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Aneuploidy is a hallmark of cancer development and occurs due to defects in chromosome segregation. The kinetochore, a complex consisting of over 100 different types of proteins, is required for the proper segregation of chromosomes. However, we lack an in depth understanding of the step-by-step assembly process resulting in a functional kinetochore due to the extreme molecular and temporal complexity of this complex. Dr. Changkun Hu will reconstitute kinetochore assembly in vitro and use TIRF microscopy to measure individual kinetochore protein recruitment times in Dr. Sue Biggins’ lab at the Fred Hutch. This approach will allow Dr. Hu to determine rate-limiting steps and key regulating mechanisms in kinetochore assembly and will serve as a blueprint for future studies examining the assembly of other large complexes. Furthermore, this work may reveal novel trouble points in chromosome segregation that lead to aneuploidy in cancer.

As a PhD student in Dr. Nicholas Wallace’s lab at Kansas State University, Dr. Hu’s research focused on the repair of DNA double-strand breaks (DSBs). Dr. Hu demonstrated that beta human papillomavirus type 8 protein E6 (8E6), long known to impair traditional DNA-repair pathways, also promotes DNA repair via a mutagenic DSB repair pathway termed alternative end joining. In this way, 8E6 promotes cancer development by increasing genomic instability. Dr. Hu will now pivot to study genome stability at the chromosome level in Dr. Biggins’ lab.