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IN BRIEF

NEURODEGENERATIVE DISEASE

IKK β protects from Huntington's disease

Ochaba, J. et al. *Proc. Natl Acad. Sci. USA* **116**, 10952-10961 (2019)

Huntington's disease (HD) is a severe neurodegenerative disorder caused by a mutation in the *Huntingtin* gene, which results in the production of an unstable Huntingtin (HTT) protein with an abnormal expansion of a polyglutamine repeat. Previous work has shown that I κ B kinase (IKK) subunit IKK β can phosphorylate HTT serine 13 in vitro, leading to an increase of HTT clearance and a reduction of mutant HTT-mediated cellular toxicity. A study now confirms the neuroprotective role of IKK β during HD progression in vivo by showing that IKK β knockout worsened HD pathological phenotype in R6/1 mutant mice (a mouse model of HD). The results also suggest that IKK β regulates neuronal health through HTT phosphorylation-mediated activation of autophagy gene expression. **ALB**

<https://doi.org/10.1038/s41684-019-0358-y>

GENETICS

Enhancing gene editing in zebrafish

Aksoy, Y. A. et al. *Commun. Biol.* **2**, 198 (2019)

CRISPR-Cas9 gene editing strategies rely on the activation of the DNA repair pathway after the generation of double strand breaks (DSBs). Non-homologous DNA end-joining (NHEJ) dominates the DNA repair pathway, which limits the efficiency of homology-directed repair (HDR), the alternative pathway allowing precise and high-fidelity gene targeting. In a new study, a team of investigators from Australia developed an in vivo visual reporter assay to quantify HDR-mediated events at single-cell resolution in zebrafish. They used this system to identify chemical compounds that shift the DNA repair equilibrium in favor of HDR, and showed that DNA-dependent protein kinase inhibitor NU7441, which blocks NHEJ, can increase precise CRISPR-mediated gene editing up to 13.4-fold. **ALB**

<https://doi.org/10.1038/s41684-019-0359-x>

GUT MICROBIOME

Gut-mediated benefits of exercise

Carbajo-Pescador, S. et al. *Dis. Model Mech.* **12**, dmm039206 (2019)

To assess the effects of exercise on early obesity and non-alcoholic fatty liver disease (NAFLD) onset, juvenile Wistar rats fed a control diet or a high-fat diet (HFD) were split into four subgroups: half of the rats from each diet group remained sedentary and the other half undertook a training protocol. Biochemical analysis and fecal microbiota sequencing of the different groups showed that exercise attenuated HFD-induced metabolic syndrome and effectively counteracted HFD-induced microbial imbalance. Exercise preserved intestinal barrier integrity, which, in turn, prevented HFD-induced activation of the gut-liver axis and of downstream inflammatory pathways involved in NAFLD. These results support the use of physical exercise to prevent and manage childhood obesity and NAFLD development. **ALB**

<https://doi.org/10.1038/s41684-019-0360-4>

IMAGING

Mitochondria in motion

Wehnekamp, F. et al. *Elife* **8**, e46059 (2019)

A new study reports the development of a 3D orbital single particle tracking (SPT) microscope allowing the high-resolution spatiotemporal tracking of individual mitochondria in sensory neurons of zebrafish larvae. Analysis of the 3D trajectory of the moving mitochondria identified 5 five motional states (a fast and a slow directional motion state in both the anterograde and retrograde directions, and a stationary state) and showed that changes in directionality were more likely to occur after longer pauses. Future possible applications of this approach include the use of 3D SPT to link single organelle dynamics to physiological and pathological neuronal changes in vivo. **ALB**

<https://doi.org/10.1038/s41684-019-0361-3>