

**Figures Accompanying:
PUBLISHABLE SUMMARY 2nd term report
Project No: 224874**

Project Acronym: Epicentromere

**Determining the Epigenetic Mechanism of
Centromere Propagation**

(4 figures total in this document)

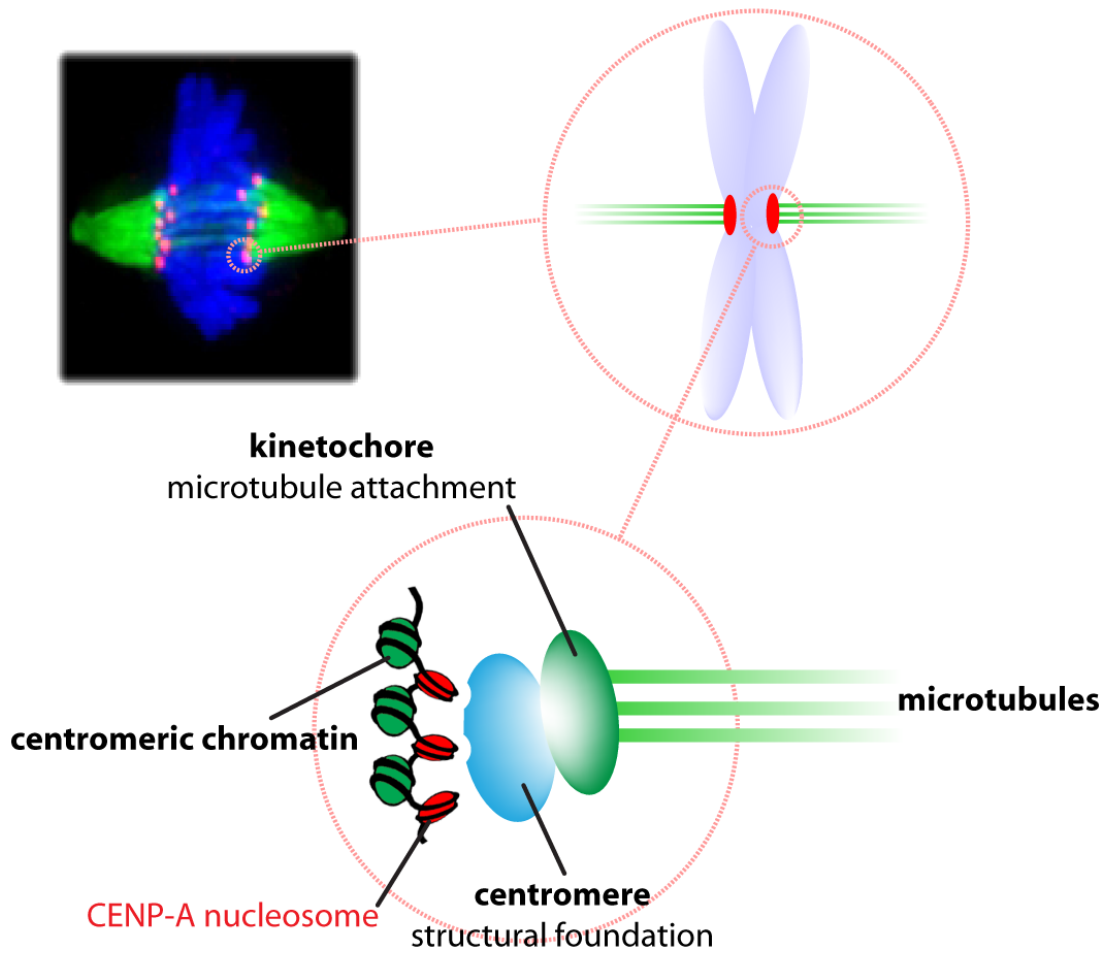


Figure 1. Cartoon of mitotic centromere organization. Micrograph shows a cell in metaphase. The centromere is a unique locus specified by the histone H3 variant CENP-A (**red foci**) present on each chromosome (**blue**) that assembles the kinetochore that in turn directs attachment to microtubules (**green fibres**) during mitosis. Cartoon shows a blow-up of the centromere complex with centromeric chromatin containing **CENP-A nucleosomes** that nucleates the constitutive **centromere complex** that in turn assembles the **kinetochore** during mitosis. The kinetochore is responsible for **microtubule** attachment that drives chromosome segregation during mitosis.

