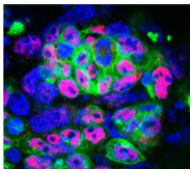
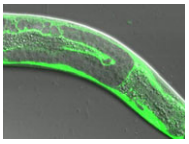


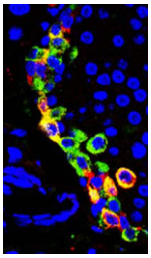
Stem cells: from EpiSCs come PGCs

Distinct pluripotent stem cells can be generated from different mouse embryonic cell types: embryonic stem cells (ESCs) from the inner cell mass (ICM); epiblast stem cells (EpiSCs) from the ICM-derived epiblast; and embryonic germ cells (EGCs) from primordial germ cells (PGCs). Since PGCs originate from the epiblast in vivo, what is the relationship between EpiSCs and PGCs? On p. 3549, Katsuhiko Hayashi and Azim Surani now report that EpiSCs can generate unlimited amounts of PGCs. By monitoring the expression of a *Blimp1* (the key PGC determinant) reporter transgene in EpiSCs, they show that self-renewing EpiSCs, unlike ESCs, spontaneously generate a continuous stream of PGCs, some of which differentiate into oocyte-like cells when co-cultured with female gonadal cells. These PGCs can also de-differentiate into pluripotent cells that resemble EGCs rather than EpiSCs, indicating that the epigenetic memory of the EpiSCs and PGCs has been erased. As mouse EpiSCs resemble human ESCs, this study could provide an inroad into studying both early human and mouse germ cell development.



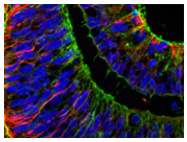
NAD$^+$ your average developmental signal

The co-enzyme nicotinamide adenine dinucleotide (NAD$^+$) is found in all living cells and serves as an electron shuttle. NAD$^+$ consumer enzymes hydrolyse NAD$^+$ to nicotinamide; this is recycled to NAD$^+$ via the NAD$^+$ salvage pathway, which differs between vertebrates and invertebrates. Now, on p. 3637, Wendy Hanna-Rose and colleagues reveal, for the first time, a developmental role for components of this well-studied pathway. They show that the *C. elegans* nicotinamidase PNC-1, the first enzyme in the worm NAD$^+$ salvage pathway, is required for normal reproductive development, with *pnc-1* mutant animals showing delayed gonad development and egg-laying defects. Interestingly, the gonad defects are caused by the lack of NAD$^+$, but the egg-laying defects by nicotinamide accumulation, indicating that both substrate and product levels are important biologically. Furthermore, the researchers find that the mouse functional equivalent of PNC in the NAD$^+$ salvage pathway, Nampt, can rescue *pnc-1* mutants. Together, these findings indicate for the first time that NAD$^+$ salvage pathway components might have evolutionarily conserved developmental functions.



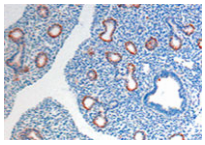
Pancreatic endocrine progenitors adopt single fate

Pancreatic islets contain several different types of hormone-producing (endocrine) cells, damage to which can lead to disease, such as diabetes. During embryonic development, all pancreatic endocrine progenitor cells express the transcription factor Ngn3, but do individual Ngn3$^+$ progenitors give rise to multiple endocrine cell types or only to one? The answer, claim Desgraz and Herrera, is the latter (see p. 3567). Using a genetic system called MADM, the researchers generated transgenic mosaic mice in which very few Ngn3$^+$ cells are fluorescently labelled, and then traced the fate of individual Ngn3$^+$ cells. They found that at birth, each Ngn3$^+$ cell had turned into a single endocrine cell. In adult mice, small homogeneous clusters of Ngn3$^+$-derived labelled cells exist, which indicates low cell proliferation. These findings suggest that the Ngn3$^+$ progenitors are heterogeneous, as they are unipotent but give rise to multiple cell types, and showcase the potential of MADM for investigating cell fate specification events in vivo at the single-cell level.



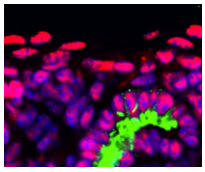
Filopodia hold lens and retina together

In the developing mouse eye, the presumptive lens and retinal epithelia stay in close contact whilst undergoing a coordinated indentation movement known as invagination. The mechanisms that underlie this invagination event have remained mysterious, although cytoplasmic processes between the two epithelia were described as early as 1902. Now, on p. 3657, Richard Lang and colleagues identify filopodia as being the processes present between these two epithelia, extending mainly from the presumptive lens. Their formation, they report, depends on Cdc42, IRSp53 and FAK, three molecules previously implicated in filopodia generation and anchoring. Using pharmacological inhibitors, the authors reveal that the filopodia can contract through the actin-myosin system and that this contractility regulates the distance between lens and retinal epithelia, as well as the depth of the lens pit. They conclude that the filopodia act as physical tethers that allow lens and retinal invagination to proceed in a coordinated fashion. Future work should address whether this mechanism of invagination occurs elsewhere during vertebrate morphogenesis.



MicroRNA creates giants through paramutation

Mammalian body size is regulated by both genetic and environmental factors. Minoo Rassoulzadegan and colleagues now add to this list a heritable epigenetic mechanism (paramutation) that results in increased body size (see p. 3647). When injecting the microRNA *miR-124*, which is normally expressed in the central nervous system, into fertilised mouse eggs, the researchers found an unexpected 30% increase in body size of the resulting mice, which persisted into adulthood. Interestingly, this increased growth was evident very early in development, with frequent blastocyst inner cell mass duplications causing a rise in twin pregnancies. The progeny of *miR-124*-injected males inherited the increased body size; this inheritance correlated with the presence of *miR-124* in the sperm. The researchers identified a candidate *miR-124*-induced paramutation in the form of a heritable chromatin modification in *Sox9*, which encodes a transcription factor involved in regulating embryonic proliferation and differentiation. From their findings, they propose that RNA-mediated paramutations might contribute to other heritable traits that Mendelian genetics cannot explain.



BMP7 signals through JNK in nephron progenitors

Nephrons, the basic filtering units of the mammalian kidney, are generated in the so-called nephrogenic zone (NZ) of the developing kidney over several days. This means that nephron progenitor cells must be replenished while new nephrons differentiate, a balance that depends on the growth factor BMP7, but not on the canonical BMP7-triggered response, SMAD-mediated transcriptional activation. Leif Oxburgh and co-workers now report that in mouse nephron progenitors, BMP7 induces Jun N-terminal kinase (JNK) signalling instead (see p. 3557). The researchers developed a novel cell culture system to study isolated NZ cells and demonstrate that these cells, like NZ cells in vivo, are unresponsive to SMAD-mediated signalling. Rather, they rapidly activate JNK signalling in response to BMP7, and BMP7 promotes their proliferation. Correspondingly, JNK signalling is disrupted in *Bmp7*-null kidneys in vivo. Together, these data suggest that BMP7 promotes nephron progenitor proliferation by directly activating JNK signalling and establish a new experimental system for investigating nephrogenesis.