be aborted at mitosis 13 without ever yielding a completed product. Cytoplasmic transcript finally appears about 20 minutes after mitosis 13, consistent with the expected transcription time of 16 minutes. To test whether this expression delay is due to transcript length, Rothe *et al.* trimmed the 23-kb *knirps-related* gene to 3 kb by removing the introns. This abridged version of *knirps-related* produces cytoplasmic transcripts and a protein product within cycle 13, confirming the adverse effect of gene length in a short cell cycle.

Size

The abridged version of *knirps-related* partially complements a *knirps* mutation, demonstrating that the *knirps-related* product has a modest amount of *knirps* function. It is, however, unclear why the endogenous full-length *knirps-related* gene does not express this function. There are numerous differences between the endogenous gene and the cDNA transgene (note that transgene expression is driven by the 5′ regulatory region of *knirps* and the *knirps* promoter), but one of them — the reduced size of the transgene — points to an explanation that fits the molecular results to a T. As the authors argue, by precluding early expression of completed product, the size of the endogenous gene might prevent expression of *knirps* function.

A gene must be small to be expressed in short cell cycles, but why is *knirps-related* large? Although its involvement in head development occurs later, there is no obvious reason to preclude early expression of *knirps-related.* Because its transcription pattern roughly parallels that of *knirps*, early production of a completed *knirps-related* product should simply provide a redundant *knirps*-like function.

More generally, why should any gene be large, if size compromises function? There are many possible reasons — it might be important to preclude expression of large genes during rapid cell cycles, or delay expression in slower cell cycles, or introduce a temporal lag in a cascade of transcriptional control — but an example of any of them remains to be documented. □

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HUMAN GENOME PROJECT

Mapping the way ahead

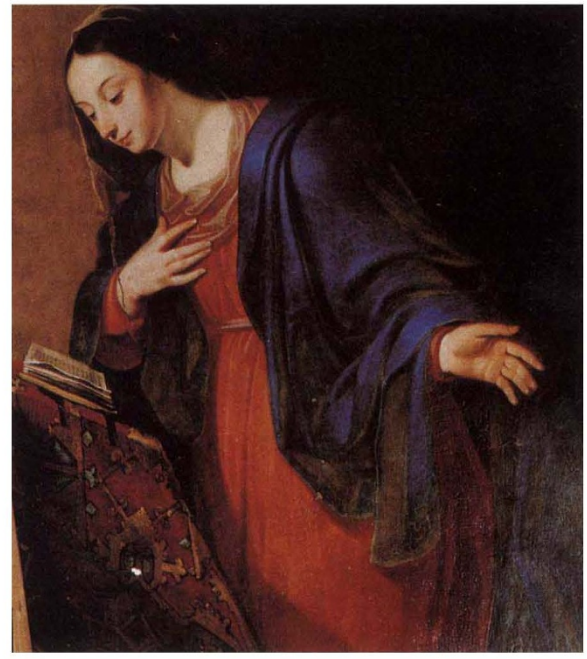
Peter Little

A REALISTIC solution to a long-standing problem in the Human Genome Project emerges this week with the publication of maps of most of two human chromosomes — chromosome 21, described on page 380 of this issue[1], and the Y chromosome, described in *Science*[2]. The Human Genome Project has a major mid-term goal, which is to construct a map of the whole human genome, and much debate has centred on the nature of this map. Should it be a physical map of restriction sites; should it be a recombination map; or should it be a map of cloned DNAs organized into overlapping arrays (so-called cloned DNA maps)? There are many models for all of these types of map. But opinion has been forming around the ideas that it should be a cloned DNA map and, because the genome is large, that yeast artificial chromosome vectors should be the cloning system; such vectors can carry up to 2 million base pairs of passenger DNA.

The two papers are the first indication that the debate has been resolved. What is exciting about them, apart from reporting the generation of the first such maps of human chromosomes, is that they both elegantly demonstrate that a reasonably simple approach can be applied to any genome without having to construct complicated libraries from individual chromosomes.

The work on the human Y chromosome, from the laboratory of David Page, and that on chromosome 21, from the consortium led by Daniel Cohen, both employ sequence tag sites[3] (STS) to generate the map. An STS is a short sequence of DNA that can be amplified using the polymerase chain reaction (PCR). STS have been positioned throughout the human (and many other) genomes and it is possible to carry out multiple PCR reactions with very little effort. The figure overleaf shows how STS can be used to construct a set of overlapping yeast artificial chromosome (YAC) clones that collectively represent

Soft option for pigment analysis



Q-TIPS or cotton buds (depending on where you come from) may come to the aid of art restorers and historians, if a technique developed by Luc. J. Moens, Wim J. Devos, Alex von Bohlen and Reinhold Klockenkämper, is taken up. Working at Ghent University and the Institute for Spectrochemistry, Dortmund, the researchers find that it is possible to analyse the few grains of pigment picked up by a clean, dry cotton bud wiped over the surface of a painting, and to get an elemental breakdown of their composition. The novelty is in the use of total reflection X-ray fluorescence, a technique which maximizes the efficiency with which X-rays excite the sample atoms to fluoresce. The simplicity of this benign method makes it an excellent alternative to the usual non-destructive (or *in situ*) techniques, which involve handling whole paintings. The workers have already used the approach in preparation for restoring several paintings, including *The Annunciation*, shown here, by the seventeenth-century Flemish master Van den Heuvel. Something like 'ultramarine sickness' has afflicted the painting, turning the deeper blue of folds in the cloak greenish. The analysis reveals the presence of smalt ($CoAs_2$) in the discoloured parts, which has probably been altered by moisture and carbon dioxide. R. P.