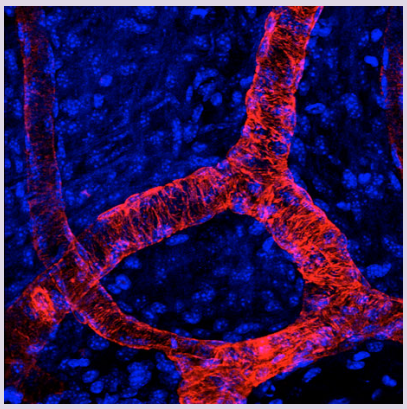

TGFβ inhibitors spring a leak in tumors

The blood supply to solid tumors is leaky, with improperly formed blood vessels and abnormal blood flow. The unique properties of the tumor vasculature may enable specific drug targeting. Sounni, Dehne and colleagues demonstrate a novel pathway, involving the matrix metalloproteinase MMP14 and the TGFβ signaling cascade, whose inhibition improves the ability of tumors to soak up high molecular weight compounds. This may be an important step forward in enhancing the delivery of both molecular contrast agents for imaging and tumoricidal drugs. *K.W.*
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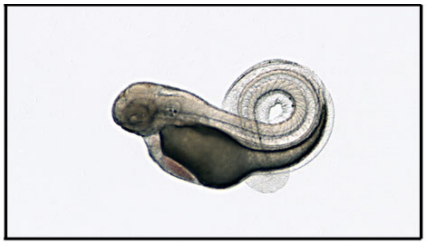
A fish-eye view of von Hippel Lindau disease

von Hippel Lindau (VHL) results from *VHL* gene loss and causes hemangioblastomas. van Rooijen et al. show that knocking out the zebrafish ortholog of *VHL* recapitulates the abnormal retinal blood vessel formation that is common in patients. Angiogenic retinopathies also occur in diseases that cause blindness, such as diabetes, suggesting a wider utility for these zebrafish mutants in research and drug development. *K.W.*
Page 343

Polycystins regulate tissue formation



Polycystic kidney disease (PKD) causes internal epithelial cysts and afflicts patients with hernias, aneurysms and cardiac valve defects. Mangos et al. describe a zebrafish model of autosomal dominant PKD, in which the fish are deficient in the polycystin genes, *pkd1a/b* and *pkd2*, linked to human PKD. The main structural element, the tail, is disrupted in mutant fish owing to overabundant collagen deposition. This suggests that polycystins influence tissue formation and demonstrates a regulatory role for the extracellular matrix in PKD. *K.K.*
Page 354

Autism mutation induces oxidative stress and toxin sensitivity in worms

Autism spectrum disorders (ASDs) affect learning and social behavior in many children, with a strong and genetically complex hereditary basis. Hunter, Mullen and colleagues mutated the autism-associated neuroligin gene (*nlg-1*) in *C. elegans*. Mutant worms have sensory deficits, increased levels of oxidative stress and are hypersensitive to environmental toxins. This model suggests that neuroligin influences sensory processing and oxidative stress, and may explain some of the hypersensitivity in individuals with ASDs. *K.K.*
Page 366

Movement disorder lessened by antibiotic

Movement disorders such as Parkinson's disease (PD) and dystonia are associated with dysfunction of the chaperone protein torsinA. Cao et al. identified FDA-approved small molecules that promote torsinA activity in *C. elegans*, including ampicillin. Ampicillin improved torsinA activity in human patient cells, and restored motor coordination and balance in a mouse model of early-onset torsion dystonia. Ampicillin derivatives may hold therapeutic potential for patients with movement disorders. *K.K.*
Page 386

Elastin pancreatic tumors wilt for lack of fibulin-5

Understanding how tumor-stromal interactions regulate the growth and metastasis of pancreatic ductal adenocarcinoma should help combat this aggressive cancer. Schluterman et al. report that grafted pancreatic tumors cannot grow properly in fibulin-5 knockout mice. Fibulin-5 normally sits in the extracellular matrix and prevents hyperactivation of integrin β1. Its loss triggers oxidative stress and apoptosis in the stromal microenvironment of the tumor, which withers away. *K.W.*
Page 333

All at sea with Alzheimer's: an ascidian model

The build-up of plaques and tangles in the brains of Alzheimer's patients marks the slow but inexorable progression of the disease. New drugs aim to halt the accumulation of amyloid beta peptides, the principal component of plaques. High-throughput drug screens, with plaque formation or its consequences as a readout, are difficult and slow in existing models. Virata and Zeller show that the sea squirt, our closest invertebrate relative, could be a useful resource for drug development. *K.W.*
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