expression, including the ways in which genes are regulated. Understanding the consequences of differences in gene expression on aging rate, and the consequences of aging on gene regulation will continue to have profound impacts on our ability to manipulate the aging process. This symposium on gene regulation in aging will focus on how genes are regulated by the aging process and can be regulated differently to affect the aging process. We have an expert on the regulation of gene expression in the immortal germline and soma of the hydra, Dr. Celina Juliano. Dr. Roger Brent is an expert on the mechanisms of cell to cell variation in gene expression. Dr. Monica Driscoll is an expert on both the genetics of aging and gene expression changes with age. Finally, Dr. Alex Mendenhall's studies are focused on understanding intrinsic (epigenetic) variation in the regulation of gene expression as a cause and consequence of aging. Together these experts will present their research as it relates to gene regulation and the aging process.

HOW THE SAME GENETIC PROGRAM RUNS DIFFERENTLY IN INDIVIDUAL ANIMALS TO AFFECT AGING AND DISEASE

Alexander Mendenhall, Bryan Sands, and Soo Yun, *University of Washington, Seattle, Washington, United States*

Monozygotic human twins will age at different rates. The same is true for isogenic laboratory animals. Some of these differences in the rates of aging are caused by differences in the expression of genes. And, some of the differences in gene expression between isogenic individuals are caused by seemingly non-heritable, stochastic epigenetic differences. Here we discuss how differences in chaperone expression can influence aging and a model of Ras-driven neoplasia risk and survival in the model nematode Caenorhabditis elegans. We review evidence suggesting differences in epigenetic silencing machinery contribute to differences in chaperone gene expression. We suggest models for germline and somatic epigenetic regulation of chaperones. We discuss potential means of targeted epigenome modification, and potential implications for human health during aging.

MECHANISMS OF DEVELOPMENT AND REGENERATION IN HYDRA

Celina Juliano, Jack Cazet, and Abby Primack, *University of California, Davis, Davis, California, United States*

Hydra vulgaris is a small and simple aquatic animal capable of whole-body regeneration and has negligible senescence. The entire animal, including the nervous system, is composed of about 25 cell types, and can regenerate from a fragment of tissue as small as ~300 cells. In addition, all cell types are continually renewed in the uninjured adult as part of normal homeostasis; every differentiated cell type is replaced approximately every 20 days, which likely contributes to its lack of aging. The remarkable features of Hydra are enabled by three distinct populations of stem cells that support the three lineages that make up the adult Hydra – the ectodermal epithelial lineage, the endodermal epithelial lineage, and the interstitial lineage (includes the neurons). A major goal of our laboratory is to understand the gene regulatory networks that control the specification of all Hydra cell types in the uninjured (homeostatic) state and then understand how injury triggers these differentiation pathways at unexpected locations during regeneration. Using high throughput genomics approaches such as scRNA-seq, ATAC-seq, and Cut&Tag, we have transcriptionally defined every cell type in Hydra and identified putative transcriptional regulators for each cell type. This includes the 11 neuronal subtypes that comprise the nerve net that spans the entire length of the Hydra body. We are currently leveraging these data to conduct functional testing of key putative regulators and to identify injury inputs into cell specification events during regeneration.

MISEXPRESSION OF GENES LACKING CPG ISLANDS IS A SHARED TRAIT OF MAMMALIAN AGING

Samuel Beck, *Boston University School of Medicine, Boston, Massachusetts, United States*

Changes in the 3-D architecture of chromatin are observed in various diseases and are also a hallmark of aging. Disruption of the nuclear lamina and associated heterochromatin are commonly observed in various aging contexts, including premature aging diseases, cellular senescence, and normative aging. Although these conserved structural changes have been reported for over two decades, their impacts on transcription and contribution to age-related degenerative changes remain unknown. By performing a large-scale computational analysis and experimental validation, here we show that genes lacking CpG islands (CGI- genes), which form heterochromatin when transcriptionally silent, are globally misexpressed in aged nuclei with disrupted chromatin architectures. We demonstrate that CGI- gene misexpression is a common feature of mammalian aging and explains the molecular basis of various age-associated defects, ranging from loss of cellular identity and increased transcriptional noise to age-associated chronic inflammation. Our findings reveal that CGI- gene misexpression is directly associated with age-related physiological deterioration, thus providing a novel biomarker of aging.

A SIMPLE ANIMAL MODEL OF EXERCISE REVEALS A MOLECULAR DETERMINANT OF LONG TERM HEALTH MAINTENANCE

Monica Driscoll, *Rutgers, The State University of New Jersey, New Brunswick, New Jersey, United States*

At all stages of life, both dynamic gene expression changes and events that "lock in" particular programs that promote health and maintenance are critical factors in aging trajectories. We have a long-term interest in the fundamental biology of healthy maintenance, a topic that has led us to consider multiple facets of healthspan. A powerful whole-organism intervention with maintenance-promoting, anti-disease, anti-aging impact is exercise. The molecular and cellular mechanisms that mediate long-term system-wide exercise benefits, however, remain poorly understood, especially as applies to "off target" tissues that do not participate directly in training activity. We are investigating the basic biology of exercise benefits using the simple 959-celled model C. elegans. We found that multiple daily swim sessions are essential for exercise adaptation, leading to enhanced expression of muscle structural genes and improved locomotory performance. Importantly, swim exercise training enhances whole-animal health parameters such as mitochondrial respiration and mid-life survival, increases functional healthspan of pharynx and intestine, and enhances nervous system health by increasing learning ability