› RESEARCH IN BRIEF

Transcriptomic signatures of malaria

It is difficult to predict how severely a patient will be impacted by an infection. Researchers working with malaria believe they have identified several biomarkers associated with severity of infection in mice (*Sci. Rep.* **7**, 41722; 2017). The team infected mice with one of two strains of *Plasmodium chabaudi*, the parasite responsible for malaria in rodents, and compared the results of high-resolution, whole-blood transcriptomic analysis. One of the strains produces severe symptoms, while the other is avirulent. The comparison revealed signatures of platelet aggregation, anemia, and lung infection in the mice infected by the virulent strain. Interestingly, the first two signatures could be detected before the mice showed clinical signs of becoming sick. If translatable into humans, these results suggest virulence could be predicted from a simple blood draw.

CARTing around mRNA

Messenger RNA has therapeutic potential for treating a variety of diseases. Getting negatively charged mRNA through positively charged cell membranes, however, is tricky. To improve *in vivo* mRNA delivery, a team at Stanford suggests using CARTs (*Proc. Natl. Acad. Sci. USA* **114**, E448-E456; 2017). CARTs, or "change-altering releasable transporters," are positively charged oligomers that will form protective rings around a stand of mRNA. With mRNA safely ensconced, the CARTs and their cargo can pass through cell membranes. Once inside, a conformational change releases the mRNA into the cell to begin instructing protein expression while leaving behind small neutral molecules that can be easily biodegraded. After confirming the functionality in cell cultures, the team designed CARTs to carry mRNA encoding a green fluorescent protein into different tissues of their mice. Compared to sites injected with naked mRNA, those that received mRNA delivery via CARTs were highly bioluminescent, as expected.

Automating histology

Proper training in histology is an important—but sometimes overlooked—detail in pathological research. Automating the process could help overcome limits in training as well as inter-observer variability when assessing tissue samples. A proprietary, automated system was recently put to the test to score drug-induced fibrosis in murine lung tissue, with promising results (*PLoS One* **12**, e0170561; 2017).

The team compared the results of the automated tissue analysis against those of a trained pathologist using a standard scoring method, as well as against micro-CT scans and lung function testing. The results suggest automation may be up to the task; the team found significant correlation between the analysis of the automated system and the standard measurement methods.

B_3 for the eyes

Vitamin B_3 is an essential vitamin with a newly suggested role in preventing glaucoma (*Science* **355**, 756–760; 2017). Researchers studying the neurodegenerative disease in mouse models observed progressive decreases in metabolites in the retina that are needed for mitochondrial metabolism and to prevent oxidative stress in retinal ganglion cells, leaving the eyes susceptible to damage from high intraocular pressure that often comes with age. The precursor to those metabolites is Vitamin B_3. The team therefore decided to supplement the diets of their mice with the vitamin, both prophylactically in young mice predisposed to glaucoma and after intraocular pressure began to spike in older individuals. The dietary B_3 boost proved protective, slowing progression in mice with the disease and reducing the probability of developing it in the first place.

Gene therapy for hearing loss

Hearing loss affects millions of people, but there are currently no biological treatments for this malady. Usher syndrome, which is a genetic disorder that causes several devastating problems, including balance problems and blindness, also causes profound deafness.

Using a knock-in mouse model of Usher syndrome, Ush1c c.216G>A, a team led by Gwenaëlle Géléoc and Jeffrey Holt at Boston Children's Hospital, Harvard Medical School, developed a novel gene therapy strategy to rescue hearing in the mutated mice (*Nat. Biotechnol.* doi:10.1038/nbt.3801; published online 6 February 2017). Using an adeno-associated viral vector, they delivered wild-type Ush1c and were able to recover normal gene and protein expression, restore sensory cell function, and most importantly, were able to recover hearing and balance behavior in the mutant mice to near wild-type levels.

The results demonstrate a critical and unprecedented recovery of *in vivo* biological function using gene therapy, and suggest that this treatment approach could be translatable to humans.

High-throughput workflows for microbial genomics

While shotgun DNA sequencing has transformed the field of microbiology, allowing genomic sequencing and analysis at high speeds and relatively low costs, there are still some hurdles slowing down progress. Sample preparation still requires significant amounts of time, and is now the key limiting factor. New research by Paul Blainey from the Broad Institute and colleagues aims to improve the speed of sample preparation (*Nat. Commun.* **8**, 13919; 2017).

Using a microfluidic platform, they developed a workflow that is capable of sequencing library sample preparation for up to 96 samples, while substantially reducing the amount of DNA sample required. Additionally, the rapid process does not come with a quality tradeoff: data quality was either maintained or improved compared to conventional methods. Using their platform they sequenced 400 clinical *Pseudomonas aeruginosa* libraries and found excellent single-nucleotide polymorphism detection.

Untangling microbial communities with MetaSort

The mircobiome is a critical variable in understanding animal—including human—health and disease. Identifying the variety of microbes forming complex communities, however, is still a challenge. Metagenomics, which seeks to identify all of the microbial members of a community, is hampered by relying on reference genomes, which don't necessarily cover novel microbial communities. To address this problem, Fangqing Zhao and colleagues at the Chinese Academy of Sciences, Beijing, developed a new bioinformatics platform, called MetaSort, for construction of bacterial genomes from metagenomic samples (*Nat. Commun.* **8**, 14306; 2017). Testing their new method using material from marine kelp, they were able to recover 75 high-quality genomes.

How the nervous system protects the gut

Maintaining a balanced intestinal microbiome is important for proper intestinal function and overall health and well-being. The gut, however, is a highly dynamic environment, undergoing waves of peristaltic activity. Controlling this gut activity is the enteric nervous system (ENS), which might also, therefore, play an important role in regulating the microbial composition of the gut.

Using a *sox10* mutant line of zebrafish, which lack an ENS, a team from the University of Oregon demonstrate that these mutant fish develop inflammation owing to increased levels of pro-inflammatory bacteria, and a decrease in anti-inflammatory bacteria (*PLoS Biol.* **15**, e2000689; 2017). Their results illustrate the importance of the ENS in maintaining healthy balances in gut microbiota.