Lack of Blm protein during *Drosophila* embryonic development impacts lifespan of surviving progeny

Nathan L. Anderson[1], Abbey L. Roy[1], Karly Lacey[1],
Eric P. Stoffregen[1]

LEWIS-CLARK STATE COLLEGE
Division of Natural Sciences and Mathematics

Intro

- In humans, mutations in BLM DNA helicase cause Bloom Syndrome, an autosomal recessive cancer predisposition syndrome.
- In *Drosophila*, Blm plays an essential role in ensuring proper DNA replication during early embryogenesis.
- Most progeny from *Blm*-mutant mothers die during embryonic development due to a lack of maternal Blm gene products (Figure 1).
- It is unknown what effect the lack of Blm during early embryogenesis has on flies that survive this Blm-null environment.
- We hypothesize that due to sub-lethal DNA damage caused by the lack of maternally loaded Blm during early development, surviving progeny from *Blm*-mutant mothers (Blm-null during early development; Blm^-) will exhibit shorter lifespans than genetically matched controls (maternal Blm protein provided during early development; Blm^+).

Method

- *Blm*-mutant females (Blm^-) were crossed to wild type males, and as a control, wild type females (Blm^+) were crossed to *Blm*-mutant males (Figure 2).
- All resulting progeny were *Blm* heterozygotes.
- These progeny differ only in that the progeny from Blm^- mothers lacked functional Blm during early development, while Blm^+ mothers provided maternal Blm gene products during this time period.
- On day 4 after eclosion, flies were segregated by sex, and deaths were scored daily.

Results

- Progeny from Blm^- mothers demonstrated significantly reduced lifespan during the first 40-50 days post-eclosion, as compared to progeny from Blm^+ mothers (Figure 3).

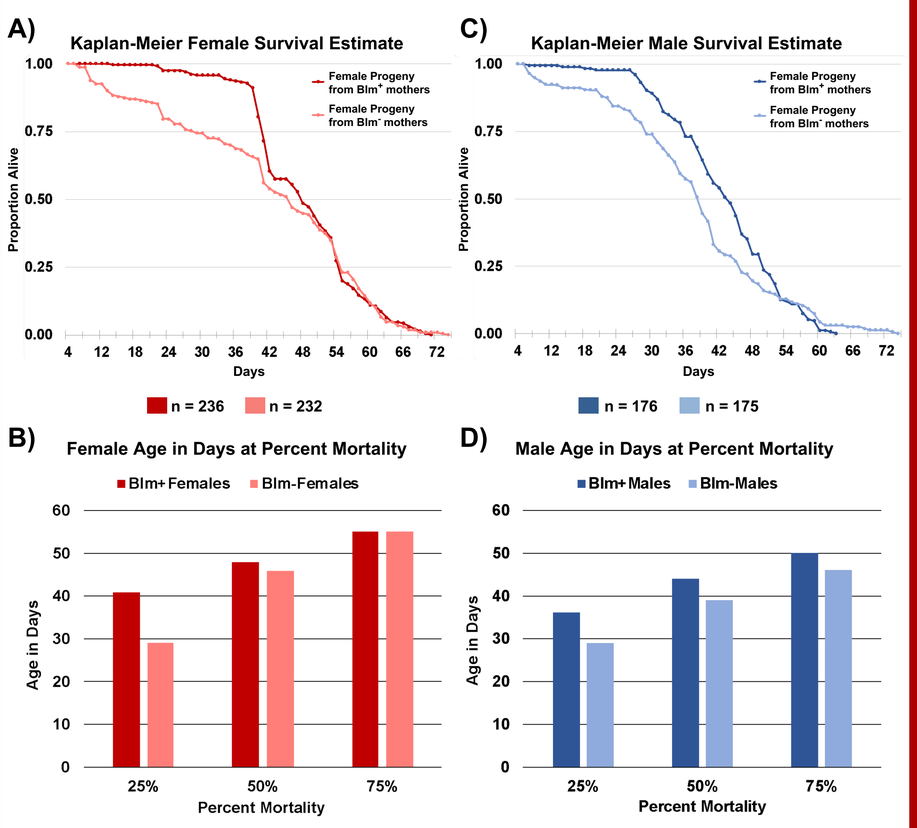
Discussion

- Our data supports the hypothesis that a lack of maternally loaded Blm during early embryogenesis reduces the lifespan of flies that survive to adulthood.
- We plan to analyze lifespan differences between males with variable Y chromosomes that develop +/- maternal Blm (Figure 4).

