GENETICS

More than essential

Cacheiro, P. et al. *Nat. Commun.* **11**, 655 (2020)

Data from two projects—one in man and one in mouse—are coming together to help researchers screen for disease-causing genetic variants. The result is a new classification scheme that refines the concept of 'essentiality' for a particular gene.

The work, dubbed Full Spectrum of Intolerance to Loss-of-function (FUSIL), combined phenotype results in mouse from the International Mouse Phenotyping Consortium with human genes dubbed by the Broad Institute's Project Achilles as either essential or non-essential in cell lines.

Based on the cross-species data, the researches define 5 FUSIL categories with different biological properties: cellular lethal, developmental lethal, subviable, viable with phenotype, or viable with no phenotype. The authors suggest that screening against the FUSIL database could help in discovering previously unknown genetic causes of rare diseases. *EPN*

https://doi.org/10.1038/s41684-020-0498-0

TRANSCRIPTOMICS

Single cells in the fly midgut

Hung, R. et al. *PNAS* **117**, 1514–1523 (2020)

The midgut of the fruit fry *Drosophila melanogaster* shares a number of conserved processes and molecular pathways with the intestines of its distant mammalian relatives—humans included. Those similarities have made the fly a useful invertebrate model for studying homeostasis, cell signaling, and stem cell regeneration and maintenance in a complex tissue.

A new resource simplifies things, breaking the fly midgut down into its cellular components. Using RNA sequencing, researchers at Harvard Medical School have assembled a transcriptomic atlas of the male fly midgut at single-cell resolution.

The effort captured the known cells of the fly midgut, revealed new details about differential expression of different cell types, and uncovered five novel ones. The single-cell RNA-seq database can be visualized and explored at https://www.flyrnai.org/scRNA/ *EPN*

https://doi.org/10.1038/s41684-020-0500-x

NEUROSCIENCE

Squid connections

Chung, W., Kurniawan, N.D. and Marshall, N.J. *iScience* **23**, 100816 (2020)

Ever more detailed brain maps are in the works for a number of different model organisms, from worms and flies to mice and marmosets. Researchers from the University of Queensland in Australia have gotten started on such a resource for another animal: the bigfin reef squid, *Sepioteuthis lessoniana*.

Others have looked at the neuroanatomy of various cephalopods before via gross anatomy and histology, but Chung et al. are approaching the brain with a mix of those classic techniques and a more modern technology adapted from vertebrates: magnetic resonance imaging (MRI).

Though still a work in progress to fully map all the connections—the reef squid's connectome rivals that of the mouse—the MRI effort offers a fresh look at different regions of the unique cephalopod brain, including those neural networks involved in vision and camouflaging. *EPN*

https://doi.org/10.1038/s41684-020-0499-z

EXPERIMENTAL ORGANISMS

DMD treatment in pigs

Moretti, A. et al. *Nat. Med.* (2020) 10.1038/s41591-019-0738-2

Duchenne muscular dystrophy (DMD) is an inherited and eventually fatal myopathy that affects about 1 in 5000 newborn boys. The mutation responsible, a frameshift mutation affecting the gene that produces the dystrophin protein in muscles, maybe however be amenable to gene therapy. Trials in patients have been limited, but CRISPR/Cas9-based therapies delivered via adeno-associated virus vectors have shown promise in mouse and canine models. New work from researchers in Munich adds another large animal: the pig.

The team generated a pig model of DMD; these animals do not express dystrophin and display muscle weakness, signs of cardiac myopathy, and experience premature death. A CRISPR/Cas9-based therapy, delivered intravenously, was able to restore dystrophin expression in muscles such as the diaphragm and heart and prolong lifespans in the pig model. *EPN*

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