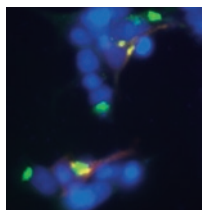


## “DNA-prime protein-boost” HIV vaccine tested

Vaccine researchers report that an HIV vaccine formulation was effective in eliciting strong and balanced immune responses in healthy human volunteers. The findings were published in the online edition of *Vaccine*. Additional independent assays on the volunteers' samples confirmed the presence of long-lasting and high-quality T-cell responses against HIV antigens; these latter results were published online in the *Journal of Virology*. Volunteers first received three injections of a DNA vaccine that expressed protective antigens from the HIV virus, followed by two injections of a protein vaccine whose components matched those in the DNA vaccine. A unique design underlying this combination HIV vaccine formulation was the use of a cocktail of five different envelope (Env) proteins collected from HIV viruses circulating in different parts of the world. Env is a key protective antigen, and the goal was to elicit broad antibody responses against a wide range of HIV viruses so as to counter the problem of frequent HIV mutations. Indeed, the high-titer antibodies found in volunteers' sera were able to recognize each of a very diverse group of Env antigens included in the study. More significantly, the majority of volunteers developed positive neutralizing antibodies against a good portion of the five HIV subtypes in the assay. (*Vaccine*, published online 30 April 2008; doi:10.1016/j.vaccine.2007.12.060, and *J Virol*, published online 30 April 2008; doi:10.1128/JVI.00068-08)

## Intrabody mops up mutant huntingtin



Mutant huntingtin accumulates in neuronal nuclei and processes, which suggests that its subcellular localization is critical for the pathology of Huntington's disease. Researchers have now generated an intrabody whose binding to a unique epitope of huntingtin is enhanced by polyglutamine expansion. This intrabody decreases the cytotoxicity of mutant huntingtin and its distribution in neuronal processes. Injection of an adenoviral vector expressing the intrabody into the brains of mice expressing mutant huntingtin improved their ability to move their limbs, although it did not prolong their lives. The results were published in the *Journal of Cell Biology*. Disease-causing mutations give rise to a region consisting of polyglutamine, which makes the proteins clump together inside cells. The authors' goal was to create a tool that could distinguish between the accumulation of mutant proteins in the nucleus and the cytoplasm. Cultured cells that make both the intrabody and mutant huntingtin were able to clear the mutant protein more rapidly and had fewer clumps of huntingtin. Even though the intrabody travels only within the cytoplasm, when injected into the striatum it alleviated the motor problems of mice that make mutant huntingtin. (*J Cell Biol*, published online 26 May 2008; doi:10.1083/jcb.200710158)

## Transgenic primate model for Huntington's

Researchers have developed the first transgenic nonhuman primate model of Huntington's disease (HD). It is hoped that the model, recently described in *Nature*, will help researchers to better understand the disease and to develop more effective therapies. In the past, researchers have used transgenic mouse models to study the disease, but such models do not completely parallel the brain changes and behavioral features observed in humans with HD. The researchers produced the HD transgenic rhesus macaques by injecting mature oocytes with a lentivirus vector expressing the mutant *HTT* gene with expanded polyglutamine repeats. The oocytes were then fertilized by intracytoplasmic sperm injection and transferred into eight surrogates. This resulted in six pregnancies and five live births (two sets of twins and one singleton). All carried the mutant *HTT* gene, and two continue to survive. Hallmark features of HD, including nuclear inclusions and neuropil aggregates, were observed in the brains of the HD transgenic monkeys. Additionally, the transgenic monkeys showed important clinical features of HD, including dystonia and chorea. (*Nature*, published online 18 May 2008; doi:10.1038/nature06975)



## Gene therapy clinical trial yields promising results for Batten disease

Results of a recent clinical trial show that gene therapy is both safe and effective at slowing the progression of Batten disease, or late infantile neuronal ceroid lipofuscinosis, a rare genetic degenerative neurological disorder that usually becomes fatal in children around ages 8 to 12. The clinical trial found that the procedure not only was safe but, on average, significantly slowed the disease progression of the subjects tested. Neurological function was assessed using a rating scale throughout an 18-month follow-up period. The results were published in *Human Gene Therapy*. The gene in question—*CLN2*—is mutated in children with the disease, causing a deficiency in the enzyme TTP-1, which is responsible for ridding central nervous system cells of waste materials. Small organelles within the cells, called lysosomes, become clogged with toxic material within the neurons of the brain. Because the disease is fatal early in life, there are only about 200 cases of the disease in the world at a given time. An adeno-associated virus vector carrying the *CLN2* gene was injected into the brains of the patients. (*Hum Gene Ther*, published online 13 May 2008; doi:10.1089/hum.2008.022)