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How to edit the epigenome
Programmable nucleases are proving very useful not only for altering DNA sequences but also for modulating the epigenetic landscape. For example, they can influence transcription by targeting effector proteins to specific loci in order to add or remove histone modifications or DNA methylation. Gersbach and colleagues discuss recent technologies for epigenome editing via DNA-binding domains of zinc fingers, transcription activator-like effectors or Cas9 fused to different effector domains. The Review explores the specificity of these tools and how to increase it with inducible components. It describes the tools’ applications to transcriptional activation and repression, chromatin organization, the design of gene regulatory networks, cellular reprogramming and disease treatment.

Review p127

Lung-on-a-chip
The human lung is a complicated organ, susceptible to a number of disorders that cannot easily be studied in vitro. Animal models of chronic diseases such as asthma and chronic obstructive pulmonary disease (COPD) exist but are of questionable relevance, as immune system and inflammatory responses differ greatly between mice and humans. Ingber and colleagues reconstructed functional human small airways by growing primary airway epithelial cells and lung microvascular endothelial cells in a microfluidic device. They succeeded in modeling asthma and lung inflammation and measured the effect of viral infection on COPD-derived small airways. The organ-on-a-chip lends itself to screening of drugs that could suppress inflammation associated with infection.

Article p151

Tools for manipulating zebrafish neurons
Genetic tools for activating or inhibiting neurons are invaluable for unraveling the mechanisms that govern behavior in animals. Optogenetic approaches have been popular, but the necessary illumination of the animals can have unwanted behavioral consequences. Prober and colleagues have established orthogonal methods for neuronal manipulation in freely behaving zebrafish that do not involve light. The researchers ectopically expressed different transient receptor potential (TRP) channels that respond to capsaicin, menthol or increased temperature in the neurons under study. Depending on the agonist and its concentration, the manipulation led to either neuronal activation or ablation. The researchers expressed these TRP channels in sensory neurons to explore effects on locomotion and neural activity in zebrafish larvae. The tools could also be used to manipulate neurons in the hypothalamus, leading to behavioral effects on locomotion and sleep.

Brief Communication p147

An inverted light-sheet microscope for imaging embryogenesis
Visualizing and tracking the fates of individual cells during embryogenesis can yield crucial insight into this fundamental process. Ellenberg and colleagues have developed an inverted light-sheet microscope system for imaging embryogenesis that allows mouse pre-implantation embryos to be grown in standard culture conditions. This setup allows for multicolor imaging of embryogenesis with an order of magnitude less light than used in conventional approaches, and it enabled the first imaging of pre-implantation embryos from the zygote to the blastocyst stage. Analysis of the data with improved cell-tracking algorithms revealed novel findings on cell specification. This inverted light-sheet setup has the potential to yield important information on early mouse development.

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