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research highlights

IN BRIEF

REGENERATIVE MEDICINE

A new immunodeficient pig model

Itoh, M et al. *Nat. Commun.* **10**, 2244 (2019)

Recent developments in stem cell technology and tissue engineering have opened new avenues for regenerative medicine. Tissues and organs such as vascular grafts, liver, and myocardium have been successfully produced from human-derived cells and implanted in small animals. However, before translation to the clinics, human cell regeneration strategies need to be evaluated in large animals. A study describes a new mini-pig model in which an immunodeficient state was induced by removing the major immune organs and administering immunosuppressive therapy. This operational immunodeficient pig (OIDP) model enabled the long-term accommodation of an artificial human vascular graft that was rejected in a conventional immunosuppressive pig (CISP) model. OIDPs might become an invaluable tool for the evaluation of preclinical human cell regeneration strategies. **ALB**

<https://doi.org/10.1038/s41684-019-0339-1>

CELL THERAPY

Fetal cells repair the adult heart

Vadakke-Madathil, S et al. *Proc. Natl. Acad. Sci.* <https://doi.org/10.1073/pnas.1811827116> (2019)

The mammalian adult heart has a very limited regenerative capacity, which explains the high morbidity and mortality associated with cardiovascular disease. Cell therapy has emerged as an attractive strategy for cardiac repair, but the efficacy of this therapeutic option remains controversial. A new study using a mouse model of myocardial infarction shows that, after injection, Caudal-type homeobox-2 (Cdx2) fetal cells isolated from end-gestation placenta can home to the injured heart and differentiate into cardiomyocytes and blood vessels, resulting in improved cardiac contractility. Cdx2 cells, which also showed the potential to evade host immune surveillance, might therefore represent a promising new cell source for cell therapy for cardiac repair. **ALB**

<https://doi.org/10.1038/s41684-019-0340-8>

IMAGING

Zebrafish in 3D

Ding, Y et al. *Elife* **8**, e44898 (2019)

Histology is widely used to characterize the phenotype of a tissue, but the technique has several limitations that include tissue loss and distortion caused by the physical sectioning of the sample. A study presents a new synchrotron-based micro-tomography (micro-CT) method that generates 3D images for quantitative histological analysis of the whole zebrafish at the sub-micron resolution. The technique, which was optimized for soft tissue differentiation (histotomography), enables tissues and cell nuclei visualization across various organ systems, such as the hematopoietic, respiratory, musculoskeletal, gastrointestinal, cardiovascular, and nervous systems. The use of X-ray histotomography could be extended to generate whole-animal reconstructions of other organisms such as *Drosophila* or *C. elegans* and enable cross-species phenotypic analyses. **ALB**

<https://doi.org/10.1038/s41684-019-0341-7>

AGING

Stronger SIRT6, longer lifespan

Tian, X et al. *Cell* **177**, 622–638.e22 (2019)

The mechanisms responsible for the differences in maximum lifespan (MLS) between various mammals are unclear. Previous studies have shown that DNA repair mutants have accelerated aging phenotypes, suggesting that DNA repair is a longevity determinant. A new systematic analysis of DNA repair in primary fibroblasts isolated from 18 species of rodents with MLS ranging from 3 to 32 years shows that DNA double-strand break (DSB) coevolves with longevity. By showing that NAD-dependent protein deacetylase sirtuin-6 (SIRT6) promotes DSB repair and that differences in SIRT6 activity contribute to the variation in DSB repair efficacy between short-lived and long-lived species, the study provides new targets for anti-aging strategies. Further analysis showed that differences in five amino acids determine the differences in SIRT6 activity between mouse and beaver, two species with very different lifespans. **ALB**

<https://doi.org/10.1038/s41684-019-0342-6>