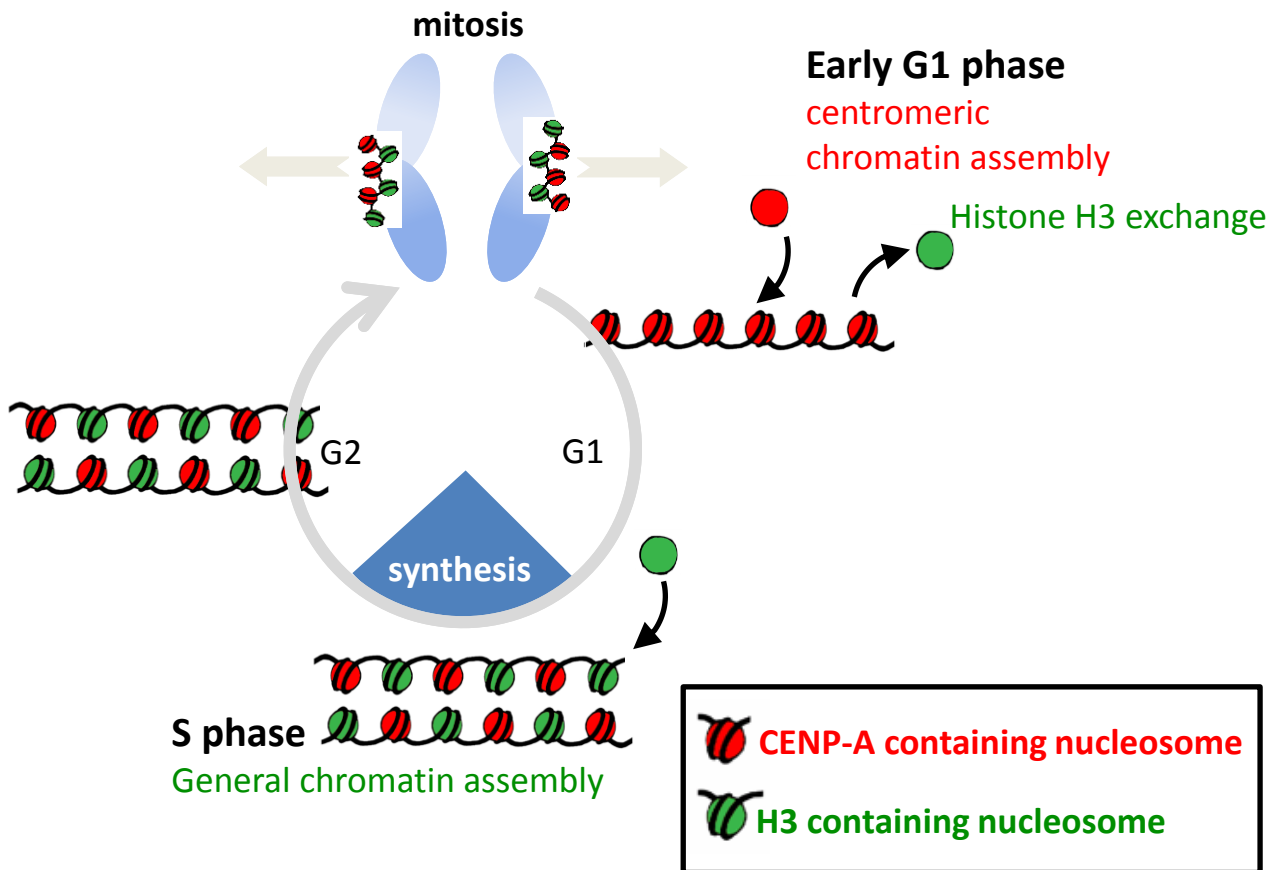


Figure 2. Schematic depicting centromeric chromatin composition in relation to the cell cycle. CENP-A containing nucleosomes (**red**) are interspersed with canonical H3-containing nucleosomes (**green**) after replication in S phase. This mixed set of nucleosomes is the substrate for nucleating kinetochore assembly in mitosis and is maintained as cells exit in anaphase. **CENP-A** assembly initiates in telophase and proceeds through early G1 (presumably concurrent with removal of **H3** nucleosomes). *Adapted from Jansen et al., JCB 2007*

