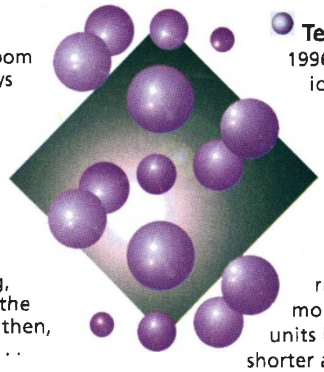
TOUCHING**base**



Genome Jingle

Whatever the task — from long days in the cold room purifying proteins to what may feel like longer days grant writing — Ira Herskowitz (University of California at San Francisco) has put it to music. For now, you can hear these well-known tunes with entertainingly novel words (but intimately familiar themes) if you are lucky enough to attend a meeting where Ira has guitar in hand — such as the recent *Yeast Genetics and Human Disease* Meeting held in Baltimore. You can also check out his first recording, released in 1993 with his twin brother, Joel (on the Cold Spring Harbor Laboratory Press label). Until then, here's one for all you 'genome jockeys' out there . . .

I've Been Workin' on the Genome
—Words by Ira Herskowitz to the tune of
I've Been Workin' on the Railroad.

Refrain:
I've been workin' on the genome
All the live-long day
I've been workin' on the genome
Just to pass my time away
Can't you hear the buffers flowin'
Gels run dusk 'til dawn
Then you read the sequence ladders
It goes on and on
A megabase to go, a megabase to go
A megabase to go 'til dawn
A megabase to go, a megabase to go
A megabase to go 'til dawn

Someone's got the Huntington gene, don't they
Someone's got the gene, I know
Someone's got the Huntington gene, don't they
Now they're callin' up the *New York Times*
[Refrain]
Walkin' down chromosome quatro
We're walkin' but it's mighty slow
We're walking down chromosome quatro
Sequencing as we go
Readin' A G C C T
A A A A A A A
A A A A A
Sequencing junk DNA
[Refrain]

The Urge to Ingest

Another bullet in the battle of the bulge has struck its target with the publication of a report in *Science* by J. Erickson, G. Hollopeter and R.D. Palmiter that shows that *ob/ob* mice lacking neuropeptide Y, though still larger than normal mice, are significantly less obese and more energetic than comparable *ob/ob* mice that still produce the peptide. In addition to increased energy expenditure, the double mutants had a lower rate of food intake. Jeffrey Friedman (Rockefeller University), who discovered the leptin (*ob*) gene, told the Associated Press that the finding was important as it "establishes a direct link between some of leptin's effects and neuropeptide Y." However, he cautioned that that this work links only two of the elements that control body weight, and that the relationship between the chemicals involved "is a complicated one." For instance, loss of neuropetide Y does not completely restore *ob/ob* mice to normal, nor does its complete absence have any discernible effect on weight and energy metabolism in normal mice, suggesting other mechanisms can compensate for its loss. "NPY is the reason for about half of the obesity caused by a lack of leptin," said Erickson to reporters."It is only part of the puzzle. There are other elements that stimulate the urge to eat." Research to ferret out these other elements continues.

Tense, Nervous Gene?

1996 was a successful year on the whole for behavioural geneticists, what with strong claims for genetic effects underlying traits such as Novelty Seeking, well-being and, as described in the November 29 issue of *Science*, neuroticism. Klaus-Peter Lesch and colleagues administered personality tests to more than 500 subjects (mostly men), and found that a polymorphism in the serotonin receptor is associated with neurosis. (The polymorphism is a variation in the number of repeat units in the promoter region of the transporter; the shorter allele is associated with lower transcription and reduced serotonin uptake.) As with the Novelty Seeking studies published at the beginning of last year, the proposed genetic effect is very subtle — accounting for just a few percent of the total variation in mood — and the authors stress that there are likely to be many other genetic and environmental factors involved in modulating a person's level of tension and nervousness. About 70% individuals carry the shorter, anxiety-associated allele, prompting some observers to question the likely evolutionary advantage of such a common variant. Dean Hamer, one of the co-authors of the new study, speculates that anxiety-ridden people may have more sex than others, whereas colleague Dennis Murphy believes that anxiety may sharpen the wits of those with a fear of public speaking.

Banking on *ATM*

For the past 20 years or so, Michael Swift of the New York Medical College has studied the possible cancer risk associated with carriers of the gene for ataxia telangiectasia, a severe neurological and cancer-associated condition. In particular, there has been considerable interest on whether women who carry this gene, *ATM*, are more susceptible than average to breast cancer, particularly because the estimated carrier frequency of *ATM* is at least 1%, and there are concerns that carriers might be susceptible to radiation as used in mammography. Last month, Swift's team published the results of a small study which they believe supports this notion (Athma, P. *et al. Cancer Genet. Cytogenet.* **92,** 130-134; 1996). Using flanking markers (rather than analysing the *ATM* gene directly), Swift's group determined the carrier status for 33 breast cancer cases from 28 known AT families. Twenty-five of the women who had developed breast cancer (between the ages of 31 and 77) were carriers, significantly more than the expected number of about 15, and calculated a relative risk for carriers compared to non-carriers of 3.8. "The AT gene occurs much more frequently in the population than the *BRCA1* and *BRCA2* genes", says Swift, "so although individual carriers of one mutated AT gene have a smaller excess risk of breast cancer than carriers of *BRCA1/BRCA2* mutations, the AT gene is probably responsible for six or seven times the number of cases caused by these highly publicized genes." That number may amount to more than 6%, Swift estimates. However, Swift acknowledges that population screening for mutations at all gene loci potentially associated with breast cancer, including *ATM*, is a priority.

Laid Back Linkage

The press release issued by *Science* magazine last November heralding the localization of *HPC1*, a gene for hereditary prostate cancer (discussed in more detail by M-C King on page 8), contained one slight but significant lapse. "Smith et al.", the statement read, "have tracked down what appears to be the general location, or locus, of a gene that confers susceptibility to prostrate [*sic*] cancer."