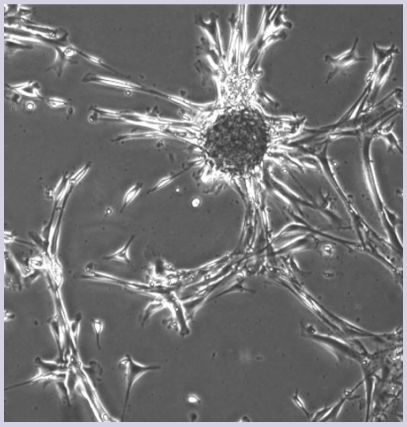

Patient-cell-based model for brain diseases

Identifying the cellular and molecular defects that underlie brain diseases has been limited by the lack of appropriate models. Matigian et al. describe a new model based on cells of the human olfactory mucosa, the organ of smell, that can be used to identify disease-specific changes in cellular processes and in gene and protein expression. They report both known and novel alterations associated with schizophrenia and Parkinson's disease, and it is likely that the model can also be applied to investigate defects underlying other brain diseases. *S.A.*

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All reseach articles are freely accessible online.

Altered axonal microtubule dynamics in neuronal dysfunction

Mutations in the *SPAST* gene are a frequent cause of hereditary spastic paraplegias, which are incurable neurodegenerative disorders characterised by progressive weakness and spasticity of the legs. Using the zebrafish CNS as a model system, Butler et al. show that *SPAST* is a crucial regulator of nerve fibre outgrowth, through its role in controlling microtubule dynamics and growth-cone motility. *K.W.*

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Modelling EPO-deficient anemia in mice

Patients with chronic kidney disease (CKD) suffer from anemia characterised by low erythrocyte counts and reduced serum erythropoietin (EPO). Recombinant human EPO is an approved treatment for CKD patients with anemia, but treatment with this biologic has several caveats, and there has been a lack of experimental models in which new treatments can be tested. Zeigler et al. now report on a new *Epo* conditional-knockout mouse with a moderate anemic phenotype that recapitulates that of CKD patients. Because these mice do not exhibit the abnormal kidney function or inflammation observed in CKD patients, this will be a useful model for studying erythropoiesis under EPO-limiting conditions in the absence of secondary complications. *S.A.*

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SHIP2 modulates metabolism through FGF signalling

In both humans and mice, high levels of the lipid phosphatase SHIP2 cause insulin resistance and susceptibility to type 2 diabetes, but the role of SHIP2 in cellular signalling is unclear. Jurynec and Grunwald show in zebrafish embryos that SHIP2 is an attenuator of the FGF signalling pathway, and that its loss causes many of the same phenotypes as exaggerated FGF signalling. The primary role of mammalian SHIP2 might therefore be to modulate endocrine FGF signalling, explaining its effects on metabolism. *K.W.*

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Excess adenosine causes wasting in flies

Adenosine metabolism is the cornerstone of energy generation in many organisms and, in addition, levels of extracellular adenosine act as a potent signalling stimulus for multiple cellular pathways. Zuberova et al. show that, in flies, a build-up of extracellular adenosine is fatal owing to its effects on glucose metabolism and storage. These observations provide new clues for unravelling mechanisms of stress-induced hyperglycemia and chronic infection leading to wasting in humans. *K.W.*

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Drosophila model of primary coenzyme Q deficiency

Coenzyme Q (CoQ) is an essential lipid component of the mitochondrial electron transport chain and is required for optimal ATP production. Mutations in genes of the CoQ biosynthetic pathway cause rare but severe diseases with symptoms ranging from deafness and myopathy to progressive neurodegeneration. In addition, it is thought that dietary supplementation with CoQ decreases the pathology of some neurodegenerative disorders, such as Parkinson's disease. Grant et al. describe a Drosophila model of primary CoQ deficiency in the developing CNS that might help to optimise treatments for primary CoQ deficiency diseases in humans, as well as to investigate the efficacy and mechanism of action of over-the-counter CoQ dietary supplements. *S.A.*

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New insights into ataxia telangiectasia

The symptoms of ataxia telangiectasia have been attributed to defects in DNA repair, caused by mutation of the ATM serine-threonine kinase. Kim et al. demonstrate that, in addition to its role in DNA repair, ATM also induces PDGFRB, a neuronal survival factor, and that loss of ATM renders neurons susceptible to apoptosis induced by oxidative stress. *K.W.*

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