Purpose: Aging is a complex biological phenomenon that involves thousands of genes orchestrated in conserved molecular pathways. Plastic surgeons strive to treat the appearance of aging in an effective and natural manner through surgical intervention, an approach that can be compromised by the limitations of aged tissue. Our goal is to define the molecular changes responsible for normal human tissue aging to identify novel therapies for the prevention and treatment of aging. Our previous work demonstrated that subcutaneous human adipose tissue, a frequent target for rejuvenation and reconstruction, is an excellent model with which to study human aging. The goal of this study is to demonstrate that histone modifications induced by the sirtuin gene family provide important contributions to adipose tissue aging.

Materials and Methods: Subcutaneous adipose tissue from the abdomen is collected from healthy patients (ages 18-85) undergoing plastic surgery at the University of Pennsylvania. Adipocytes, stromal vascular fraction (SVF) and adipose-derived stem cells (ASCs) are isolated from each specimen and examined in parallel. The aging phenotype is established in patients by the expression of senescence-associated markers and sirtuin genes, and by telomere length. Histone and sirtuin target gene acetylation is analyzed via Western blotting and ChIP-seq analyses in old versus young tissues.

Results/Complications: We confirm that biological age is consistent with chronological age in our model of adipose tissue aging using purified populations of adipocytes, SVFs, and ASCs from subcutaneous adipose tissue of young and old patients. We demonstrate that the human sirtuin genes regulate human adipose tissue aging in a differential manner via effects on histone and target gene acetylation. Significantly, we demonstrate for the first time that specific histone modifications, including H3K9ac and H3K56ac, may serve as critical markers for adipose tissue aging.

Conclusion: Our work demonstrates a significant role for histone modifications in adipose tissue aging. These modifications, thought to be enacted by the sirtuin genes, can serve as specific regulatory targets for anti-aging therapies. Future experiments will investigate regulatory molecules that reverse these histone modifications in ASCs in an attempt to prevent or reverse aging in these cells. These findings and planned future experiments are critical for advancing the understanding of how human tissues age and have significant implications for regenerative medicine applications in plastic surgery.