IDAHO INBRE
IDeA Network of Biomedical Research Excellence

Surviving adult progeny that were **deficient for Blm** DNA helicase during early embryonic stages exhibit a **reduced lifespan.**

Figure 3: Lifespan Differences Between Progeny from *Blm*$^-$ versus *Blm*$^+$ Mothers



Full figure legends can be viewed by pointing your cell phone camera at this QR code:

Figure 1: Embryos Lacking Blm Incur Widespread DNA Damage

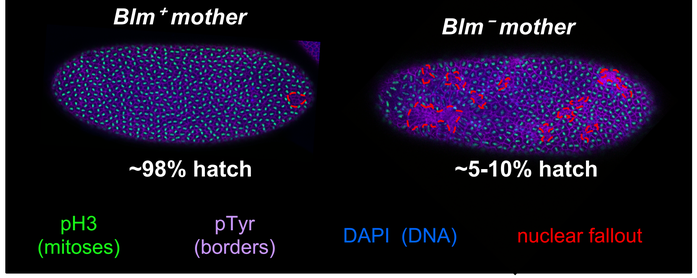


Figure 2: Experimental Crosses

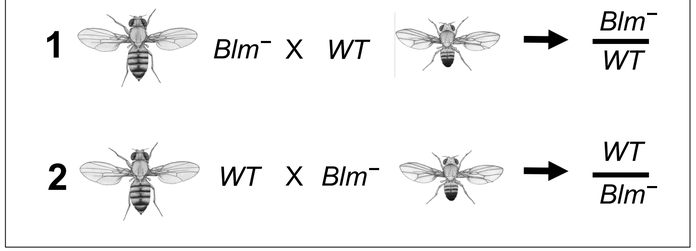
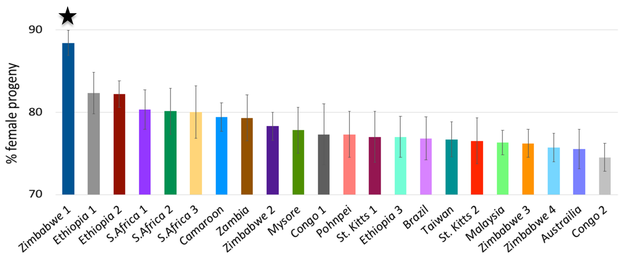


Figure 4: Identification of Natural Blm-dependent Variation



Geographically diverse males crossed to *Blm*$^-$ females

References

- Aeschliman J, Brady M, McMahan S, Lacey K, Sekelsky J, Stoffregen EP. *Blm Helicase Facilitates Rapid Replication of Repetitive DNA* (in preparation).
- McVey, M *et al. Multiple functions of Drosophila BLM helicase in maintenance of genome stability.* Genetics (2007).
- Han *et al. OASIS 2: online application for survival analysis 2 with features for the analysis of maximal lifespan and healthspan in aging research.* Oncotarget (2016).
- Dunkler, D., Ploner, M., Schemper, M., & Heinze, G. (2018). Weighted Cox regression using the R package coxphw. Journal of Statistical Software, 84(1), 1-26.
- R Core Team (2019). R: A language and environment for statisticalcomputing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

Acknowledgements

- The project described was supported by an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under Grant #P20GM103408.
- *Drosophila* images (Fig.2) courtesy of @lifeofmaro.
- Thank you to Dr. Leigh Latta for help with statistical analysis.