



TOUCHING BASE

QUESTIONS? THOUGHTS? IDEAS?
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Time for backyard GMOs?

Public opinion of GMOs currently ranges from passive ignorance to outraged revulsion. What will it take to turn the tide to general acceptance? It seems that we are lacking a consumer product that will allow simultaneous modification of selected combinations of genes in domestic plants and animals; for example, a cat processor that would permit interactive selection of coat color, temperament and wing aspect ratio. Historical precedents indicate that people will embrace genetic modification in their lifestyles. From the craze for virally variegated tulips in 17th-century Netherlands to the passion for radiation-induced finch traits introduced into canaries in Italy, we can infer that when GM enthusiasm erupts, it is largely consumer-driven. But can we trust the consumer not to take this power too far? Handguns and computer viruses are frequently cited examples of consumer choice with risky but accepted side effects. But are members of the public really less responsible and less accountable than large corporations? Body modification, as currently practiced, involves scarification, implants, piercing and tattooing. These art forms link personal boldness with varying degrees of reversibility; their effects are limited to the individual and are not heritable. Prevailing consumer values are, therefore, despite their ethically poor foundation, in alignment with the stronger moral principles of dignity and responsibility that keep us from attempting human germline modification. Pigs might fly, but let's try cats first. MA



HHMI turns 50

Fifty years ago this month, the Howard Hughes Medical Institute was chartered, bearing the name of the enigmatic entrepreneur who founded it. Although Howard Hughes saw success as an aviator and as a defense contractor and maker of spy satellites, his business failures were so frequent that Hughes biographers Donald Bartlett and James Steele were moved to say, "It was as if he was missing the gene for corporate success". The saving grace of the Hughes fortune was the rotary drill bit with 166 cutting edges that his father patented, and that revolutionized oil drilling. Otto Friedrich wrote, "...no matter how much money he wasted, the Hughes drilling bit would always pay his bills". When the HHMI was founded in December 1953, its initial income came from ownership of 75,000 shares of the Hughes Aircraft Company. Its mission: "the promotion of knowledge within the field of the basic sciences

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(principally the field of medical research and medical education) and the effective application thereof for the benefit of mankind". The Hughes Aircraft Company was sold to General Motors in 1985, establishing the HHMI endowment at about \$5 billion, making it one of the world's largest philanthropies, and it remains so today. Although the HHMI has devoted significant resources to the improvement of science education, its hallmark has been a generous grant program for individual scientists. Innovative researchers are funded as HHMI employees but remain on their home campuses, in a mutually beneficial arrangement. The world is better for it, and not just by a bit. AP

Idealistic guitar-playing man returns

In time for the festive season, Cold Spring Harbor Laboratory Press (<http://www.cshlpress.com>) have re-released "Selected Songs for Cynical Scientists" by Cambridge Professor Ron Laskey. Writing in *The Biochemist* last December, he described the "indescribable satisfaction of pouring out frustration or irritation in the form of satirical songs...Singing and performing music in public are good training for the disasters that can occur when lecturing". One song that Dr. Laskey wrote in outrage at the security services impounding his bicycle during a diplomatic visit became the only protest song (to my knowledge) filed as a formal complaint with the police. His own lyrics to a memorable 1960s protest song lampooned the transcription field for clonally following fashion. If I remember rightly from the last CSH meeting when he entertained an enthusiastic audience of cell cycle researchers, he is keeping his wit current with the evolution of this field:

"Little boxes, little boxes, little boxes, all the same,

Now they all use little microchips, the results all look the same."

Jump on the bandwagon and give these little modules to all the friends in your functional network. MA

Mutant of the Month

Shhh! Let sleeping dogs lie—especially when they are Dobermans. Our January MoM, Prancer, has autosomal recessive narcolepsy. She carries an insertion of a SINE element upstream of exon 4 of *Hcrtr2*, encoding hypocretin receptor-2, which makes her excessively sleepy and causes rapid transitions from awake to REM sleep.



Courtesy of Stanford University Center for Narcolepsy

The insertion causes skipping of exon 4, which leads to a premature stop codon and thus a nonfunctional receptor. Hypocretin receptor-2 is a G protein-coupled receptor for the neuropeptide hypocretin (also called orexin), which has been tied to feeding behavior and changes in metabolic rate. In addition to the Doberman pedigree, different mutations in *Hcrtr2* have been found in Labrador and Dachshund pedigrees. Notably, only a single mutation in the human preprohypocretin gene has been found to be associated with narcolepsy (none in the receptor). In fact, it is usually sporadic and not inherited. Human narcolepsy seems to be associated with a loss of hypocretin-producing cells in the hypothalamus. It has also been shown to be tightly associated with human leukocyte antigen (HLA) allele DQB1*0602, suggesting that it might be autoimmune in nature. MS