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Gene linked to Down's decline

A single duplicated gene may cause the neurological decline seen in long-living sufferers of Down Syndrome (DS), according to a new study in mice. If confirmed in humans, this finding could lead to better treatment for the roughly 4,000 children born in the US every year with DS.

DS, caused by trisomy of human chromosome 21, is characterized by mild to moderate mental retardation and a significant risk for development of medical problems, including hearing deficits and heart defects. In addition, most DS sufferers develop Alzheimer's disease by the age of 40, but the basis of this early neurodegeneration is unclear.

Using mice segmentally trisomic for mouse chromosome 16 as a model for DS, a research team led by Ahmad Salehi and Jean-Dominique Delcroix at Stanford University (Stanford, CA), found that overexpression of the amyloid precursor protein (App) compromises transport of nerve growth factor (NGF), thereby promoting neuron degeneration (*Neuron*, 6 July). Surprisingly, artificial delivery of NGF alone was sufficient to rescue the condition in mice, indicating that much of the cognitive decline in people with DS may be caused by the overexpression of this single gene. This research suggests that reduction of *App* gene expression may mitigate cognitive decline in DS sufferers.

Trojan horse platelets treat hemophilia

By devising a gene therapy strategy in which platelets 'smuggle' clotting factor to injury sites, researchers have moved toward solving a huge problem in the treatment of hemophilia A.

Hemophilia A is a congenital disorder characterized by a lack of clotting factor VIII (FVIII). This shortage of FVIII causes clotting abnormalities in hemophiliacs that can include excessive bleeding following even minor injuries. Standard treatment for the disease is infusion of exogenous FVIII. Although highly effective in most patients, up to 30% develop antibodies to FVIII, rendering the protein ineffective.

Now, Robert R. Montgomery and colleagues at the BloodCenter of Wisconsin, Medical College of Wisconsin, and Children's Hospital of Wisconsin (all in Milwaukee) report a gene therapy approach that eliminates this problem in a knockout mouse model of hemophilia A (*J. Clin. Invest.*, July). These researchers show that expression of FVIII in blood stem cells can lead to storage of the protein in platelets, where it is protected from attacks by inhibiting antibodies. When the platelets are activated at an injury site, they release FVIII, which normalizes the clotting process. Local delivery of FVIII to injured blood vessels results in clotting even in mice with high titers of anti-FVIII antibodies, suggesting that this approach may be the key to treating hemophilia patients who, because of antibody resistance, no longer respond to exogenous FVIII treatment.

New study examines murine empathy

Can mice feel one another's pain? New research at McGill University (Montreal, Canada) suggests that mice empathize with the pain they observe in their cage mates. This result runs contrary to the popular notion that higher primates are the only animals capable of such advanced conspecific feelings.

Jeffrey S. Mogil and colleagues used the so-called 'writhing test' to measure the responses of pairs of same-sex mice placed in adjacent transparent Plexiglas containers. The two mice were simultaneously injected in the abdomen with 0.9% acetic acid and observed for writhing behavior. The researchers found that mice exhibited more writhing after injection when paired with cage mates of 14–21 days than when the mice were injected in isolation (*Science*, 30 June). Moreover, the 'mouse empathy,' as measured by increased writhing, seems to be dependent on visual cues, as opaque containers nullified the effect of cage-mate pairing. The researchers also noted that male mice paired with strangers showed significantly less writhing than when tested in isolation.

The researchers hope that further evidence of empathy in mice will lead to the development of an animal model to study the mechanistic components of empathy that can now only be investigated in humans in a limited way.