Lamin leveraged for progeria

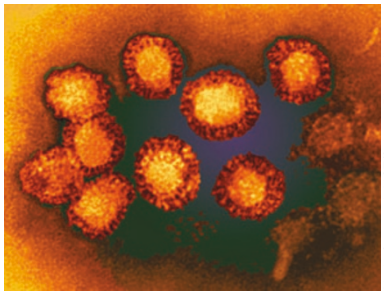
A drug in development to treat cancer eases symptoms in a mouse model of Hutchinson-Gilford Progeria, a rare disease in which children seem to age rapidly (*Science*, doi:10.1126/science.1124875).

In this condition, lamin A, a component of the nuclear scaffold, is incorrectly processed so as to retain a farnesyl lipid group. The result is misshapen cell nuclei. Previous studies in cells had suggested that a farnesyltransferase inhibitor could add shape back to the nuclei.

Now, Loren Fong *et al.* administer the inhibitor to a mouse model and find it forestalls symptoms and increases survival. Just three years after the discovery of the disease-causing mutations in the lamin A gene, the results set the stage for a clinical trial. —*CS*

Receptor dilemma

A gene variant that protects against HIV seems to make people more susceptible to infection with West Nile virus, report Philip Murphy and colleagues (*J. Exper. Med.* 203, 35–40).



Linda Stannard, UCT/Science Photo Library

West Nile virus discriminates.

The *CCR5Δ32* variant disables the chemokine receptor CCR5 and is present in about 1 percent of the Caucasian population in the United States. Because HIV uses CCR5 to enter cells, people with the variant have reduced susceptibility to HIV infection.

The researchers previously found that mice deficient in CCR5 invariably died from West Nile infection. The receptor seems to be involved in attracting protective immune cells to the brain, where the virus does its damage. The new study found a greater frequency of homozygous *CCR5Δ32* mutations in people with symptomatic West Nile infection than in the general population. Homozygosity also seemed to increase the risk of death from the virus.

The findings sound a cautionary note for efforts to develop HIV drugs targeting CCR5—such drugs might increase susceptibility to West Nile. 16,577 cases of the infection were reported to the US Centers for Disease Control from 2001 to 2004, likely a vast underestimate. —*CS*

Beating botulism

A single infusion of antitoxin can effectively treat infant botulism, according to the results of a controlled trial by Stephen S. Arnon *et al.* (*N. Engl. J. Med.* **354**, 462–471). Although extremely rare, infant botulism is still the most common form of botulism in the United States—and affected infants often spend weeks in the hospital.

The antitoxin, Human Botulism Immune Globulin Intravenous (Human) (BIG-IV), was tested on 382 infants over six years. The drug, derived from human plasma, more than halved the duration of the hospital stay, from 5.7 to 2.6 weeks. Hospital charges were reduced by about $89,000 per patient—about twice the cost of the drug, which is now available from the California Department of Health Services.

Botulinum toxin is considered a potential bioweapon and a recombinant version of the antitoxin is being developed. —*CS*

Written by Jasmine Bhatia, Eva Chmielnicki, Juan Carlos López and Charlotte Schubert

Is schizophrenia irreversible?

Mice that model the cognitive symptoms of schizophrenia have been engineered by overexpressing dopamine type 2 receptors (D2R) in the striatum, a multitasking subcortical structure in the brain (*Neuron* 49, 603–615, 2006).

Hyperactivity of the dopamine system mediates the delusional thoughts that typify schizophrenia, but whether dopaminergic dysfunction is involved in the cognitive symptoms of schizophrenia was not clear. Christoph Kellendonk *et al.* found that their engineered mice had abnormalities in dopamine metabolism in the prefrontal cortex, an area of the brain that is involved in working memory. The mice showed deficits in working memory and behavioral flexibility, symptoms commonly seen in schizophrenic individuals.

Even when the D2R gene was turned off at birth, the cognitive symptoms persisted in the mice. Schizophrenia may therefore be caused by abnormal brain wiring during development, rendering relief of symptoms in adulthood all the more difficult. —*EC*

Angiogenesis and ALS

Mutations in a gene that regulates angiogenesis are associated with some cases of amyotrophic lateral sclerosis (ALS), report Matthew Greenway *et al.* (*Nat. Genet.* doi: 10.1038/ng1742). Missense mutations in the gene for angiogenin were found in 15 of 1,629 people with the disease, many of Scottish or Irish descent. Angiogenin is expressed in motoneurons, but it's unclear how the protein prompts blood vessel growth or operates during ALS—a disease more famously pinned to defects in SOD-1, a protein that mops up free radicals. —*CS*

Harm to SARMs

Men with prostate cancer are commonly treated with selective androgen receptor modulators (SARMs) to stop hormone-dependent proliferation. But resistance to the drugs often develops, and David Rose and colleagues propose one reason why (*Cell* 124, 615–629).

The researcher suggest that a specific interaction between macrophages and prostate cells may cause resistance to SARMs. They provide evidence that macrophages interact with prostate cells through VCAM-1. The bound macrophages produce proinflammatory cytokines, which cause derepression of SARM-bound androgen receptor, leading to resistance. The findings point to new ways to treat hormone-dependent cancers. —*JB*

Lincoln legacy

A quest to uncover the molecular basis for ataxia has homed in on a glutamate transporter—and on the pedigree of Abraham Lincoln (*Nat. Genet.* **38**, 184–190).

People with spinocerebellar ataxia type 5 suffer from poor coordination and other symptoms owing to damage to nerve cells in the cerebellum. Through an analysis of three different families, Laura Ranum and colleagues traced the disease to mutations in the gene encoding β-III spectrin. β-III spectrin is highly expressed in neurons of the cerebellum and is known to stabilize a glutamate transporter. The researchers provide evidence that the mutant form results in lower levels of this transporter at the synapse.

One of the families studied is related to Abraham Lincoln. Lincoln has no present-day direct descendants, but the analysis suggests that one of his grandparents carried the gene. That means there is a 25% chance that Lincoln had the disease, consistent with descriptions of the time suggesting that the towering US president had an uneven, shambling gait.

Scientifically, the results dovetail with findings from studies of other types of spinocerebellar ataxia, hinting at the involvement of glutamate.