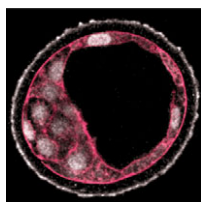


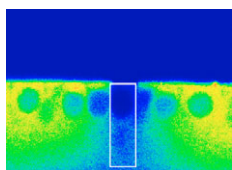
Heparanase releases and primes FGF10 for action

Heparan sulfate (HS) proteoglycans (for example, perlecan) are involved in many developmental processes, particularly those regulated by fibroblast growth factors (FGFs). HS regulates FGF activity by acting as an FGF co-receptor at the cell surface and as an FGF reservoir in the extracellular matrix. FGF10 signalling is critical for salivary gland development in mammals and now, on p. 4177, Matthew Hoffman and colleagues report that the cleavage of perlecan by heparanase modulates FGF10 activity during branching morphogenesis in the mouse submandibular gland (SMG). They show that the inhibition of heparanase in organ culture decreases SMG branching and that the addition of FGF10, but not other FGFs, rescues branching. Heparanase, they report, releases FGF10 from the basement membrane, where it binds to perlecan. Importantly, the HS fragment that heparanase releases from perlecan also increases FGF10's bioactivity, which increases branching complexity in the SMG. Thus, heparanase, by releasing an HS fragment and FGF10 from the basement membrane, plays a key role in salivary gland development.



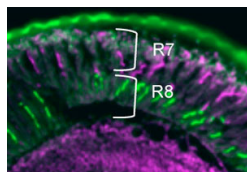
Pre-implantation patterning by chance?

During pre-implantation mammalian development, a blastocyst forms that contains three distinct cell types: trophoblast (which gives rise to the placenta) and the primitive endoderm and epiblast (which together form the inner cell mass from which the fetus develops). But does blastocyst patterning originate in the egg (the pre-patterning model) or do differences between blastomeres only appear after the 8-cell stage of embryonic development (the regulative model)? On p. 4219, Dietrich and Hiiragi now provide evidence that patterning in pre-implantation mouse embryos involves stochastic (random) processes. To identify the critical events in blastocyst patterning, the researchers analyzed the expression of Oct4, Cdx2 and Nanog (three transcription factors that help to specify the blastocyst lineages) at precisely defined times during pre-implantation development. Their results lead them to propose a regulative model for blastocyst patterning in which the first lineages in the early mouse embryo emerge after the 8-cell stage as a result of random processes and/or of earlier asymmetric cell divisions.



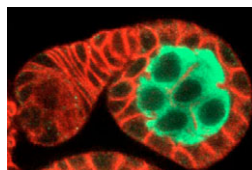
Nuclear ins and outs of Dorsal gradients

The dorsoventral axis of the *Drosophila* embryo is specified by a ventral-to-dorsal concentration gradient of the NF- κ B/REL transcription factor Dorsal in the nuclei of the syncytial embryo. This gradient's formation involves the nuclear import of cytoplasmic Dorsal in response to an extracellular signal. Now, Robert DeLotto and colleagues report that the maintenance of the gradient is actually a dynamic process that also involves the Exportin 1-mediated nuclear export of Dorsal (see p. 4233). Using real-time, live imaging of embryos that express a Dorsal-GFP fusion protein, the researchers show that nuclear Dorsal concentrations change continuously during interphase and that the Dorsal gradient breaks down and reforms with every mitotic division. Dorsal, they report, constantly shuttles in and out of the nuclei during interphase. Furthermore, its diffusion is partly constrained to cytoplasmic domains around each syncytial nucleus. The researchers propose, therefore, that the generation and maintenance of the Dorsal gradient during fly embryogenesis involves both restricted long-range diffusion and the regulated nucleocytoplasmic shuttling of Dorsal.



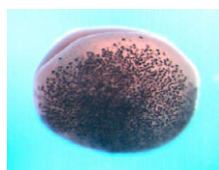
A Senseless but colourful switch

Different specialized cell types arise from common progenitors many times during development. In the *Drosophila* eye, for example, the different subsets of photoreceptor cells (PRs) needed for colour discrimination arise from the R7 and R8 neuronal precursors. Xie and co-workers now report that the transcription factor Senseless (Sens) acts as molecular switch for PR differentiation in *Drosophila* (see p. 4243). Recent studies have shown that the transcription factor Prospero (Pros) represses R8-related characteristics in R7-based PRs. Xie et al. now extend these studies by showing that *sens* can both induce R8-like characteristics and repress R7-related features in terminally differentiating PRs in vivo. They also show that Pros and Sens function with the transcription factor Orthodenticle to oppositely regulate the expression of R7- and R8-specific rhodopsins in vitro. Since *pros* and *sens* are expressed in similar but distinct cell types in many developing tissues, antagonistic *pros/sens* regulation of gene expression may help to create cellular diversity in many developmental contexts.



GSCs and the Argonautes

Germline stem cells (GSCs) in the *Drosophila* ovary are an excellent model system in which to study the mechanisms that regulate stem cell maintenance and differentiation. Now, on p. 4265, Yang and co-workers report that Argonaute 1 (AGO1), a protein that is involved in small-RNA-mediated gene regulation, controls the fate of *Drosophila* GSCs. Piwi, another Argonaute protein, helps to maintain GSCs by silencing *bag of marbles* (*bam*), a gene that is required for GSC differentiation, but do other Argonaute proteins play similar roles? The researchers report that the overexpression of *Ago1* leads to GSC overproliferation, whereas its loss causes a reduction in GSC numbers. This result, together with an analysis of the fate of germline clones that lack a functional *Ago1* gene, suggests that an AGO1-dependent miRNA pathway probably plays an instructive role in repressing GSC differentiation. Finally, the researchers show that some GSCs partly differentiate in *Ago1 bam* double mutants, which suggests that AGO1 (unlike Piwi) might regulate GSC fate in a *bam*-independent manner.



Polarity proteins seal cell fate

Cell polarity is thought to generate cell fate diversity through asymmetric cell divisions, but which components of polarized cells convert polarity information into cell fate determination? On p. 4297, Sergei Sokol and co-workers report that the answer in *Xenopus* epidermal ectoderm is the conserved polarity proteins atypical protein kinase (aPKC) and partitioning-defective 1 (PAR1). Early asymmetric divisions in *Xenopus* embryos produce superficial (apical) and deep (basal) ectodermal layers. These contain superficial epidermal cells and ciliated cells, respectively. In gain- and loss-of-function studies, the researchers show that aPKC, which is localized to the apical domain of the superficial cells, inhibits ciliated cell differentiation and promotes superficial cell fates. aPKC, they report, phosphorylates PAR1 and targets it to the basolateral domain of the superficial cells and PAR1, they show, stimulates ciliated cell differentiation and inhibits superficial epidermal cell fates, possibly through Notch signalling. This aPKC/PAR1 pathway, the researchers suggest, may link cell polarity to cell fate determination in epithelial tissues in many species.

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