Y Chromosome Variation and Male Lethality in Drosophila Embryos Lacking Blm DNA Helicase

BLM DNA helicase is a conserved protein that plays multiple roles in DNA replication and repair. Mutations in human BLM lead to a cancer predisposition disorder, Bloom Syndrome. In Drosophila melanogaster (the fruit fly), Blm has been well-studied. We have been investigating an unexplained observation about Blm in Drosophila that was made decades ago; mothers who lack functional Blm produce far more female than male progeny. Our data support the hypothesis that this female progeny skew occurs because maternally deposited Blm is essential to respond to DNA replication challenges in the early embryo. Blm mutant mothers, who are unable to package functional Blm into their eggs, exhibit a maternal effect lethality (most of their embryos fail to survive to adulthood), and their sons are particularly vulnerable. We hypothesize that this increased male lethality is due to the vast amount of repetitive DNA sequences on the Y chromosome, which pose an increased challenge to DNA replication. To further explore the basis of these Y chromosome replication challenges, we sought to identify Y chromosomes that show variability in their dependence on Blm. We screened global populations of Drosophila and identified Blm-dependent Y chromosome variability. We are assessing the nature of this Blm-dependent sequence variability and the effects that these sequences have on a variety of biological processes.