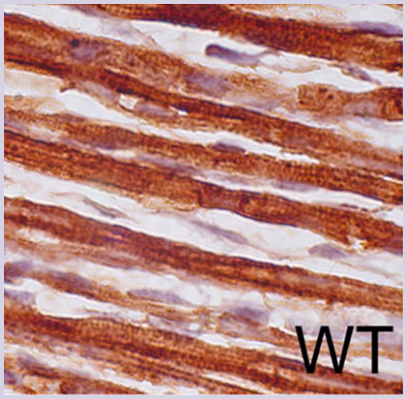

Muscular dystrophy traced to prenatal origins

There are several types of muscle dystrophy (MD), each causing different types of progressive weakness and skeletal muscle degeneration. Duchenne muscular dystrophy (DMD) is the most severe form of MD and results in respiratory muscle failure, cardiomyopathy and early death. DMD results from the loss of the protein dystrophin. Using mouse models of MD, Deborah Merrick and colleagues establish a key role for dystrophin in early muscle formation. They demonstrate that dystrophin and caveolin-3 (a dystrophin-associated glycoprotein complex protein) are essential for muscle fiber formation and emergent stem cell function. This work indicates that these protein changes could be early indicators of MD, allowing earlier diagnosis and treatment to enhance the quality of life for MD patients.

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A mouse model for motor and sensory dysfunction

Hereditary motor and sensory neuropathies progressively debilitate leg and arm movement and impair sensation. The wide variability in symptoms and genetic etiology, as well as the lethality of known mutations in mice, has delayed the development of model organisms. Francesca Achilli and colleagues made a dominant mutation in glycyl-tRNA synthetase (GARS), which appears in some cases of familial Chariot-Marie-Tooth (CMT) and infantile hereditary motor neuropathy (HMN). The mice have muscle weakness, loss of electrical conduction in neurons, and neuromuscular junction defects. An increasing number of nervous system diseases are linked with tRNA synthetase mutations, and this model should help determine the role of protein translation in these and other similar diseases. *This research article is freely accessible online.*

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Polycomb proteins shape the brain and spinal cord

The Chiari malformation is a developmental defect characterized by abnormal growth of the brainstem and cerebellar herniation. Malformation severity ranges from inconsequential to incapacitating or lethal changes; no genes that are causally involved in these changes have been identified. Here, Xavier Miró and colleagues identify a genetic factor that causes Chiari-like malformations in mice. This factor, Suz12, is a member of a polycomb complex, a group of proteins that act as epigenetic regulators of gene expression. Furthermore, the authors also demonstrate that Zac1, a regulator of neuronal proliferation, is part of the same molecular pathway affected by the Suz12 deficiency. These data help illuminate our understanding of genetic misregulation and how it can cause brain and neural tube defects.

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Cancer gene mutations make a zebrafish melanoma model

Metastatic cutaneous melanoma is an aggressive cancer that is resistant to current therapy. The mutations in epidermal melanocytes that lead to cancer are often propelled by changes in the oncogenes encoding RAS, RAF, MEK, ERK or PI3K. Here, Christina Michailidou and colleagues show that expression of mutant RAS (V12RAS) in zebrafish produces a similar phenotype to familial atypical mole and melanoma syndrome (FAMM) in humans. Similarities include variable melanocyte morphology and growth, and the spontaneous formation of invasive melanoma. Using this model, they demonstrate that blocking PI3K, an effector of the RAS signaling pathway, is sufficient to inhibit melanoma formation.

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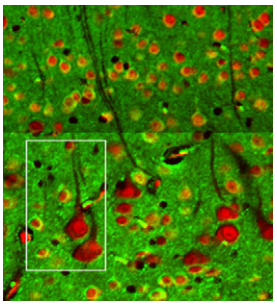
Pten mouse models of childhood seizures



Childhood epilepsy can result from malformations of the cerebral cortex known as cortical dysplasia. The treatment of these seizures is limited by a lack of animal models with key features of the disease, such as characteristic alterations in cell morphology and structural abnormalities in the cortex. M. Cecilia Ljungberg, C. Nicole Sunnen and colleagues report that a conditional *Pten* knockout mouse has characteristics that support its utility as a model for cortical dysplasia, such as enlarged cortical neurons and spontaneous seizures. As *Pten* is part of the PI3K-mTOR pathway, they have also identified an important molecular signaling pathway in cortical dysplasia. These data suggest that pharmacological inhibitors of this pathway, specifically the mTOR inhibitor rapamycin, are a potential therapy for controlling seizures in cortical dysplasia patients.

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