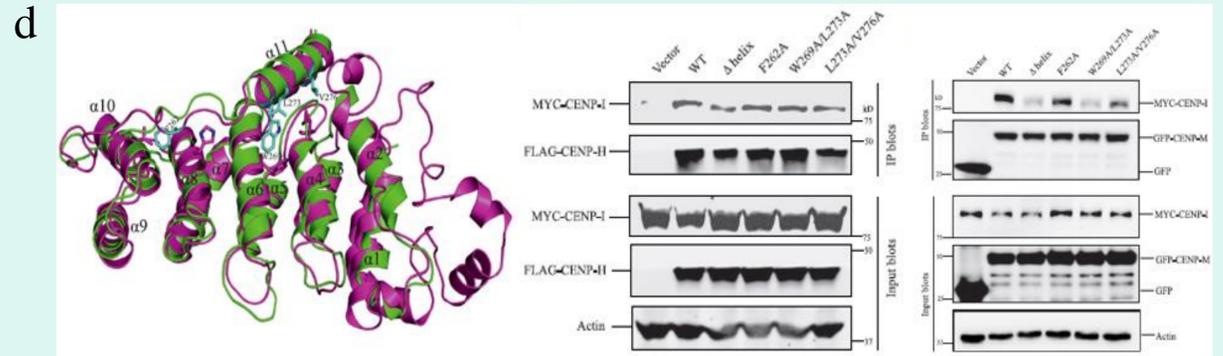
Model of kinetochore complex



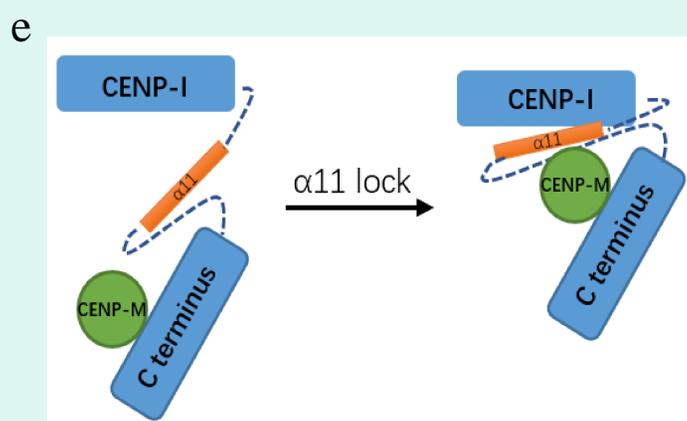
The unique helix is conserved and crosses against the concave surface of the HEAT repeats as a safety belt



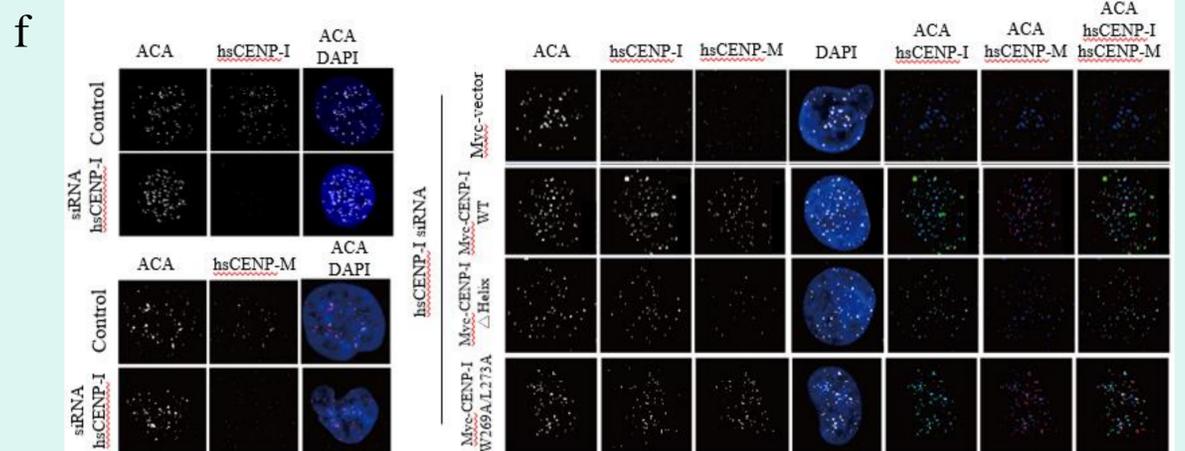
The helix  $\alpha 11$  was required for maintaining the proper folding and function of CtCENP-I<sup>NT</sup> in vitro



The corresponding helix of hsCENP-I was important to mediate the full interaction with CENP-M, not CENP-H, as a part of CENP-I function among kinetochore.



The corresponding helix and intramolecular interactions might be responsible for the conformational change among the CCAN



Depletion and mutation of hsCENP-I may influence the centromeric localization of CENP-I and CENP-I during cell cycle