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Selected Publication

Yuen K, Nabesima K, Oegema K, and Desai A. Rapid De Novo Centromere Formation Occurs Independently of Heterochromatin Protein 1 in *C. elegans* Embryos. *Current Biology.* 2011.21(21):1-8.

Research Aims and Interests

Centromere Propagation and Establishment

Centromere is the specialized chromatin domain for directing chromosome segregation. Conserved kinetochore structure assembles on the centromere to mediate chromosome-microtubule attachment. All active centromeres contain a histone H3 variant, CENP-A. which serves as an epigenetic mark for centromere identity, and a foundation for kinetochore assembly. Yet, centromeric DNA sequences and sizes vary, from 125b in the budding yeast to megabases of repeats in vertebrates, and to a diffuse centromere (holocentromere) in the nematode *C. elegans*, some insects and plants. The repetitive nature of most centromeres hinders them from sequencing analyses. We mapped the genome-wide localization of CENP-A in holocentric *C. elegans* by chromatin immunoprecipitation. We found that CENP-A binds to non-expressed regions in *C. elegans* embryos. How CENP-A is epigenetically maintained through cell cycles and generations is not well understood. Recently, we identified a histone chaperone that localizes CENP-A in *C. elegans.*

Occasionally, neocentromeres can form on non-centromeric DNA in patients with cancers or developmental defects caused by chromosomal rearrangements. Introduction of centromeric sequences into cells may also form stably propagating artificial chromosomes. How the centromeric domain is established is mysterious. We found that in *C. elegans,* injection of naked DNA can result in frequent formation of artificial chromosomes containing neocentromeres. We are investigating what epigenetic and sequence factors determine neocentromere formation, and we found that specific chromatin structure and histone modifications is important. This knowledge will provide insights into the history of centromere repositioning in karyotype evolution and advance the engineering of artificial chromosomes for gene therapies.

Chromosome Instability (CIN) in Yeast

To systematically determine the genetic basis of CIN, we developed genome-wide chromosome stability assays in S. cerevisiae. We identified over 200 non-essential CIN mutants. For instance, we found that the ubiquitin ligase for H2B monoubiquination, Bre1, is required for sister chromatid cohesion establishment, by recruiting replication and cohesion factors. Understanding the genetic and phenotypic differences between CIN and normal cells will facilitate the development of therapies that specifically selects against CIN tumor cells.