Genetics Day Poster Submission

Presenter: Eric Hillpot

Category: Graduate Student

Authors: ERIC HILLPOT, S. Ramachandran, A. Wolfe, A. Seluanov, V. Gorbunova

Title: THE 1.9 Å BEAVER SIRTUIN6 CRYSTAL STRUCTURE

Abstract: Sirtuins are NAD+ -dependent enzymes with histone deacetylase and/or mono-ADP-ribosyltransferase activities that regulate diverse cellular functions related to metabolism, disease, tumor suppression, and aging. The nuclear Sirtuin, SIRT6, promotes lifespan by; regulating chromatin expression of genes related to metabolism and oxidative stress, repressing LINE1 elements, and promoting DNA double-strand break repair and promoting genome stability. Our group recently published that DNA doublestrand break repair coevolves with maximum lifespan in rodents . SIRT6's ability to repair double-strand breaks was compared across 18 rodent species. The ability of SIRT6 to repair double-strand breaks correlates with maximum lifespan. At the extremes, the mouse is an example of a shortlived rodent with weak SIRT6 enzymatic activity, and the beaver is an example of a long-lived rodent with strong SIRT6. Mouse and beaver SIRT6 activities were directly compared. Importantly, fve amino acid residues were determined to be key in the differential activities between mouse and beaver SIRT6. However, the enzymatic and structural differences between mouse and beaver SIRT6 are not fully understood. To determine the key structural differences between mouse and beaver SIRT6, X-ray crystallography was used.