The Men Who Would Be King

Steve Case and Bill Gates: You don’t have to be CEO anymore to want to rule the Internet.
experts think otherwise. Last month a Nasdaq dive pushed the options messaging system to 90% of its capacity.)

An unintended consequence may be a rash of stock splits, predicts Susan Woodward, chief economist for OffRoad Capital.

The ratio between the spread and the average stock price has created a steady profit margin for decades, she says. To attract market makers (in an effort to stabilize prices), companies might split their stock to potentially raise the profit margin, she says. Until the switch, the biggest beneficiaries are the Y2K techies. The industry postponed the change until after the 2000 panic passed—perfect timing to employ the same people that guided Wall Street through its last “disaster.”

— Carol Virzi

THE REVIVAL OF GENE THERAPY

Wash That Gray Right Out of Your Hair

A BREAKTHROUGH BY A GROUP OF RESEARCHERS IN PHILADELPHIA may help reinvigorate the struggling field of gene therapy and portend a future in which Just For Men hair color is history.

Scientists at Jefferson Medical College reported in the January issue of Nature Biotechnology that they have turned hair dark in albino mice using chimerastransplantation, a type of gene therapy that repairs faulty genes rather than replacing them. The work boosts enthusiasm who hope that gene therapy will eventually treat everything from grayness to balding. It was also happy news for Kineragen, a small private company with just 37 employees in Newtown, Pa., that holds an exclusive license on chimerastransplantation. The experiment “is one more step forward [showing that] the technology is robust,” exults Lisa Maliseed, vice president for strategic planning and licensing.

Chimerastransplantation differs from standard gene therapy, in which scientists use disabled viruses to deliver whole new genes intended to function in place of defective ones. Standard gene therapy is hampered by imprecision. A gene may insert itself anywhere in the genome, which can throw off its regulation: the gene might “turn on” at the wrong time or make abnormal amounts of the protein whose production it directs. Another danger is that the viruses that act as messengers for the inserted genes can cause the immune system to go into overdrive and eliminate what it perceives as foreign invaders. Researchers think that this is a big part of what killed Jesse Cel-
singer, an 18-year-old research volunteer at the University of Pennsylvania who died in September while undergoing gene therapy to treat a rare metabolic disease.

Chimerastransplantation doesn't rely on viruses for delivery. Instead of inserting new genes haphazardly, it repairs faulty genes with surgical precision, using molecular messengers to correct misspellings in the genetic alphabet. For instance, in the case of the albino mice, the misspelling blocked an enzyme that's crucial for the production of the pigment melanin, which gives hair its color. The repair tools were actually DNA-RNA pieces, dubbed chimeras, which contained the correct spelling. They repaired the faulty gene with surgical precision by harnessing the cell's own DNA repair mechanism. The upshot: In the albino mice, the genetic imprecision was reversed, and the mice began sprouting dark hair.

Don't rush to your doctor for restoration of your lustrous locks just yet. “We were able to generate only a few black hairs, detectable only under the microscope,” notes lead researcher Kyungsoon Yoon, a chemist and molecular biologist at Jefferson. And the change in the mouse hair color lasted just three months because of the short life span of the pigment-producing cells. To spur permanent change, scientists will need to find a way to repair genes in the precursor cells that give rise to all pigment-making cells.

Still, some argue that gene therapy will yield a future of 80-year-old full-headed blondes. “Gene therapy has just taken a cosmetic step forward,” wrote Robert Hoffman in a commentary accompanying Yoon's report. Hoffman is president of Anti-Cancer, a privately held biotechnology company in San Diego that is a pioneer in hair gene therapy. Hoffman's firm is targeting ordinary graying, which is caused by the natural deterioration of pigment-producing cells that comes with aging, not by genetic misspelling. Anti-Cancer hopes to stimulate pigment production by inserting extra copies of the gene that Yoon repaired or by inserting the gene into other kinds of hair cells and hijacking them to do the job.

But Yoon herself—who launched her experiment with the ultimate goal of treating not graying heads but disfiguring skin diseases—cautions that widespread commercial applications are “more than premature.” “The technology is not ready for the kind of venture,” she says.

— Meredith Wadner

CEOs AREN'T MILLIONAIRES

Much of America is addicted to ABC's game show Who Wants to Be a Millionaire? But FORTUNE 500 CEOs don't feel the same way. Perhaps they're fearful of the softball questions—or just envious of the easy wealth.

Can't wait for it to come back on the air 17%

Dumb idea and dumb show 36%

Strangely intriguing 20%

Haven't seen it 54%