Plasmodium falciparum. For example, HbC – in which substitution of lysine for glutamate at position 6 of the β-chain accelerates the oxidation of Hb to insoluble hemichromes – reduces the risk of developing severe malaria in homozygous individuals. On p. 1091, James Dvorak and colleagues report that this protection may result from HbC’s effects on the clustering of host erythrocyte membrane band 3. This protein normally exists as dimers in erythrocyte membranes but forms larger clusters when hemichrome is deposited below the membrane during erythrocyte senescence or a P. falciparum infection. Autoantibody recognition of these clusters targets the erythrocyte for destruction. When the authors used a quantum dot technique to determine the surface distribution of band 3 molecules on P. falciparum-infected erythrocytes, they found more and larger clusters on HbC homozygous erythrocytes than on normal erythrocytes. They conclude that increased band 3 clustering may enhance autoantibody recognition sites and thereby help HbC to protect against malaria.

Errant chaperone in Bardet-Biedl syndrome

So far, eight genes have been linked to Bardet-Biedl syndrome (BBS), a human disorder characterised by obesity, retinal degeneration, kidney dysfunction and other ailments. MKKS/BBS6, which is also mutated in the developmental disorder McKusick-Kaufman syndrome, is among the least understood of the BBS-linked proteins, but now Michel Leroux and co-authors report that MKKS/BBS6 is a divergent group-II-chaperonin-like protein that is required for cytokinesis (see p. 1007). They show that BBS6 evolved recently from a subunit of CCT, the eukaryotic cytosolic chaperonin. However, unlike chaperonins, BBS6 resides mostly within the pericentriolar material, and its localization is disrupted by disease-linked mutations within its apical domain. The authors provide evidence for a centrosomal role for BBS6 by showing that knocking down BBS6 causes cytokinesis defects. Finally, because BBS6 is enriched in tissues containing ciliated cells, the authors propose that, like other BBS proteins examined, BBS6 may have a basal body/ciliary function that, when lost through mutation, causes Bardet-Biedl syndrome.

Bone growth: the integrin connection

Most mammalian skeletal bones are formed by endochondral ossification – the replacement of a cartilaginous mould by bone. Cartilage development depends on the integrin-mediated interaction of the collagen-forming chondrocytes with the surrounding extracellular matrix. α10β1 is the major integrin mediating this interaction and mice lacking β1 integrin develop severe bone defects. Surprisingly, Reinhard Fässler and colleagues now report that mice lacking α10 integrin exhibit only slightly retarded growth of the long bones, which is caused by mild defects in the growth plate, a specialized structure in long bones that is responsible for linear bone growth (see p. 929). These defects include abnormalities in chondrocyte arrangement, shape and proliferation. In addition, the density of the collagen fibrillar network in these mice is reduced compared with that in normal mice. The authors conclude that integrin α10β1 is important but not essential for endochondral ossification, presumably because other collagen-binding integrins, such as α2β1, compensate for its loss, something that cannot happen in β1-integrin-null mice.

Ste20 relative gets the Nak of polarity

The shape of individual cells, which contributes to the final form of multicellular organs and tissues, is controlled by polar growth, which is itself regulated by the microtubule and actin cytoskeletons. On p. 1033, Klaus Leonhard and Paul Nurse report that the Ste20-related protein kinase Nak1/Orb3 polarizes the actin cytoskeleton of fission yeast during the cell cycle. The cylindrical cells of fission yeast grow from F-actin-rich tips at opposite ends of the cell. At the onset of mitosis, F-actin relocates to the medial ring of the cell, where it regulates cytokinesis. The authors show that inactivation of Nak1/Orb3 in a temperature-sensitive orb3 mutant disrupts the normal cell-cycle-dependent pattern of F-actin localization and produces orb-shaped fission yeast cells that fail to separate after mitosis. They also describe how the localization of Nak1/Orb3 normally changes during the cell cycle and propose that the periodic phosphorylation of Nak1/Orb3 may control its localization, thereby coordinating the reorganization of the actin cytoskeleton and the regulation of cell separation with cell-cycle progression.

Transcription before decondensation

It is generally accepted that for genes to become transcriptionally active the chromatin surrounding them has to decondense. However, this proposal is supported only by data from systems in which foreign promoters drive gene expression. Now, Peter Shaw and co-workers describe the induction of large-scale chromatin decondensation in two transgenic wheat loci under the control of their normal, developmentally regulated promoter (see p. 1021). The storage protein glutenin is expressed in the endosperm of the developing wheat grain. The authors use fluorescence in-situ hybridization and confocal imaging to examine two transgenic wheat lines containing about 20 or 50 copies of the genes encoding two glutenin subunits together with their promoters. Each transgene locus is visible as one or two condensed foci in tissues where glutenin is not transcribed but decondenses extensively into many foci upon activation of transcription. Unexpectedly, the authors find that the initiation of transcription can precede extensive decondensation but not vice-versa. Future experiments should determine the DNA and/or chromatin modifications that underlie these changes in higher chromatin order.

Development in press

Ploughing a straight furrow

Precise changes in plasma membrane shape underlie many morphogenetic processes. During the cellularisation of Drosophila embryos, furrow canal formation – a specialised process of membrane invagination – and actin cytoskeleton reorganisation ensure the nuclei of the syncytial blastoderm become enclosed to generate distinct cells. In a paper published in Development, Großhans and colleagues report that the guanine-nucleotide-exchange factor RhoGEF2 and the formin Diaphanous (Dia) play crucial roles in regulation of the position, shape and stability of the furrow canal by controlling actin filament assembly. Both proteins normally localise to the invagination site before furrow formation. The authors show that RhoGEF2 and dia mutant embryos have enlarged furrows and that F-actin levels at the furrow canal are reduced in these mutants. Because RhoGEF2 and Dia appear to act in a pathway parallel to that involving Nullo and Sry- or (early furrow canal markers that are involved in junction formation) these two pathways might control complementary aspects of furrow canal formation.