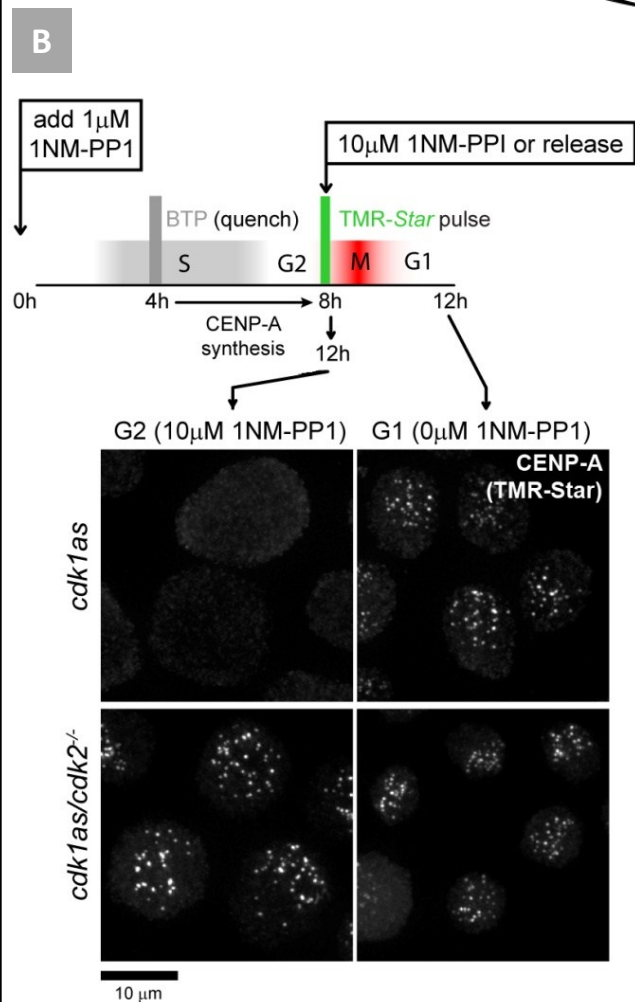
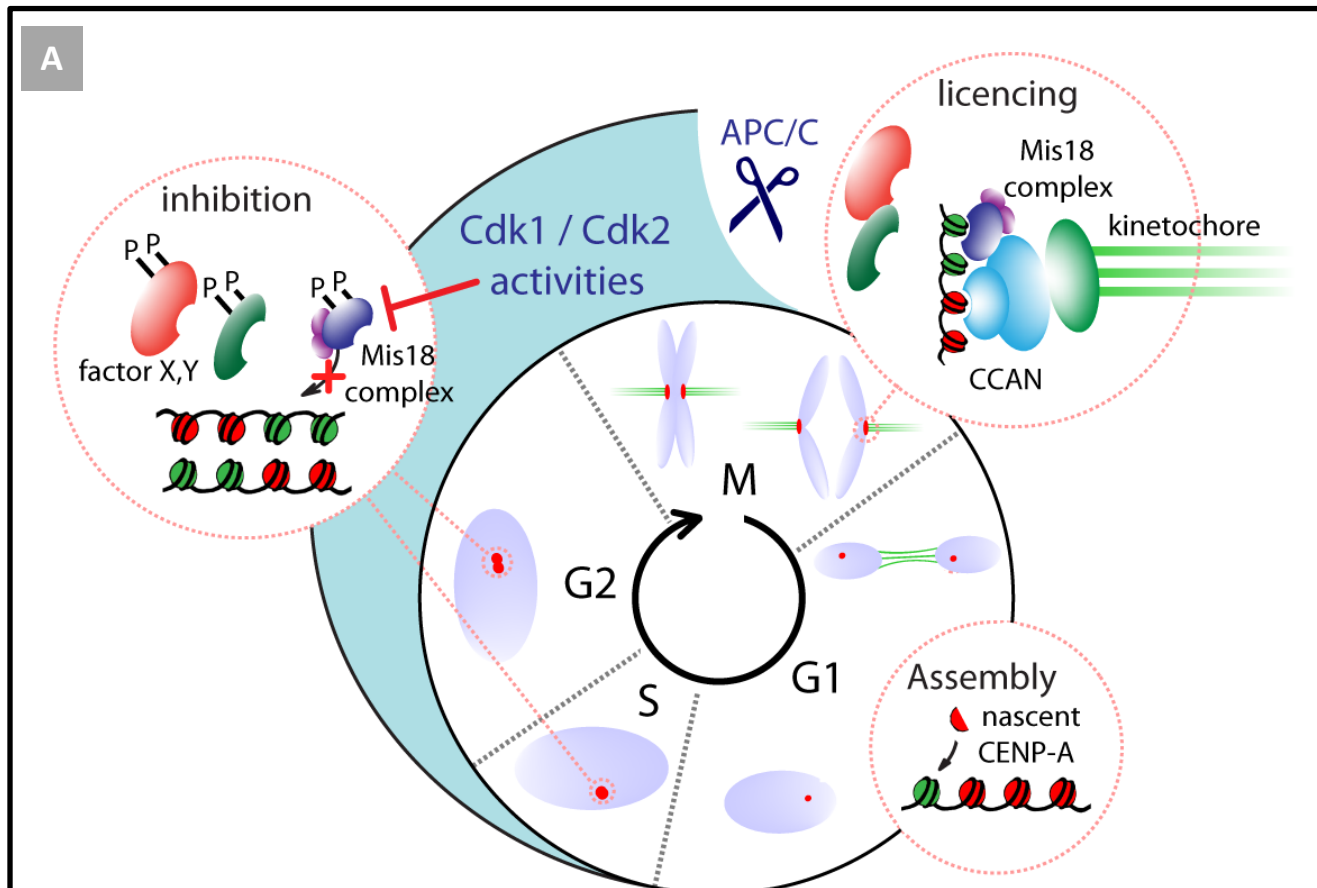


Figure 3. Cdk1/2 control timing of CENP-A assembly.

A) Model illustrating Cdk1/Cdk2-mediated inhibition of CENP-A assembly, exerted in part through phosphorylation (P) of Mis18BP1 (member of the Mis18 complex) during S, G2, and M phases. Factors X and Y symbolize the involvement of other, yet to be identified, components. Inhibition is alleviated through APC/C-mediated loss of Cdk1 activity in anaphase, targeting the Mis18 complex to the centromere (licensing) followed by CENP-A assembly in G1 phase. Canonical (H3 containing) nucleosomes are shown in green, CENP-A nucleosomes in red. B) DT40 cells carrying an analog sensitive *cdk1* allele, either alone or in a *cdk2* knockout background are cell synchronized in G2 phase while a nascent CENP-A SNAP pool is labeled. Both lines assemble CENP-A at centromeres in G1 but only *cdk1/2* double mutants have lost cell cycle control (with full blown assembly in G2 phase). Adapted from *Silva et al. Developmental Cell 2012*

