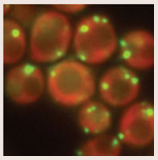
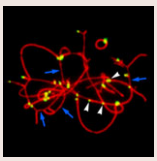
In this issue



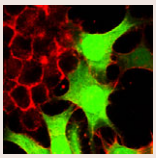
Turning up the heat on stress granules

Eukaryotic cells form various mRNA-containing assemblies in response to environmental stress. These include stress granules (SGs), which contain the translation initiation factor eIF3 and small ribosomal subunits, and P-bodies, which share some components with SGs but specifically contain mRNA decapping and deadenylating complexes. The formation of SGs has primarily been studied in mammalian cells, but Jiří Hašek and colleagues (p. 2078) now investigate their formation in the budding yeast *Saccharomyces cerevisiae*. The authors subject yeast to robust heat shock, and report the energy-dependent formation of cytoplasmic accumulations (putative SGs) that contain several typical components of mammaliam SGs, including the initiation factor eIF3a and the small ribosomal subunit. The yeast SGs also colocalise with typical P-body proteins and, in contrast to mammalian SGs, they can form in the absence of eIF2α phosphorylation. Notably, heat-shock-induced SGs differ in their composition from SGs that have recently been reported to form in glucose-deprived *S. cerevisiae* [Buchan et al. (2008). *J. Cell Biol*. 183, 441-455], and the authors also show that different scaffolding proteins are required in heat-shock- and glucose-deprivation-induced SGs. Their results underscore the diverse composition of mRNA-containing assemblies in *S. cerevisiae*.



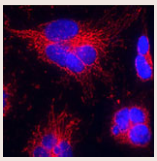
Meiosis: CDK2 keeps it together

Along with its well-established role in mitotic progression, the cyclin-dependent kinase CDK2 has recently been shown to be important during gametogenesis – *cdk2*$^{-/-}$ mice are infertile (although otherwise viable) and spermatocytes in male mice arrest during meiotic prophase I. Little has been known, however, about the details of CDK2's meiotic role. Now, José A. Suja and colleagues (p. 2149) analyse meiotic progression in spermatocytes of *cdk2*$^{-/-}$ mice, and show that homologous chromosomes pair (synapse) incompletely – notably, however, the synaptonemal complexes and cohesin complexes (both of which connect homologous chromosomes) form normally in these mice. In addition, synapsis occurs extensively between non-homologous chromosomes. The authors next show that, in spermatocytes lacking CDK2, meiosis arrests at a pachytene-like stage (when recombination between homologous chromosomes normally occurs) and chromosomes fail to recombine fully; instead, unrepaired double-strand breaks accumulate. Finally, the authors note that some telomeres do not attach to the nuclear envelope in *cdk2*$^{-/-}$ spermatocytes, and sex chromosomes fail to form a sex body. Thus, they conclude, CDK2 has a role in ensuring accurate homologous pairing and recombination during mammalian meiosis. These data expand the functional repertoire of CDKs.



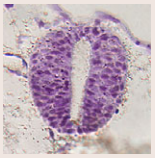
Rac3 rounds it up

Despite their high degree of similarity, the Rho GTPases Rac1 and Rac3 have opposing effects on neuronal morphology and differentiation – Rac1 induces cell spreading and neuritogenesis, but Rac 3 promotes cell rounding and prevents differentiation. On page 2127, John Collard and colleagues report new findings on the protein-protein interactions of Rac3 that help to explain these striking functional differences. Using a neuroblastoma cell line, the authors show that Rac3 (like Rac1) interacts with GIT1, a scaffolding protein that also acts as an Arf GTPase-activating protein (GAP) and has roles in cell adhesion and spreading. In contrast to Rac1, however, the Rac3-GIT1 interaction is not mediated by βPix (which interacts with GIT1). Moreover, Rac3 disrupts the interaction between GIT1 and the focal-adhesion protein paxillin (which is stimulated by Rac1). Notably, the authors show that Rac3-induced cell rounding results from the GIT1-dependent inactivation of the GTPase Arf6, and that expressing Arf6 or its activator ARNO restores spreading in Rac3-expressing cells. On the basis of their data, the authors propose that Rac1 and Rac3 oppose each other by differentially modulating GIT1 function. This work sheds light on the mechanism of neuronal differentiation.



