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research highlights

IN BRIEF

EXPERIMENTAL MODEL

A new rat model of  
hydrocephalus

Scott Emmert, A. et al. *Dis. Model Mech.* **12**, pii: dmm040972 (2019)

Hydrocephalus, one of the most common congenital abnormalities affecting the nervous system, is defined by an excessive accumulation of cerebrospinal fluid (CSF) in the brain. Surgical treatments are available to prevent brain damage, but a better understanding of the condition could lead to new therapeutic strategies.

Investigators from Cincinnati Children's Hospital Medical Center generated a rat model of hydrocephalus by using a CRISPR/Cas9 approach to introduce a gene mutation within the *Ccdc39* gene. *Ccdc39<sup>prlu/prlu</sup>* mutants demonstrated progressive postnatal hydrocephalus, impaired neural differentiation and glymphatic-mediated CSF circulation, as well as increased inflammation responses compared with wild-type rats. *Ccdc39<sup>prlu/prlu</sup>* rats should be useful to understand the mechanisms underlying impaired neurogenesis, glymphatic fluid exchange and cognitive and motor development in neonatal hydrocephalus. ALB

<https://doi.org/10.1038/s41684-020-0469-5>

GUT MICROBIOTA

A microbial link to  
neuroprotection

Kundu, P. et al. *Sci. Transl. Med.* **11**, eaau4760 (2019)

A variety of studies have reported changes in gut microbiota (GM) composition during the aging process, but the effects of these changes on host physiology remain poorly understood. Studies in mice have shown that aging-associated GM promote age-related inflammation, but a study in humans revealed that GM of extremely long-living people is enriched in health-associated microbes.

A new study suggests that the GM of old mice has beneficial properties by showing that young germ-free mice receiving a GM transplant from old donor mice exhibited increased neurogenesis in the hippocampus and increased intestinal growth. The study also reports that old donor GM induced the expression of FGF21, a longevity hormone that can influence neuronal viability. ALB

<https://doi.org/10.1038/s41684-020-0471-y>

ATRIAL FIBRILLATION

Studying arrhythmia in  
zebrafish

Collins, M. M. et al. *PNAS* **116**, 24115–24121 (2019)

GWAS have identified the 4q25 genomic region as a risk locus for atrial fibrillation (AF), and evidence suggests that AF-associated 4q25 variants act by regulating the expression of *PITX2*, a gene encoding a transcription factor required for cardiac development. Studies using *pitx2<sup>+/-</sup>* mice have confirmed the role of *PITX2* in AF pathogenesis, but the underlying mechanisms remain unclear.

Here, a team of investigators from the Max Planck Institute and the University of Copenhagen used zebrafish — a model increasingly used to study cardiac diseases, including AF — to further understand the role of *PITX2* in AF. By showing that *pitx2c<sup>-/-</sup>* zebrafish develop AF phenotypes caused by developmental perturbations to sarcomere organization and metabolic pathways, they provide new insights into the mechanisms of AF. ALB

<https://doi.org/10.1038/s41684-020-0470-z>

EXPERIMENTAL MODEL

A new mouse to study IFN  
signaling

Stifter, S.A. et al. *Cell Rep.* **29**, 3539–3550 (2019)

Interferons (IFN) are cytokines involved in the defense against infection. Although the role of IFN is well known, the identity and tissue distribution of IFN-responsive cells in vivo remain poorly defined, mainly because the only IFN signaling reporter mouse available (the *Mx2-luciferase* mouse) could not detect the IFN response at the level of individual cells.

In a new study, investigators from the University of Sydney describe an immunity-related GTPase m1 (*Irgm1*) reporter mouse strain (M1Red) allowing the visualization of IFN-responsive cells in vivo following inoculation with recombinant IFNs or influenza A virus. The *Irgm1* gene was selected to drive dsRed expression because *IRGM1* is expressed in both hematopoietic and non-hematopoietic cells and its expression is strongly induced by different types of IFNs. ALB

<https://doi.org/10.1038/s41684-020-0472-x>