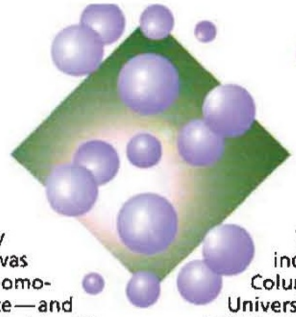
TOUCHINGbase



Hairy genetics

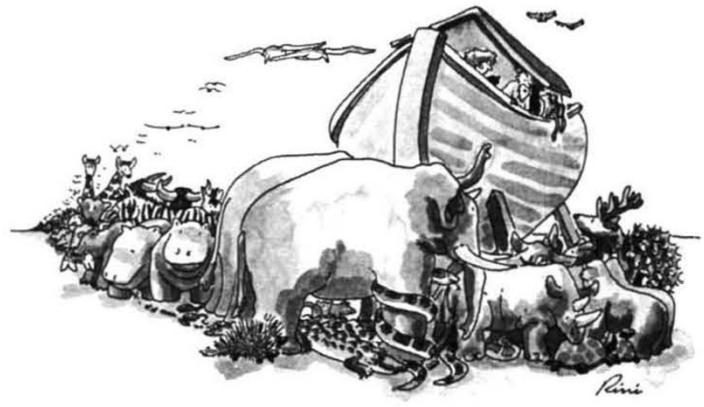
The first gene defect causing human hereditary hair loss has been identified by a research team led by Angela Christiano at Columbia University, New York. There are several forms of hereditary baldness—known collectively as alopecias—the most extreme example being alopecia universalis (AU), where sufferers have a complete lack of scalp and body hair. In the hunt to find the AU gene, the locus was mapped to a region that contains the human homologue of the gene mutated in hairless mutant mice—and mutations in this gene were subsequently identified in AU patients. These findings, published in 30th January issue of *Science*, will ruffle hairs in dermatology circles, which have long considered hereditary alopecias as autoimmune diseases, rather than a consequence of single gene defects. While an immunological component may still be involved, Colin Jahoda (University of Durham, England) believes these findings will shift the focus towards looking for genetic mechanisms underlying other forms of hair loss in humans and naturally-occuring bald mice whose aetiology is yet to be revealed. Putting *hairless* back into hair should be 'relatively straightforward', according to Christiano, particularly as topical application of liposomes has previously been shown to be an effective means of gene delivery into hair follicles. While a cure for alopecia seems within reach, it is not so simple for more common forms of hair loss, such as androgenetic alopecia, better known as male pattern baldness. Despite optimism in some pharmaceutical quarters that this may also be a single gene defect, Christiano's research so far suggests that it is likely to be yet another complex polygenic disease that plagues man, possibly involving several susceptibility loci. So, although research into the genetics of the hair cycle is in its growth phase, it may some time before we can open a jar and smear on a new head of hair.

Mitochrondrial pseudo-mutations?

A large proportion of Alzheimer's disease (AD) cases were reported to be associated with mutations in the two mitochondrial genes, *CO1* and *CO2*, which encode the catalytic core of cytochrome c oxidase (CO), a key enzyme in the cell's energy-producing machinery (*Proc. Natl. Acad. Sci. USA* **94**, 4526–4531). These findings have now been challenged by two independent research teams lead by Eric Schon of Columbia University and Doug Wallace of Emory University (*Proc. Natl. Acad. Sci. USA* **94**, 14894–14899, 14900–14905). They conclude that the 'AD mutations' are most likely sequence variants of nuclear-encoded 'pseudogenes', which migrated from mtDNA to the nuclear genome early in hominid evolution, and are therefore likely to be of no functional significance. The new reports suggest that the earlier findings may have resulted from artifactual PCR amplification of 'mtDNA-like sequences' embedded in the nuclear genome. This will come as a blow to researchers at the San Diego biotech company MitoKor who are currently developing a diagnostic test for AD based on the mutation assay. It is also a warning to other research efforts aimed at identifying mitochondrial mutations associated with human diseases. With approximately 1000 mtDNA-derived sequences estimated to be integrated into the nuclear genome and the increasingly sensitive analytical techniques for detecting low-frequency mutations, there is a growing risk for sequence variants of 'mtDNA pseudogenes' being mistakenly interpreted as pathogenic mutations.

Whose chips are they anyway?

The fight about intellectual property issues of DNA-chip technology has taken another twist: Incyte Pharmaceuticals, Inc., recently announced a definitive agreement to acquire Synteni and their flagship GEM (Gene Expression Micro-Array) technology. Incyte, a genomic database company, has, in the past, had a friendly working relationship with Affymetrix Inc., another DNA-chip company. Affymetrix has now announced the filing of a patent infringement suit against Synteni and Incyte; "it's just another move in a chess game", according to Bob Lipshutz of Affymetrix. Based on their past experience with Incyte, Affymetrix still hopes to "reach an agreement with them that provides a fair compensation to Affymetrix for the use of our intellectual property", but they have obviously decided to sue first and talk later. A third player in this sunny but not so tranquil Californian (mine)field is Hyseq, Inc. Hyseq has filed two lawsuits last year against Affymetrix; both of them covering Affymetrix' entire product line. It looks like all we need is for Synteni to chip in and sue Hyseq, and we'll have everyone chasing each other's tails.



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"Actually, we're only taking tissue samples."

Leaps and bounds for the dog genome project

A comprehensive canine genetic map is nearing completion, through collaborative efforts of researchers led by Elaine Ostrander at the Fred Hutchinson Cancer Research Center, Seattle, Gustavo Aguirre at the James A. Baker Institute for Animal Health at Cornell, and Jasper Rine at the University of California, Berkeley. The recently-published 'first-generation' map (*Genomics* **46**, 326–396) covers 70% of the genome and was generated from the typing of 150 informative microsatellite markers on a panel of three-generation canine pedigrees of different breeds. With complete coverage of the genome to be finished in the very near future, the next step is aimed toward establishing a synteny map between humans and dogs and the identification of genes involved in heritable canine disease. The outcome of this research will be embraced by the dog breeding community, which already utilises commerically available DNA-testing kits for establishing parentage and pedigree and for the diagnosis of several genetic diseases. Many of the diseases suffered by dogs also occur in humans, including epilepsy, retinitis pigmentosa and cancer. As dogs have larger familes and are much less genetically heterogenous than humans, man's best friend offers a powerful genetic means of sniffing out those elusive disease genes in humans.