## › RESEARCH IN BRIEF

### No bones about it

The CLARITY imaging technique was originally developed for use in the brain, making the soft tissue transparent without losing fluorescent reporters. To visualize biological processes through intact bone, with both a hard mineral layer and soft marrow, researchers at the California Institute of Technology present the Bone CLARITY protocol (*Sci. Transl. Med.* **9**, eaah6518; 2017).

The bone to be analyzed—a tibia, femur, and vertebral column in this paper—is demineralized, stabilized with an acrylic hydrogel that preserves 3D architecture, and then cleared of lipids with common laboratory detergents. The resulting samples are optically transparent, allowing molecular and cellular processes to be visualized with a custom light-sheet fluorescence microscope. With the new protocol, the team was able to estimate osteoprogenitor cells with improved precision over stereologic sampling strategies.

### Closing the dosing loop

Despite all of the physical parameters considered, determining drug dosages involves estimation, which means physiological differences in how an individual reacts to and metabolizes a compound are difficult to take into consideration. A new device offers a closed-loop solution that can measure and adjust a drug's concentration in real time (*Nat. Biomed. Eng.* **1**, 0070; 2017).

The device consists of three elements: a biosensor that uses aptamer technology to detect a given drug in the bloodstream; a controller programmed with a feedback algorithm that calculates what's needed; and an infusion pump that responds accordingly. The team fine-tuned the technology and put it through its paces with Doxycycline in rabbits, and then demonstrated its translational potential in Sprague-Dawley rats.

### Mom and pop mouse

Mammalian offspring usually receive some level of parental care, though that varies by sex and by species. To test for the evolutionary underpinnings of parental care, researchers examined the behavior and genetics of two closely related but behaviorally divergent mice species, the monogamous old-field mouse and the promiscuous North American deer mouse (*Nature* **544**, 434–439; 2017).

Monogamous mice cared more closely for their pups, with fathers investing similar amounts of attention as mothers, while promiscuous fathers were considerably less paternal. Switching pups between parents suggested nature over nurture, and genetic analysis revealed 12 genomic regions associated with differences in parental care, 8 of which were sex-specific. One particular behavior with a genetic component, nest building, could be manipulated by altering the hormone vasopressin, an observation repeated in the laboratory staple, *Mus musculus*.

### Brains: dead or alive?

Our understanding of the anatomy of the brain is undeniably indebted to post-mortem analysis of donated organs, but new research suggests that *ex vivo* studies may be of limited value in physiological studies that test for brain imaging and stimulation artifacts (*Proc. Natl. Acad. Sci. USA* **114**, 5243–5246; 2017).

The researchers recorded electric fields from transcranial electrical stimulation in the brain of a Cebus monkey *in vivo*, thirty minutes are euthanasia, and then six and seven days post-mortem. The first two measurements were fairly close, but the later recordings diverged significantly in both strength and frequency, even when controlling for temperature effects and other confounding factors. The results stress the continued need for *in vivo* neuroscience research.

## Big picture brain imaging using adaptive optics

Adaptive optics (AO) help correct for the inevitable differences in refractive indices that occur across complex biological tissues, like the brain. But conventional AO techniques require users to make a difficult choice: if they want to capture fast dynamics they can only correct a small field of view; if they want to correct aberrations in a larger section, it has to be done piecemeal, one small field of view at a time, severely limiting temporal resolution of large-field dynamics.

Reporting in *Nature Methods*, Meng Cui's group at Purdue University, West Lafayette, IN, have developed multi-pupil adaptive optics (MPAO) that enables neuroscientists to apply AO simultaneously over a wide field of view (*Nat. Methods* **14**, 581–583; 2017). The method takes the standard AO process of wavefront correction, and boosts it using prism arrays that enable independent and simultaneous image correction at multiple regions across a wide field of view. The team demonstrates MPAO's capacity for creating crisp images quickly using calcium imaging of neurons in mouse cortex, as well as vasculature dynamics.

## Cancer cells commit suicide

What if cancer cells could be reprogrammed to kill themselves? In a new paper published in *Nature Biotechnology*, a group from University of Pittsburgh, Pittsburgh, PA, constructed viruses to do just that (*Nat. Biotechnol.* doi: 10.1038/nbt.3843; published online 1 May 2017).

Using modified adenoviruses constructed to carry Cas9 nickase and a herpes simplex virus type-1 thymidine kinase (HSV1-tk), the team relied on specific genomic rearrangements occurring in human prostate cancer or hepatocellular carcinoma cells to ensure the suicide gene (HSV1-tk) was only expressed in cancerous cells. Testing their new assisted-suicide method for cancer cells using mouse xenografts, they found that cancer stricken mice with injections of both viruses (and a drug to activate the destruction process in infected cells) had reduced tumor burden and no mortality over the period of the study.

## Using bacteria to suppress virus transmission from mosquitoes

*Wolbachia* bacteria, when living inside insects, can hinder the ability of those insects to act as viral vectors for humans, providing a potential method to decrease the spread of mosquito-borne infections such as dengue and Zika.

In a paper recently published in *PLoS Biology*, a group of researchers led by Michael Turelli from University of California, Davis, Davis, CA, took isolated populations of *Ae. aegypti* infected with *Wolbachia* and released them into two areas within Cairns in northeastern Australia to study the extent of the mosquitoes' spread (*PLoS Biol.* **15**, e2001894; 2017). The team found that mosquitoes maintained their infections with *Wolbachia* even as the population spread at a rate of 100–200 meters per year (release date of 2013). The population dynamics provide a valuable resource for further exploring the utility of *Wolbachia* infected mosquitoes for fighting deadly human viral infections.

## News drugs for targeting colorectal cancer

MACC1 (Metastasis Associated in Colon Cancer 1) is an important driver and biomarker for cancer progression and metastasis, particularly colorectal cancer (CRC). Using a high-throughput screening method based on luciferase-reported MACC1 expression, Ulrike Stein from Charité Universitätsmedizin Berlin and Max-Delbrück-Center for Molecular Medicine, Berlin, Germany, and colleagues tested ~30,000 compounds from the ChemBioNet library and found two that significantly suppressed MACC1 expression levels (*PLoS Biol.* **15**, e2000784; 2017).

The team tested both of the compounds, lovastatin and rottlerin, *in vivo* in mice with xenograft colorectal cancer and found that they suppressed MACC1 expression and also reduce metastasis to the liver. The results provide the first preclinically-identified compounds that specifically target MACC1 and may prove valuable for translational development.