WEB WATCH

Genetics policy

The ethical, legal and social implications (ELSI) of genetics rightly occupy a central position in genetics research. But what progress is being made with these issues? Which organizations are making the key statements, and how are they likely to influence policy-making in human genetics? The website HumGen has been launched to help interested parties to navigate through the wealth of ELSI information and research. The stated aim of HumGen is to put scientists, policy-makers, legislators, industrialists and the general public in touch with "credible, relevant policy statements on topics related to human genetics around the world".

The project director of HumGen is Bartha Maria Knoppers, a professor at the Public Law Research Centre (CRDP) of the University of Montreal. She leads a substantial team, drawn mainly from the CRDP, to maintain and develop HumGen.

The information in HumGen is divided into three main areas. The current-awareness function of HumGen is served by GenInfo, which provides information such as recent statements and press releases. GenBiblio is a search engine that allows users to find and collate archived information. Finally, GenConnect provides contact information for over 200 organizations (governmental and non-governmental) that provide the statements that are made available at HumGen.

The site is attractively designed, simple to navigate and should become a valuable portal to information on the full range of implications of genetics research.

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Links

WEB SITES Center for Bioethics at the University of Pennsylvania and The Eubios Ethics Institute

HUMAN GENETICS

Expanding insight into myotonic dystrophy

Myotonic dystrophy (or dystrophia myotonica, DM) — the most common adult muscular dystrophy in humans — has a complex, dominantly inherited pathology caused by a triplet repeat (CTG) expansion in the 3′ untranslated region (UTR) of the serine-threonine kinase-encoding *DMPK* gene. Certain aspects of this disorder have been accounted for in previous mouse models of DM, apart from the myotonia (hyperexcitability) of the skeletal muscle. A recent paper now indicates that this characteristic of DM is not mediated by the *DMPK* gene itself but by a toxic gain-of-function effect caused by the expanded CUG repeat in the mutant *DMPK* mRNA.

Because inactivating *Dmpk* in mice causes muscle weakness but not myotonia, Mankodi *et al.* assayed for the phenotypic effects of the untranslated repeat by expressing 250 CUG repeats in the 3′ UTR of a human actin transgene. The expression of this transgene in mouse skeletal muscle caused myotonia by four weeks of age and mortality in 41% of the mice by 44 weeks of age — effects that were not seen in mice expressing a short-repeat actin transgene.

Why is the CUG repeat toxic? So far, this remains unknown. The expanded repeat sequesters the mutant transcript in the nucleus (shown in green and blue, respectively, in the picture), where Mankodi *et al.* speculate it might

GENOME EVOLUTION

Arabidopsis 4, Tomato 1

Although the lineages of the *Arabidopsis* and the tomato families separated about 112 million years ago, what their respective genomes have being doing since is witnessed in the order and the number of the genes that they share. A comparison of the genomes of *Arabidopsis* (Familia Brassicaceae) and tomato (Familia Solanaceae) should open a window on how plant genomes have evolved since the radiation of dicotyledonous plants — knowledge that can be extended to the important crops (sunflower, coffee and cotton) that fall in the *Arabidopsis*/ tomato clade.

Ku and colleagues sequenced a 105-kilobase bacterial artificial chromosome (BAC) from tomato chromosome 2. Of the 17 predicted ORFs found in the BAC, 12 cross-matched repeatedly not to one, but to four separate *Arabidopsis* regions (on chromosomes 2, 3, 4 and 5). The individual *Arabidopsis* segments contain incomplete but overlapping subsets of the 12 ORFs found on the tomato BAC; furthermore, the ORFs are arranged in the same relative order in all segments (including the BAC). The simplest explanation for this finding is first, that there have been two rounds of large-scale duplications (perhaps even polyploidy) in the *Arabidopsis* lineage since it diverged from tomato and second, that all segments have derived from an ancestral, tomato-like template that predates the divergence of tomato and *Arabidopsis*.

The preserved gene order also tells us that chromosomal rearrangements (for example, inversions, translocations and transpositions) had a relatively minor role in shaping the evolution of the plant genome, which is conducted instead by repeated rounds of genome duplication followed by progressive gene loss.

The data reveal more. Despite the seven-fold difference in the genome size of tomato and *Arabidopsis* (900 versus 120 megabase pairs) there is no evidence from the homeologous segments examined here that tomato genes are scattered more sparsely. If we were to believe that the BAC is representative of the tomato genome as a whole, it would take 145,000 genes to make a tomato!

Where does research go from here? The idea that polyploidy has been an important contributor to the evolution of the *Arabidopsis* lineage should lead us to search for evidence of duplication elsewhere in its genome. In fact, earlier this summer, Grant and colleagues reported a comparative mapping study between soybean and *Arabidopsis*, using conceptual amino-acid comparisons. This allowed them to resolve large regions of conserved synteny between soybean and *Arabidopsis* and to identify regions suggestive of polyploidy in *Arabidopsis*.

More questions emerge: do other dicots also show signs of duplications? Are we likely to uncover more and more polyploid events as comparisons are made between genomes

A medley of tomato (genus *Lycopersicon*) varieties. Courtesy of Claudia Schmidt, Tomaten im Web.