touching base

Solving Part of the Pycno Puzzle

Last year, two groups reported in *Nature Genetics* that they had mapped the gene for pycnodysostosis, a form of dwarfism notable for the theory that it was the condition that afflicted the great French artist, Henri de Toulouse-Lautrec. One of those groups, headed by Robert Desnick and colleagues from Mt Sinai Medical Center in New York, has recently described the gene for the malady (Gelb, B.D. *et al. Science* **273**, 1236-1238; 1996). Desnick's group finds that in three families, the gene for cathepsin K, the only cysteine protease known to be highly expressed in osteoclasts, is mutated in various ways, including an elongation of the C terminus, a nonsense and a missense mutation. The finding may have important ramifications for the treatment of other bone disorders such as osteoporosis, but the nature of the French artist's condition remains a mystery — for now. The New York group is holding discussions with the artist's family about the possibility of reaching an unequivocal DNA diagnosis. Some might argue, why bother? As the *New York Times* concluded its report on the Toulouse-Lautrec controversy last year, 'The fact that so many great figures of the past have triumphed over physical adversity suggests that nothing can hold a determined person from achieving greatness — except, perhaps, a lack of talent.'

Sudden Impact II

The 1995 average citation index figures, compiled by the Institute for Scientific Information (ISI) in Philadelphia, make for interesting reading. The figures, representing the average number of citations in 1995 for papers published the preceding year, give *Nature Genetics* an 'impact factor' of 28.5, placing it second among all research journals, and ahead of all weekly journals including *Nature* (27.0) and *Science* (21.9). Some other figures of note: Genes & *Development* (18.79), *Neuron* (16.62), *Proceedings of the National Academy of Sciences* (10.52), *American Journal of Human Genetics* (9.26), *Human Molecular Genetics* (5.27) and *Genomics* (4.09).

Life As We Know It?

The recent fuss about the possibility on life on foreign planets stimulated by the Martian meteorite ALH84001 would not have been nearly so great without the intriguing pictures of microscopic tubular bodies embedded in the red rock, resembling forms of bacteria. Now, a high priority for the scientists trying to discover once and for all it there was indeed life on Mars is to slice open these 20-nm wide structures. They might be in for some surprises, however. As the magazine *Newsweek* reported, 'the next step is to make ultrathin slices of the microfossils and try to find cell membranes or — even better — amino acids, the building blocks of DNA.'

No Shows in Rio

A recent international event held every few years was marred by serious lapses in organization, inadequate transportation and random acts of violence against attendees. No, not the centennial Olympic Games in Atlanta, but the Ninth International Congress of Human Genetics (ICHG), held in Rio de Janeiro in August. At least a dozen invited speakers and session organizers failed to turn up, causing the cancellation of at least two entire symposia and decimating several others. Many speakers, invited well over a year in advance to attend the congress, said they were unable to obtain confirmation from the organizers until just weeks before the meeting. Other scientists were asked to fill in at the last minute and arrange workshops following sudden cancellations. Whether it was the expense of Rio de Janeiro, the crime (at least two groups of conference delegates were mugged at knifepoint on the Copacabana), or the glut of conferences that prompted people to stay away, sadly only about a third of the thousands of delegates expected turned up. The Organizing Committee is now entertaining bids for the site of the next ICHG meeting, scheduled to be held in 2001. The Rio fiasco suggests that it should be held in conjunction with the rapidly improving European Society for Human Genetics conference, or the annual American Society of Human Genetics meeting, as happened successfully in 1991 in Washington D.C. — or not held at all.

The Double Helix Revisited

In 1953, the structure of DNA was solved by Francis Crick, James Watson ... and Dr Jason Waters, the brilliant third man on the team who was mysteriously passed over when the Nobel Prizes were awarded nine years later. This is the premise of *Threshold* (HarperCollins, New York; $24), the debut novel by Harvard graduate Ben Mezrich whose résumé, which includes stints as a cartoonist and legal researcher, does not immediately suggest that the author has what it takes to write a successful thriller in the mold of Michael Crichton on gene mapping and genetic engineering. In the book, Dr Waters is head of the secretive Tucsome Project for Genetic Research. Tucsome comes under the scrutiny of a young medical student named Jeremy Ross, after his ex-girlfriend's father, the Secretary of Defense no less, dies under mysterious circumstances exhibiting self-mutilation symptoms eerily reminiscent of Lesch-Nyhan syndrome. Ross' heroic qualities are never in doubt, from the moment he stuns his fellow residents in the emergency room by saving the life of one of the New York Knicks basketball team, whom he diagnoses with haemochromatosis. His Ph.D thesis, on the use of HIV-1 as a vector for gene therapy, was published in the *New England Journal of Medicine*. When Ross discovers that the ex-defence secretary had high levels of retrovirus in his blood, he becomes obsessed with solving the crime while averting worldwide catastrophe — and naturally winning back his glamorous ex-girlfriend — in the process. *Threshold* is nothing if not fast-paced, but aside from the clichéd characterizations there are a surprising number of glaring scientific errors. A marker on chromosome 13 is termed 'D78G452'; the most common flaw in the cystic fibrosis gene is described as a 'four-base mutation'; worse yet, the premise of Dr Waters' nefarious activities is hopelessly flawed. Mezrich says that his book 'is not meant to disparage ... the Human Genome Project, [which] overshadows everything else in the history of science,' and he proclaims the 'utmost respect' for the people working on it. After reading *Threshold*, the feeling may not be mutual.