STEM CELLS

## Stem cells with potential

Gao, X. et al. *Nat. Cell Biol.* **21**, 687–699 (2019).

Expanded potential stem cells (EPSCs) can differentiate into extraembryonic and embryonic lineages. Culture conditions for establishing and maintaining murine EPSCs have been described, but the same conditions are not suitable for deriving human or porcine EPSCs. Gao et al. screened 400 combinations of small molecules and cytokines for their potential to inhibit differentiation in porcine induced pluripotent stem cells. A cocktail of GSK3, SRC and Tankyrase inhibitors along with vitamin C, activin A and LIF did the trick. This cocktail also allowed them to derive porcine EPSCs from pre-implantation embryos. After establishing these conditions, the researchers tested the cocktail on human embryonic stem cells and found that minor modifications were necessary in order for the cocktail to establish the expanded potential. The human EPSCs may be helpful in gaining a better understanding of embryonic development in humans. *NV*

https://doi.org/10.1038/s41592-019-0487-7

LAB-ON-A-CHIP

## In vitro intestine model for gut microbiome

Jalili-Firoozinezhad, S. et al. *Nat. Biomed. Eng.* https://doi.org/10.1038/s41551-019-0397-0 (2019).

Recent studies of human gut microbes and their interactions with hosts have uncovered their key roles in human health and disease. These studies have relied mainly on metagenomic analysis of in vivo samples. In vitro models that mimic the complex gut environment are still needed. Jalili-Firoozinezhad et al. introduced an intestine-on-a-chip that integrates intestinal endothelium, epithelium, a mucus layer, and gut microorganisms, as well as two microscale oxygen sensors, into a microfluidic organ-chip device. The integration of oxygen sensors allows in situ measurement and control of oxygen levels, thus creating a physiologically relevant oxygen gradient across the endothelium–epithelium–microbiome interface. The hypoxic intestine-on-a-chip supports more bacterial diversity than aerobic chips or conventional liquid culture, and thus better reflects the abundance pattern of human intestinal microbiota. Ultimately, researchers aim to offer patient-, disease-, or organ-specific host-microbiome models for personalized medicine. *LT*

https://doi.org/10.1038/s41592-019-0489-5

STRUCTURAL BIOLOGY

## Graphene-on-gold grids for cryo-EM

Naydenova, K. et al. *Proc. Natl Acad. Sci. USA* **116**, 11718–11724 (2019).

Solutions of proteins and biomolecular complexes to be studied by single-particle cryo-electron microscopy (cryo-EM) are applied to a metal grid that is then rapidly frozen. Such metal grids are typically coated with a thin carbon film to encourage proteins to stick, but standard grids are subject to contamination and movement during imaging, which can compromise data quality. Naydenova et al. now report a method to coat gold grids with a monolayer film of graphene. This choice of cryo-EM support has near-ideal properties: gold grids are very stable, showing little movement during imaging in an electron beam. The graphene monolayer provides a conductive material that is invisible in the resolution range for cryo-EM and also provides a functionalizable surface to optimize the protein-orientation distribution. Using 30S ribosomal subunit and apoferritin test samples, the researchers demonstrate that the graphene-on-gold grids are compatible with high-resolution cryo-EM structure determination. *AD*

https://doi.org/10.1038/s41592-019-0488-6

IMMUNOLOGY

## Looking at xenografts in zebrafish

Yan, C. et al. *Cell* **7**, 1903–1914.e14 (2019).

Researchers routinely transplant human cancer cells into immunocompromised mice to study tumor growth and metastasis. However, following the transplanted cells over time is not straightforward in mice, especially at single-cell resolution. Instead, Yan et al. use immunodeficient, transparent zebrafish to visualize xenografted cells. *Prkdc*$^{-/-}$*Il2rga*$^{-/-}$ zebrafish lack both an adaptive immune system and NK cells, and the *Casper* background makes the fish transparent. The researchers transplanted cells from 16 different cancer cell lines, as well as xenografts from six human subjects, into these fish and were able to obtain tumor-bearing zebrafish in all cases. The transparent nature of the fish allowed them to monitor individual tumor cells over time and analyze their behavior. The zebrafish model also made it possible to study the effects of drugs alone and in combination on xenografted cells. *NV*

https://doi.org/10.1038/s41592-019-0485-9

Allison Doerr, Nicole Rusk, Rita Strack, Lei Tang and Nina Vogt