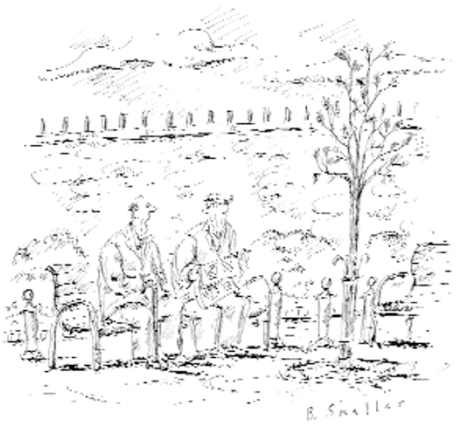
TOUCHING**base**

Zeroing in on a zebrafish circler

What do deaf fish do? Some of them swim in circles. Whereas their general appearance is quite different from a land-dwelling vertebrate, a number of zebrafish models of human disease have been reported. And like the human, the zebrafish has an inner ear which senses sound and establishes equilibrium. It also has a lateral line organ, which is homologous to the inner ear and detects water movements. Screens for zebrafish defective in these mechanosensory organs have led to the isolation of *circler* mutants, which swim in vertical loops and (in some cases) do not respond to vibrations. Preliminary characterization of *circler* mutants has shown that many have defective stereocilia—a feature central to many types of deafness in humans and mice (see page 6 of this issue for more on stereocilia and deafness). In a paper published in the current issue of *Human Molecular Genetics*, Sylvain Ernest and colleagues describe cloning the gene mutated in *mariner*, a *circler* mutant, which turns out to be none other than that encoding myosin VIIA. As the human orthologue is mutated in people with hearing disorders, including Usher 1B syndrome, it would seem that both the structure of fish mechanosensory organs and the function of myosin VIIA are conserved in vertebrates. The findings also raise the possibility that the zebrafish—an animal that lends itself to classical genetic screens—can serve as a model to dissect hereditary deafness in humans.



"My goal is to die before there's a technology breakthrough that forces me to live to a hundred and thirty."

Send in a sendai vector

Targeted molecular therapy, whether it be with genes or antibodies or fragments thereof, has fallen at a number of hurdles. The physical barrier—for example, the pulmonary epithelium, or mucous that lines the respiratory tract—is one such hurdle. Apparently, it is mucous that is to blame (along with factors affecting vector binding) for the low efficiency of gene transfer to the airway epithelium of people and animal models experimentally treated for cystic fibrosis. These obstacles are the first of many that a vector must cross before it can approach the genome of its target cell, as explained by Yoshikazu Yonemitsu and colleagues, in a study published in this month's issue of *Nature Biotechnology* (vol. **18**, 970–973; 2000). Their results, however, indicate that modified sendai virus (SeV) is a good deal more efficient at this task than cationic liposomes or adenovirus (AV). They established this by introducing recombinant SeV, AV, or a plasmid encoding the reporter construct (luciferase) complexed with a cationic liposome, separately, into the nasal cavities of mice. On observing a dose-dependent increase in expression of luciferase on an order of 3–4 logs higher in the lungs of mice exposed to SeV, the authors went on to explore the possibility that the robust performance of the vector was not simply due to the fact that SeV naturally infects the rodent lung. They tested out constructs on the lungs of ferrets, whose lungs are more similar to those of humans, and on primary human nasal epithelium *in vitro*. The results are encouraging. Perhaps this should not come as a surprise, as SeV shares the same receptor (the sialic acid receptor) as the influenza virus, which seems to know a thing or two about penetrating the respiratory tract. Nonetheless, the results reported by Yonemitsu *et al*. are extremely encouraging, and should send those researching cystic fibrosis racing for SeV constructs that contain *Cftr*, the mouse orthologue of the gene mutated in people with cystic fibrosis.

"How about 'What free love is free of, is love'? Another little gem. You could put 'what' on the end of it...'What free love is free of is love, what?' and the words would go on replicating themselves like a spiral of DNA... 'What love is free of love? free love is what love, what?'

—Henry (in *The Real Thing* by Tom Stoppard)

Who's afraid of *Biotech*?

For its annual street production, the Theater for the New City (New York) embarked on a crusade against genetically modified (GM) organisms, corporate America and globalization. Written and directed by Crystal Field, *Biotech* is a sci-fi thriller musical comedy (phew!), campaigning for a confusing pot-pourri of political measures, from long-term testing of GM food to affordable healthcare and housing for all. The story takes off when a three-headed chicken incites consumers to revolt and chant: "before we become defective, let's find a detective and get to the bottom of this." Our heroes demonstrate outside the headquarters of the evil "Genome Corporation," where patent owners are having a party, singing: "These seeds are perfect! We own the world!" The demonstrators are severely beaten by the police and end up in jail. A bohemian embodying "Mother Nature" is gagged with a transgenic tomato and frozen away "for spare parts". As a result of the investigation by two private eyes, executives and scientists are convicted for provoking disastrous mutations in their own employees and sentenced to a life of organic farming. Our heroes are freed, Mother Nature is woken by a kiss and, optimistic, proclaims to humankind: "I feel much better. You're not as stupid as you look!" The play gets some laughs, especially from children in the audience, who love the giant puppets embodying GM products. It might well inspire them to become private investigators, but probably not scientists, for the latter are portrayed as arrogant, greedy and evil. In reaction, rare real-life biologists present in the audience giggled contemptuously over a few flagrant inaccuracies. But how many geneticists know the percentage of GM-soybean actually grown in the USA today? 20%? 60%? 100%? The thespians are close, at 60% (according to *The New York Times*, it was 59% in 1999 and is 52% today). The play is no masterpiece and its prejudice is alarming. But it may serve as yet another reminder of a possibly underestimated gap between society, science and industry.

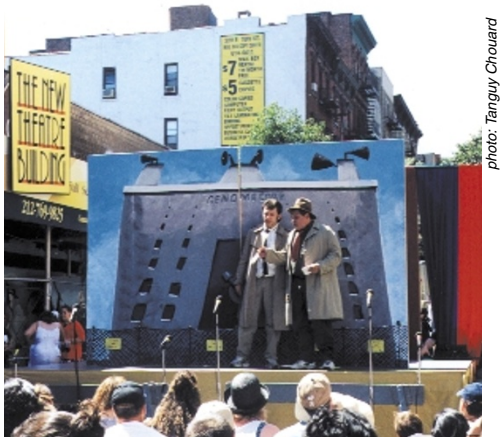


photo: Tanguy Chouard

Private eyes for the public: Genome Corp. is under investigation in *Biotech*.