MICROSCOPY

Absorption-based multicolor imaging

Garbacik, E. T. et al. *Biophys. J.* https://doi.org/10.1016/j.bpj.2018.07.008 (2018).

Multiplexed imaging can be crucial for the study of molecular processes in their proper context. However, the number of colors that can be imaged in a given sample is typically limited by the number of fluorophores whose emission spectra can be clearly distinguished. Garbacik et al. introduce a method for multicolor imaging that, unlike most methods, makes use of differences in fluorophore absorption spectra rather than emission spectra. In this method, samples are illuminated with multiple excitation wavelengths, and emission is detected with a single color-blind detector. Colors are then discriminated on the basis of the emission intensity at different excitations. The researchers demonstrated their approach by carrying out simultaneous three-color confocal imaging of cells and show that by implementing a spectral unmixing algorithm they could resolve six colors using four excitation wavelengths. *RS*

https://doi.org/10.1038/s41592-018-0126-8

SENSORS AND PROBES

Improved photoacoustic imaging probes

Li, L. et al. *Nat. Commun.* **9**, 2734 (2018).

Photoacoustic imaging (PAI) has emerged as a powerful method for sensitive and high-resolution imaging in vivo, but the development of genetically encoded probes for PAI has lagged behind that for fluorescence imaging. Li et al. report the engineering of a photoswitchable near-infrared fluorescent protein for improved photoacoustic computed tomography (PACT). The protein, DrBphP-PCM, is based on bacterial DrBphP but is an improvement over that phytochrome in that it is smaller, folds better, and gives higher photoswitching contrast. The researchers showed that DrBphP-PCM outperforms DrBphP for imaging deep within the mouse brain and can be used in multiplexed PACT. They also used DrBphP-PCM as the basis for a split version of the protein, termed DrSplit, which enabled the detection of protein–protein interactions deep within tissues. These new probes should provide versatile tools for deep-tissue imaging. *RS*

https://doi.org/10.1038/s41592-018-0127-7

STEM CELLS

Three tissues to gastrulation

Sozen, B. et al. *Nat. Cell Biol.* **20**, 979–989 (2018).

The ability to recapitulate early mammalian embryogenesis in a culture dish would give unprecedented access to study development and disease. Although the embryo is derived from one tissue, the epiblast, it cannot develop without extraembryonic tissue interactions. The Zernicka-Goetz group previously showed that coculture of mouse embryonic stem (ES) cells with trophoblast stem (TS) cells (placenta progenitors) in extracellular matrix leads to the spontaneous generation of structures with two compartments that closely resemble natural embryos. These synthetic 'ET' embryos form a preamniotic cavity, but fall short of specifying mesoderm and initiating gastrulation. In their new work, Sozen et al. develop conditions for coculturing of ES and TS cells with extraembryonic endoderm (XEN) cells (yolk sac progenitors). Remarkably, even in the absence of matrix, the resulting 'ETX' embryos go on to specify mesoderm and a XEN-derived visceral endoderm-like tissue. ETX embryos have morphology and gene expression resembling that in the mid-gastrula stage, and highlight the dramatic self-organizing capacity of the embryo. *TN*

https://doi.org/10.1038/s41592-018-0128-6

STEM CELLS

Organoid hosts for parasitic infection

Heo, I. et al. *Nat. Microbiol.* **3**, 814–823 (2018).

Disease modeling can be difficult with obligate parasites because of their complex life cycle requirements. The parasite *Cryptosporidium* is responsible for a potentially fatal diarrheal disease known as cryptosporidiosis, which takes a significant toll on the health of infants in developing countries. Heo et al. show that small intestinal and lung organoids derived from healthy human donors can be used as models for *Cryptosporidium* infection. Differentiated intestinal organoids microinjected with oocysts supported the entire life cycle of the parasite in long-term and serial infections. Organoids cultured under conditions that produce less differentiation are less susceptible to infection. Bronchial airway organoids also support infection, thus allowing closer inspection of the poorly studied lung epithelial infection route. These new models will help to unravel *Cryptosporidium* biology and cell–microbe interactions. *TN*

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