

layers overlay and the cabled appearance of the skein where the threads run circumferentially along the outer surface. — MSL

Nat. Comm. 10.1038/ncomms4534 (2014).

GENETICS

Blood and Brains

Epigenetic changes, such as gene methylation, can be detected directly by examining the status of DNA within specific tissues. However, it is desirable to identify epigenetic changes from afar, especially in tissues that may be hard to survey, such as the brain. Working with a mouse model of Cushing's disease, characterized by changes in methylation as a response to exposure to glucocorticoids, Ewald *et al.* found that methylation and expression of the *Fkpb5* gene within the hippocampus correlated with its degree of methylation in the blood. Although limited by the examination of only a single gene, the observed correlation highlights that for some diseases, it may be possible to use blood monitoring to infer epigenetic changes in the brain. — LMZ

Psychoneuroendocrinology 44, 112 (2014).

CELL BIOLOGY

Sleep Circuit

The neurotransmitter molecule γ -aminobutyric acid (GABA) promotes sleep in mammals and flies, but the molecular details of this regulation have not been clear. Chen *et al.* provide new



insight into this complex pathway, finding that GABA transaminase (GABAT), a mitochondrial enzyme that breaks down GABA, controls GABA amounts to affect sleep in *Drosophila*. Sleep is controlled by the protein sleepless (SSS), which is expressed in neurons of the fly brain. Its absence in mutant flies increases neural activity and decreases sleep. Mutant flies lacking SSS expressed more GABAT in the brain. Consequently, GABA amounts decreased by 30% in the brain, and compared to control flies, mutant flies slept less. Disrupting GABAT expression increased

GABA amounts and boosted total daily sleep. Furthermore, reducing GABAT in mutant flies lacking SSS restored sleep. Flies expressing mutant GABAT showed an increase in overall daily sleep, and the time it took flies to fall asleep was reduced. Moreover, treatment of adult flies lacking SSS with ethanolamine O-sulfate, an inhibitor of GABAT, rescued sleep. These results suggest that SSS promotes sleep and that its absence increases neuron excitability, which may demand more energy. This could alter cell metabolism in neighboring glia, including changes in GABAT activity in the mitochondria. Changes in GABAT activity have been implicated in epilepsy (characterized by increased neural activity) and other neuropsychiatric disorders. The connection of GABAT and cell metabolism to sleep control may explain sleep problems associated with these conditions. — LC

Mol. Psychiatry 10.1038/mp.2014.11 (2014).

BIOPHYSICS

AFM Uncompromised

Atomic force microscopy (AFM) is a powerful tool used both for subnanometer imaging and for mechanical probing of molecules. The key measurement in AFM is the deflection of a cantilever, which depends on the force it experiences. AFM is used in single-molecule force spectroscopy to monitor the folding and unfolding of biomolecules. This application requires sensitivity to very small changes in force on short time scales, but also requires long-term force stability. Current AFMs are optimized either for short-term force precision (achieved by using shorter, stiffer cantilevers to reduce hydrodynamic drag) or for long-term force stability (better performance comes from longer, softer cantilevers). Bull *et al.* modified a short cantilever with a focused ion beam to achieve excellent short-term precision and long-term stability. AFM cantilevers are typically gold-coated to improve signal intensity, but the gold reduces stability. Removal of the gold except for a protected patch at the end of the cantilever maintained high signal without compromising stability. A protein unfolding assay highlighted the short-term precision, whereas stretching a surface-anchored protein showed sub-pN performance over a force bandwidth of 0.01 to 1000 Hz. Monitoring abrupt unfolding of a protein showed that the cantilever had a temporal response time of about 70 μ s. These responsive yet stable cantilevers should benefit diverse AFM studies. — VV

ACS Nano. 10.1021/nm5010588 (2014).