› RESEARCH IN BRIEF

Putting *Plasmodium* on a diet

Parasites, like the *Plasmodium* species responsible for malaria, rely on their hosts for the nutrients they need for replication and survival. Consequently, studies have suggested that caloric restriction could be protective against malaria. A new letter in *Nature* looks more closely at how *Plasmodium* react when their hosts cut calories (*Nature* **547**, 213–216; 2017).

The researchers infected two groups of mice: a control fed *ad libitum*, and a caloric restricted (CR) group that received 30-40% fewer calories than the controls. The CR mice had lower parasite burdens and survived longer than controls. Testing *Plasmodium* lines with different genetic modifications, the team narrowed in on the *KIN* gene, a protein kinase, as responsible for detecting available nutrients and modifying pathways that reduce replication when there's not enough to go around.

Cre & CRISPR for sarcoma modeling

Though Cre-recombinase has been a go-to method for genetically engineering mouse models for specific cancer-causing mutations, CRISPR/Cas9 seems poised to replace stem cell manipulations and multiple breeding rounds with a quicker—and cheaper—method to directly edit desired cells in an animal model. But with any new technology, it takes time to determine if the newcomer does beat the standard. Research from David Kirsch's lab at Duke tests an established Cre-LoxP method against CRISPR for modeling sarcoma (*Nat. Commun.* **8**, 15999; 2017).

The lab generated soft tissue sarcomas in genetically modified and wild type mice using Cre-LoxP alone and in combination with CRISPR/Cas9 and then compared the resulting histopathology, tumor growth kinetics, and further mutations. Ultimately, they found no significant differences between the two methods.

Pee predictions

Though one might expect that clone-like cohorts of laboratory mice will respond identically to a particular treatment, phenotypic differences usually emerge. For example, mice fed a high-fat diet will gain weight and develop altered glucose tolerances, but some more extremely than others. The microbiome may be responsible, and new research demonstrates a novel way to link the gut to variable outcomes (*Cell. Rep.* **20**, 136–148; 2017).

In the study, researchers put 50 isogenic C57BL/6J mice on a high-fat diet, collecting urine samples along the way. Untargeted ^{1}H-NMR spectroscopy-based metabolite phenotyping identified pre-diet signatures that are related to microbial activity in the gut. These signatures correlated with 25 of 44 phenotypes observed at the end of the 20-day diet, from weight gain and glucose intolerance to different measures of anxiety, suggesting a predictive value in what can be found in pee.

It's electric

As the name suggests, the electric eel is an electrifying animal. It has evolved three specialized organs for the purpose: two produce relatively weak but fairly constant currents to aid navigation and communication, while the third is responsible for the eel's high-voltage discharge that can stun both prey and predators. Researchers at the University of Wisconsin-Madison have delved into the genetics of the electric eel in the past, and they are now looking at the proteome and phosphoproteome of the animal's electric organs and skeletal muscle (*Sci. Adv.* **3**, e1700523; 2017). With the new protein data, they report variations in sodium transporters and potassium channels and different transcription factors and protein kinases between the three electric organs, observations that they think drive the different voltages.

Fewer calories provides more wiggle room for learning in worms

Dietary restriction (DR) has been shown to provide several benefits, from improved health to extended lifespans, but the precise mechanisms by which DR provides these benefits are not well known. Using *C. elegans*, a popular model for understanding DR-induced extended lifespans, a new report demonstrates how DR can improve learning in worms (*PLoS Biol.* **15**, e2002032; 2017).

Using an associative learning paradigm, the team explored the role of DR and several other pathways, including mechanistic target of rapamycin (mTOR), AMP-activated protein kinase (AMPK), and autophagy, on both lifespan and learning. Their results show that, despite the activation of several molecular effectors, these pathways enhance learning via depletion of kynurenic acid (KYNA) and activation of a specific pair of inhibitory interneurons, providing an important link between longevity and learning.

Fizzled out: disruptions to Wnt signalling in the gastric epithelium of mice

Wnt signalling is a crucial molecular pathway for maintaining proper cellular homeostasis in several organs, including the gastric epithelium (GE). Using a combination of cultured organoids of GE cells and a GE-targeted mutant mouse line, researchers now show the importance of one specific Wnt molecule, Fzd7, in helping to maintain GE homeostasis (*Dis. Model. Mech.* **10**, 971-980; 2017). Specifically, the paper demonstrates that when the *Fzd7* gene is deleted *in vivo*, it causes rapid epithelial repopulation and was deleterious.

A mouse model for restless legs syndrome

Restless legs syndrome (RLS) is a debilitating disorder marked by an uncontrollable urge to move one's limbs, owing to discomfort. Because the discomfort is typically noticeable when trying to sleep, RLS can cause severe sleep loss and accompanying health detriments.

Genome-wide association studies using RLS patients have consistently linked the gene *MEIS1*, but an understanding of its role in RLS etiology is not clear. Salminen *et al.* developed and phenotyped a heterozygous *Meis1*-knockout mouse line to help define the role that *Meis1* might play in RLS, and report their finding in *Disease Models and Mechanisms* (**10**, 981-991, 2017).

Flies lend a leg to understanding neurodegenerative disease

Studying the role of specific proteins in various diseases is a costly and time consuming process, especially when done in an *in vivo* context. In a new paper, Josefin Fernius and colleagues at the Linkoping University, Linkoping, Sweden, demonstrate a novel assay system using *Drosophila* adult legs to monitor the cellular effects of several neurodegenerative disease-related proteins (*Dis. Model. Mech.* **10**, 1027-1038; 2017).

The group used their novel system to test the effects of expressing several proteins, including Aβ, tau, and ATX1. Their results provide a proof-of-principle for their assay system to efficiently detect and study the cellular and subcellular effects of neurodegenerative protein expression on adult (fly) neurons.