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 deacylating 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 knock-out 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.