Growing and dividing with IQGAP1

In proliferating cells, growth and division must be tightly coupled to ensure that cells maintain an appropriate size. However, many of the key proteins that maintain this coordination remain to be identified. On page 2024, Mahasin Osman and colleagues present evidence that IQGAP1 – a Cdc42 effector that has been implicated in human cancer and in exocytosis regulation – integrates cell growth and cell-cycle progression. The authors first show that expression of the C-terminal region of IQGAP1 (IQGAP1-C) promotes the proliferation and migration of cells in culture and reduces cell size. Moreover, they demonstrate that IQGAP1 phosphorylation at a residue in the C-terminus, as well as an interaction between IQGAP1 and Cdc42, are necessary for cell transformation. By contrast, the N-terminal region of IQGAP1 inhibits cytokinesis, increases cell size and impairs transformation and migration. Importantly, the N-terminus of IQGAP1 interacts with mTOR (a key cellular nutrient sensor), and this interaction is necessary for IQGAP1-mediated cell proliferation. The authors propose, therefore, that IQGAP1 acts as a phosphorylation-sensitive switch, and coordinates cell growth and division through its interactions with mTOR and Cdc42, respectively.



Hinges and (Zn) fingers in neurulation

During neural-tube (NT) formation in mammals and birds, newly formed neural folds bend inwards at dorsolateral hinge points (DLHPs) before fusing to close the NT. The mechanism of DLHP formation is not well understood, although it is known to require the zinc-finger transcription factor Zic2 and an apical actomyosin network. Now, Molly Nyholm and colleagues (p. 2137) investigate the role of zic genes during neurulation in zebrafish (in which DLHPs also form, albeit after NT closure). The authors create morphants of *zic2a* and *zic5*, and show that both proteins are required for DLHP formation; moreover, the ventral *zic2a* expression border predicts where DLHPs will form. *zic2a* and *zic5*, they show, are required for the apical localisation of actomyosin components (F-actin and active myosin II) and for the integrity of apical cell-cell junctions. They go on to demonstrate that canonical Wnt signalling (which activates zic gene transcription) is necessary for DLHP formation, localisation of active myosin II and junctional integrity. The authors conclude that zic genes act downstream of Wnt signalling to control cytoskeletal organisation during neurulation, and argue that zebrafish is a valuable model organism for studying mammalian NT formation.

Development in press

β-catenin and dopaminergic differentiation

The loss of dopaminergic (DA) neurons is a hallmark of Parkinson's disease (PD), a common human neurodegenerative disorder. Stem-cell replacement therapy is a promising strategy for alleviating PD, but is currently limited by the difficulty of generating large numbers of DA neurons. Now, in a paper published in *Development*, Eric Huang and co-workers reveal that several stages of DA neurogenesis depend on β-catenin. The authors show, using conditional gene knockout approaches, that regional deletion of the gene encoding β-catenin in the neurogenic niche of the mouse ventral midbrain (which gives rise to DA progenitors) disrupts progenitor-cell adherens junctions and radial glial cell integrity. This leads to reduced DA neurogenesis and defects in DA neuron polarity, migration and segregation. By contrast, removing β-catenin from DA neural progenitors reduces DA neurogenesis by impairing the later progression of committed progenitors to DA neurons. From these findings, the authors suggest that β-catenin-mediated regulation of DA differentiation could be exploited for the development of cell-based therapies for PD.

Tang, M., Miyamoto, Y. and Huang, E. J. (2009). Multiple roles of β-catenin in controlling the neurogenic niche for midbrain dopamine neurons. *Development* **136**, 2027-2038.