research highlights

IN BRIEF

STROKE

Modeling stroke in pigs

Castaño, C. et al. *JCI Insight* **8**, e163398 (2023)

Rodent models of ischemic stroke have been instrumental to study stroke pathophysiology, but new models, more representative of the human condition, are needed to identify novel therapies. Pig models have an important translational potential, but they usually require invasive surgical interventions to access and occlude the middle cerebral artery (MCA). A new study reports the development of a reproducible pig stroke model through a minimally invasive endovascular approach.

To create the model, the investigators introduced a guide catheter and guide wire through the femoral artery of the pigs and propelled an embolizing agent to occlude brain arteries up to the origins of MCA. The model induced a large cerebral infarction, neurological dysfunction and recapitulated some features of human stroke including the presence of specific blood biomarkers. *ALB*

https://doi.org/10.1038/s41684-023-01185-2

AGING

Strain and social rank affect the lifespan of stressed mice

Razzoli, M. et al. *Proc. Natl. Acad. Sci.* U S A **120**, e2211755120 (2023)

Individuals exposed to chronic psychosocial stress have a higher risk of disease and reduced life expectancy, but the underlying mechanisms are still unclear. A study in *PNAS* provides new insights into the factors influencing mouse survival under socially stressful situations.

Investigators exposed more than 300 male mice from three different strains (C57BL/6J, CD1, and Sv129Ev) to a lifelong chronic psychosocial stress protocol to analyze the effects of social ranking and strain on lifespan. They found that a low social status was generally associated with a shorter lifespan in mice, but this effect was modulated by the genetic background, notably in Sv129Ev in which a high social rank was associated with lower survival. Strain and social rank also affected DNA methylation in the mouse liver, indicating that epigenetic mechanisms might be linking social stress, genetic background, and affect individual biological age. *ALB*

https://doi.org/10.1038/s41684-023-01188-z

STROKE

Profiling mouse cerebral microvessels after stroke

Callegari, K. et al. *Proc. Natl. Acad. Sci. U S A.* **120**, e2205786120 (2023)

During ischemic stroke, cerebral artery occlusion leads to reductions in blood flow that cause not only neuronal death and glial activation but also extensive injury to the cerebral microvasculature. Stroke-induced cerebral microvascular dysfunction contributes to worsening stroke outcomes, and therapeutic strategies aiming at restoring vascular function after stroke could mitigate brain injury or improve stroke recovery

In a new study, researchers at Weill Cornell Medicine used a recently optimized method which preserves RNA integrity to profile the transcriptomic changes in mouse cerebral microvessels after stroke, and compared these changes to those observed in patients with stroke. They identified common alterations in mouse microvessels and human lesions after stroke, including changes in modulators of microvascular dysfunction, and sphingolipid metabolism and signaling. These results could guide the development of endothelial-targeted therapies to restore microvascular function after stroke. *ALB*

https://doi.org/10.1038/s41684-023-01186-1

REGENERATIVE MEDICINE

ERK regulates regeneration in spiny mice

Tomasso, A. et al. *Sci. Adv.* **9**, eadf2331 (2023)

While most mammals, including laboratory mice, heal injured tissues with scar tissue, spiny mice can completely regenerate several tissues in their body without scarring. This surprising property makes them a unique mammalian model for regenerative biology and medicine. A study in *Science Advances* provides new insights into the cellular and molecular processes driving regeneration in this species.

The researchers used an ear punch injury model to compare injury response in spiny mice and CD1 mice. They found that while both species showed an initial burst of ERK activation after injury, only spiny mice sustained ERK activation after 10 days. Further experiments revealed that ERK activation induced proliferative response in keratinocytes and stromal cells, and stimulated the expression of proregenerative components. Altogether these results suggest that ERK is a master regulator of tissue regeneration in spiny mice. *ALB*

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