Research News

Gene tripped by violence

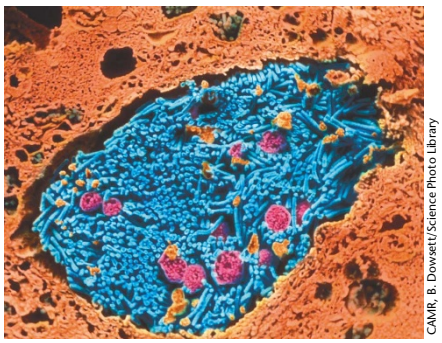
An abusive home can foster children who become aggressive adults. Now it seems that the spiral of family violence could get amplified by a bad gene, according to a study in the 2 August *Science*. The X-linked gene, *MAOA* (monoamine oxidase A), has been previously implicated in aggression in mice and humans. A 1993 study of a Dutch family, for example, correlated a null allele of *MAOA* with male anti-social behavior. But such null alleles are rare in the human population. Instead, genetic variation occurs in a variable number of repeats at the *MAOA* promoter. Repeat number is associated with *MAOA* expression levels. Caspi *et al.* found that men with low-activity *MAOA* alleles had violent, anti-social tendencies. But these men were only more aggressive if they came from homes where maltreatment occurred. Caspi *et al.* came to this conclusion by genotyping 422 men enrolled in a study tracking their health and development since birth, during or after 1972. 36% of the men had experienced some form of maltreatment as children. 12% had both the low-activity gene and had experienced maltreatment—and as adults they had committed 44% of the study's violent crimes. *MAOA* encodes an enzyme that metabolizes a number of neurotransmitters. But exactly how low-activity alleles of *MAOA* increase susceptibility to an emotionally damaging environment remains unknown.

Nr-CAM surfaces in cancer

β-catenin and other members of the Wnt pathway can become deregulated and contribute to tumor progression. But exactly how is an open question. Now, Conacci-Sorrell *et al.* suggest that the neuronal cell adhesion molecule Nr-CAM might have a lot to do with it. The researchers began by over-expressing β-catenin in human renal cancer cells and then performing microarray analysis. In the 15 August *Genes and Development*, they report that Nr-CAM was consistently up-regulated by β-catenin overexpression. Boosting Nr-CAM levels in cells in culture gave them the characteristics of cancer cells, such as enhanced cell migration and proliferation. When injected into mice, the cells produced tumors, and human tumors expressed high levels of Nr-CAM. Because Nr-CAM is expressed on the cell surface, it may present an easier target for anti-cancer therapies than intracellular proteins.

New weapon against anthrax

The anthrax bacterium has its enemies and among them is the γ phage. γ phage breeds inside the bacterium before melting its cell wall and bursting out. Schuch *et al.* have now harnessed γ phage as a therapy—and an agent for the detection of anthrax (shown in a lung capillary). The authors purified the phage enzyme that destroys the anthrax cell wall, PlyG. In the 24 August *Nature*, they report that PlyG killed *Bacillus anthracis* in culture, but did not affect most strains of closely related *Bacillus* species. The authors injected anthrax-infected mice with the enzyme within 15 minutes of bacterial exposure. The mice, otherwise doomed to die, had an 80% survival rate. The authors found that no enzyme-resistant strains developed in response to treatment, suggesting that PlyG could outperform conventional antibiotics in cases of antibiotic-resistance. But the main constraint of current treatment still holds; the enzyme must be administered soon after exposure. The enzyme's usefulness does not end with an injection. The authors also found that it could be used to light up anthrax in a dark room. When lysed, anthrax releases ATP, which can be detected using the luciferase enzyme. Luciferase, in the presence of ATP, degrades luciferin and produces light detectable with a hand-held luminometer. The authors suggest that the enzyme could enable rapid anthrax detection, something that now takes days while cultures grow in petri dishes.



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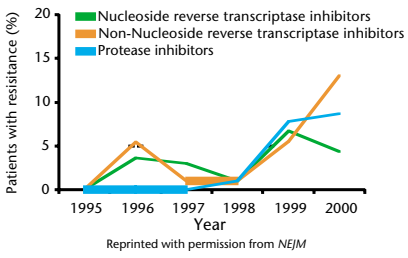
Farming modulates immunity

Asthma and respiratory allergies have been on the rise for decades. One theory holds that a more hygienic environment contributes to such problems. Now that theory has gained momentum from a 10 August study in the *Lancet*. Lauener *et al.* compared 25 children on farms with 71 children from rural towns in Europe. The authors had previously found that farm children were 5 times less likely to develop allergic diseases. Farm homes also contain measurably higher levels of bacteria. Using quantitative PCR, Lauener *et al.* showed that farm children have higher levels of expression of two genes that fight a broad response against microbes, compared with children in towns. Farm children had over a two-fold higher expression of CD14 and Toll-like receptor 2 (TLR2), which respond to bacterial lipopolysaccharide. *In vitro*, exposure of blood cells to bacterial lipopolysaccharide was previously known to also boost CD14 and TLR2 expression. Precisely how CD14 and TLR could counteract allergic diseases is unclear. But binding of TLRs by microbial components activates antigen-presenting cells, which could enhance both innate and adaptive immunity.

HIV drug resistance increases

Drug-resistant HIV strains are on the rise, according to a 10-city study of 377 HIV-infected patients in North America. In the 8 August *NEJM* Little *et al.* report that antiretroviral drug resistance increased from 3.4% in 1995 to 12.4% among the 377 patients studied. The frequency of multidrug resistance at the time of diagnosis also increased, from 1.1% to 6.2%. Furthermore, it took longer for antiretroviral drugs to take effect in patients who harbored a resistant viral strain. However, the drugs still have the advantage. For patients with resistant strains, viral suppression still occurred within 24 weeks, with the exception of one individual. The authors conclude that patients initiating treatment for HIV should now be tested for antiretroviral drug resistance.



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