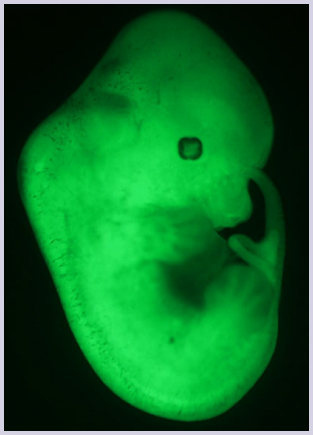

Dre recombinase, another tool in the mutagenesis toolbox

Many valuable mouse models of disease are produced through conditional mutagenesis. This technology often uses the site-specific Cre recombinase in conjunction with *loxP* recombination target sites to produce controlled mutations in somatic tissues. Konstantinos Anastassiadis, Francis Stewart and colleagues use the site-specific recombinase Dre, which exhibits similar precision and efficiency to Cre, but uses a unique *rox* recombination target site, to induce specific recombination in mice. Dre recombination was highly specific to *rox* sites, even in the presence of *loxP*. The Dre mouse offers an alternative method for the introduction of gene mutations and, in combination with current Cre and FLP techniques, could produce mouse models with multiple conditional mutations.

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This resource article is freely accessible online.

Bacteria benefit from mitochondrial dysfunction

Patients with mitochondrial disease suffer from metabolic abnormalities but are also highly susceptible to bacterial infections. Here, Lisa Francione and colleagues use Dictyostelium with altered mitochondria to show a positive correlation between AMP-activated protein kinase (AMPK) signaling and the intracellular growth of Legionella. AMPK activity serves as an internal sensor to coordinate energy synthesis with energy needs, and thus acts as a stress signal in cells with diseased mitochondria. Chronic activation of AMPK in cells with compromised mitochondria facilitates the proliferation of infectious bacteria. These findings indicate that the cellular stress response to mitochondrial dysfunction may predispose patients to secondary disease.

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Altered RNA splicing in expanded repeat disease

Expanded glutamine repeats trigger protein misfolding and contribute to a variety of neurodegenerative diseases through unknown mechanisms. In Kennedy disease, the repeat expansion occurs in the androgen receptor and results in a hormone-dependent loss of motor neurons, causing cramps and muscle weakness. Here, Zhigang Yu and colleagues report that the mutant protein produced in Kennedy disease alters RNA splicing by a mechanism that requires male hormones and correlates with the length of the glutamine repeat. Since pathological changes in RNA splicing are recognized in related diseases, other mutant proteins that are formed from extended repeats may produce similar RNA processing changes that contribute to cellular dysfunction.

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clueless, a possible contributor to Parkinson's disease

Three known genes contribute to inherited forms of Parkinson's disease: *parkin*, *pink1* and *DJ-1*, all of which affect mitochondrial functions. Here, Rachel Cox and Allan Spradling describe a novel gene in Drosophila, *clueless* (*clu*), that also affects mitochondrial function. As with the Drosophila homologue of parkin (Park), Clu affects mitochondrial clustering, and impairment of the Clu pathway disrupts mitochondrial function. Furthermore, *clu* and *parkin* interact genetically to influence the subcellular localization of mitochondria. Since *clu* is highly conserved among other organisms, its human homologue may contribute to mitochondrial damage in neurodegenerative disease.

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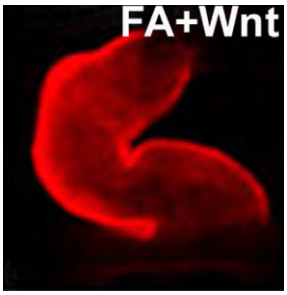
Folic acid protects Wnt signaling during development



Fetal exposure to the mood-stabilizing drug lithium causes heart and neural tube defects by unknown mechanisms. Here, Mingda Han, Maria Serrano, Rosana Lastra-Vicente and colleagues find that folic acid prevents lithium-induced changes to the Wnt–β-catenin signaling pathway in chick and mouse embryos. They show that lithium-induced defects are similar to those associated with elevated plasma homocysteine, which results from insufficient dietary folic acid. Both lithium and homocysteine suppress expression of the Wnt-regulated genes *Hex* and *Isl1*. Folic acid protects against this disruption of Wnt–β-catenin signaling during heart development and ameliorates the cardiac defects associated with homocysteine or lithium exposure.

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