› RESEARCH IN BRIEF

Uncaging copper images

Metals are critical for health but must remain in homeostasis; an imbalance, whether from too much accumulation or too little, can be highly disruptive. A new probe with the ability to track deposits or deficiencies of copper has recently been developed at the University of California, Berkeley (*Proc. Natl. Acad. Sci. USA* **113**, 14219–14224; 2016).

The bioluminescent reporter system uses a copper-caged luciferin. The caging is designed to only release the luciferin in the presence of copper, allowing for *in vivo* monitoring of concentrations over time. Compared to images of control mice with normal concentrations of copper in their livers, organs with too much copper appear brighter while those with too little look darker. Though this initial reporter is copper-specific, it could be modified to be unlocked by other metals in future applications.

Zebrafish scaffolds for heart repair

The ability to regenerate damaged tissue varies between organisms. Mammalian hearts tend to scar while those of more evolutionarily primitive species, such as fish, easily repair themselves. Underlying regeneration is the extracellular matrix (ECM), the scaffolding cells need to grow (or regrow) into tissues. Researchers from the University of Pittsburgh recently investigated whether cardiac ECM from zebrafish could help mice recover from ischemia (*Sci. Adv.* **2**, e1600844; 2016).

The team details their physical protocol to decellularize cardiac ECM, needed to remove any cellular traces that could cause an immune reaction across species. They found that ECM prepared from zebrafish hearts effectively restored cardiac function in mice following surgically induced myocardial infarction, compared to murine ECM and a saline control. Properly prepared, materials from zebrafish may be a potential new source for regenerative therapies.

Adult plasticity influenced by *Mecp2*

Rett Syndrome is an x-linked disease attributed to mutations in the gene *MECP2*. Heterozygous females can survive into adulthood but experience developmental delays with lasting mental and motor consequences within the first year. Synaptic disruptions during infancy have been established, but it was not clear how the syndrome continues to impact the brain into adulthood.

Hypothesizing that it interferes with brain plasticity, researchers at Cold Spring Harbor Laboratory performed a pup gathering assay with new surrogate dams that were heterozygous for *Mecp2* mutations or that had the gene knocked out entirely in the auditory cortex (*Nat. Commun.* **8**, 14077; 2017). Pup gathering is a learned behavior triggered by ultrasonic calls from the pups. With functional hearing but without functional *Mecp2* genes, both the heterozygotes and the knock-outs were unable to learn the behavior, implicating the gene's role in disrupting plasticity related to auditory cues.

Modeling gender differences in liver cancer

The prognosis for hepatocellular carcinoma (HCC) has a negative male bias. Attempts to recapitulate gender differences in chemically induced rodent models have proved inconsistent between different trials. As a potential alternative, transgenic zebrafish are currently under consideration.

Recent research in *Scientific Reports* (**7**, 41280; 2017) looked to characterize gender differences associated with HCC in the *kras*^{v12} zebrafish line, previously developed to model liver cancer. In the current study, the team found that males developed liver tumors more quickly and more severely than females. As suggested in rodent models, estrogen treatments suppressed tumor growth while androgen accelerated it, by inhibiting or promoting cell proliferation, respectively. The results suggest that zebrafish models are capable of reflecting gender differences in disease development and progression.

The SEARCH framework for sharing *in vivo* material

The 3Rs, originally drafted by Russell and Burch, aims to replace, reduce and refine experiments with animals. However, the use of animals is critical to biomedical progress, and the numbers of animals used is increasing, owing to advances in genetically engineered models for human diseases. In a new report, Morrissey *et al.* describe the SEARCH framework (Sharing Experimental Animal Resources, Coordinating Holdings), that helps researchers find and share left over material from *in vivo* research useful to others in their field (*PLoS Biol.* **15**, e2000719; 2017).

The SEARCH framework, exemplified by their pilot project SEARCHBreast for sharing breast cancer xenograft models and materials, allows researchers to potentially save significant costs by using materials already collected by other groups, and could also help spur new collaborations between labs; not to mention saving significant numbers of animals used in experiments.

Social transmission of associative learning in honeybees

Social insects provide a unique model to explore how complex behaviors emerge and are transmitted within a group environment. A new paper in *PLoS Biology* (**14**, e1002564; 2016) explores how honeybees can learn and teach reward-driven associative behaviors.

The group of researchers, led by Lars Chittka at Queen Mary University of London, devised a training paradigm to train bees to pull a string to receive a rewarding sucrose stimulus. After learning this associative task, the researchers then sought to determine if trained bees could pass on what they had learned by allowing naïve bees to observe the trained bees performing the task. The paradigm could help scientists use social insects to further dissect fundamental mechanisms sufficient for social transmission of learned behaviors.

A large animal model for ricin-induced respiratory distress

Ricin is an extremely toxic naturally occurring lectin that can be lethal to healthy human adults in doses as small as a few milligrams. To date, there are few clinical treatments available for those exposed to ricin, owing to a dearth of appropriate animal models to study pathophysiology. Using swine as large animal model, researchers report on ricin-induced disease progression that meets the diagnostic criteria for acute respiratory distress syndrome (ARDS) (*Dis. Model Mech.* **10**, 173–183; 2017).

Owing to their similarities in pulmonary anatomy and physiology, the group treated pigs with lethal doses of ricin and followed the animals for 30-70 hours post-exposure, monitoring them with a combination of pulmonary function tests, blood chemistry and histology. Results demonstrated that animals suffered from severe hypoxia and alveolar damage, resulting in increased lung permeability. With a model in-hand, the group hopes to understand and develop better clinical responses to ricin-induced ARDS.

An optimized protocol in guinea pigs for modeling type-2 diabetes

Brendan K. Podell and colleagues at Colorado State University, Fort Collins, developed a novel model of type-2 diabetes using guinea pigs and a unique combination of high-fat, high-carbohydrate diet with streptozotocin treatment (*Dis. Model Mech.* **10**, 151–162; 2016). Streptozotocin, a toxin particularly lethal to insulin-producing beta cells in the pancreas, has been used previously in rodent models of type-2 diabetes because of its ability to damage beta cells after diet-induced insulin resistance, recreating feature characteristics of human type-2 diabetes.

Although rodent models are more common, the authors believe their model using guinea pigs could provide some advantages, given the guinea pig's similarities to human lipid metabolism, as well as immunological and pathological responses to infectious disease with linked comorbidities to diabetes.