

In situ architecture of the human kinetochore visualized by cryo-electron tomography

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Chromosome segregation during mitosis relies on a carefully coordinated interplay between the centromere, kinetochore, and spindle microtubules. Despite its importance, the architecture of this interface remains elusive. Here we combined in situ cryo-electron tomography and cryo-light microscopy to visualize the native architecture of the kinetochore-microtubule interface in human U2OS cells at different stages of mitosis. Our data reveal that upon microtubule binding, the centromere forms a pocket-like structure around kinetochore microtubules. This centromeric pocket contains sparsely distributed nucleosome chains and two morphologically-distinct fibrillar densities from the kinetochore that form both lateral and end-on attachments to the plus-ends of microtubules within the pocket. Our data shows that the curling of protofilaments is impeded by the thick end-on fibrils, suggesting a direct relationship between these fibrils and microtubule depolymerization. Our data thus suggest that the pocket configuration of centromere scaffolds a dynamic kinetochore-microtubule interface in which multiple interactions facilitate stable attachment to microtubule plus-ends that are continually switching between growing and shrinking states.

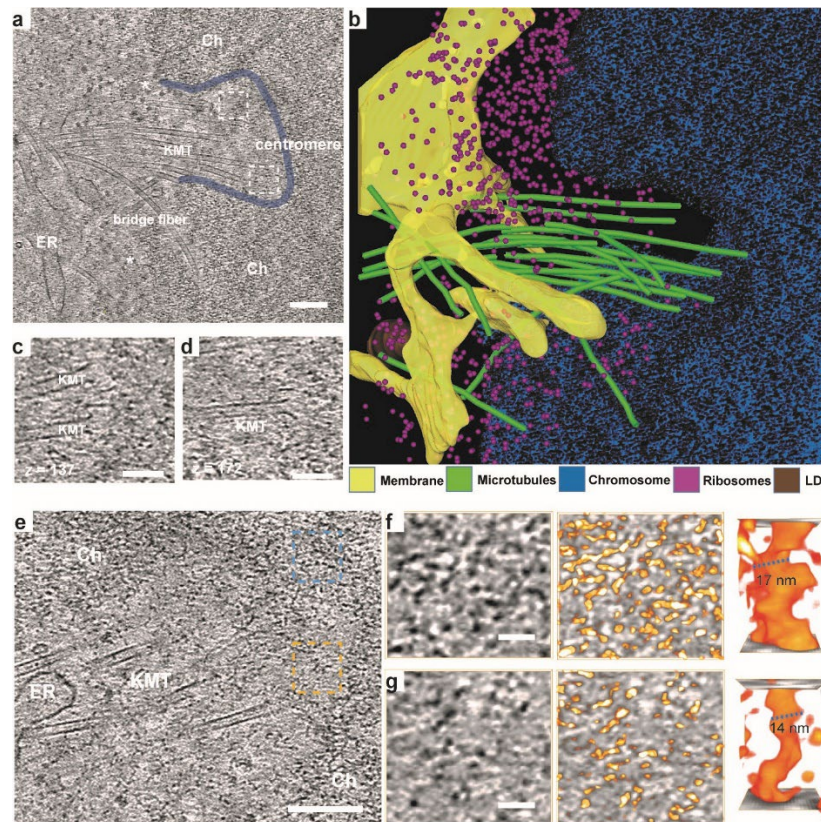


Figure 1.