Articles of Significant Interest in This Issue

Sirtuin 5 Is Regulated by the SCF-Cyclin F Ubiquitin Ligase and Is Involved in Cell Cycle Control

Sirtuin 5 (Sirt5) is a deacetylating enzyme influencing several aspects of cellular metabolism. However, little is known about how SIRT5 is regulated. Mills et al. (e00269-20) report that SIRT5 levels are controlled by the SCF family of ubiquitin ligases. Cyclin F, a substrate receptor F-box protein for the SCF that controls cell cycle progression, regulates the abundance, stability, and ubiquitination of SIRT5. Interestingly, SIRT5 knockout alters the cell cycle, and global phosphoproteomics reveal altered signaling consistent with these cell cycle changes. Together, these data reveal a connection between metabolism and cell cycle control.

Regulation of Sex-Specific Enhancer CpG Methylation by Growth Hormone-Activated STAT5b

STAT5b, a growth hormone-activated transcription factor, plays a pivotal role in regulating the sex dependence of liver gene expression and metabolic function. Using a hepatocyte STAT5-deficient mouse model, Hao and Waxman (e00166-20) show that many male-biased genes are repressed upon loss of STAT5 binding. In contrast, female-biased genes, which show low STAT5 binding in male liver, are derepressed by an indirect mechanism. STAT5 deficiency induced a near-global loss of sex-dependent liver CpG methylation, involving the hypermethylation of gene-distal enhancers enriched for accessible chromatin, enhancer histone marks, STAT5 binding, and DNA motifs for STAT5 and other factors implicated in liver sex differences.