GENOMICS

Of mice and… fish

Fugu rubripes, a small South-East Asian fish, was proposed ten years ago as a genomic model vertebrate whose small genome could aid the understanding of vertebrate genome evolution and the functional study of complex genomes. Aparicio *et al.* now report the sequence of ~95% of the *Fugu* genome. Their analysis hints at the mechanisms that might be responsible for the compactness of *Fugu*'s genome, and its comparison to the human genome reveals aspects of genome and protein evolution.

At 365 Mb, *Fugu*'s genome — sequenced to around sixfold coverage using the shotgun method — is one-eighth of that of human's. This difference is mainly due to smaller intergenic regions and introns, which seem to be kept trim by frequent deletions. In the absence of experimental data, annotation of the genome was homology based, and ~33,000 genes have so far been predicted — closely matching the number estimated for humans. As in the human genome, gene density varies across the *Fugu* genome and, because of smaller introns, most *Fugu* genes are smaller than their human orthologues, although the intron–exon structure of most genes is preserved. However, some 'giant' genes (with large introns) have also been found, which the authors speculate might shed some light on the balance between gain and loss of DNA and therefore in genome evolution. Although many segments are conserved between the *Fugu* and human genomes, gene order has been considerably scrambled.

Differences between the *Fugu* and human proteomes reflect differences in physiology, but also highlight systems that are rapidly evolving in humans, such as T-cell-mediated immunity. Although there are more similarities than differences, ~25% of the human proteome does not have a *Fugu* counterpart.

So, *Fugu* has passed the test as a genomic model organism, and this first analysis of the whole genome sequence has already provided a wealth of information on vertebrate genome and proteome evolution.

Fugu's genome is the first publicly available vertebrate genome sequence after that of the human genome, and it is the first large genome to be sequenced that didn't rely on a physical map. But maps aren't only useful for genome sequencing, they are a valuable resource in experimental models. Although the sequence of the mouse genome isn't yet complete, Gregory *et al.* report the generation of a mouse physical map.

The authors assembled 296 contigs of overlapping BACs (~9.3 Mb long), thereby providing a nearly complete coverage of the estimated 2.9-Gb mouse genome. When 97% of the mouse BAC map was aligned to the human genome, 88% of mouse clones were collinear. The authors used SSLP and radiation hybrid data to assign 203 clones to individual chromosomes, generating an invaluable resource for the mouse community. Even before the mouse genome is completed in 2005, we can expect further insights to come from the analysis of this physical map and its alignment to the human genome.

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References and links

ORIGINAL RESEARCH PAPERS Aparicio, S. *et al*. Whole-genome shotgun assembly and analysis of the genome of *Fugu rubripes*. *Sciencexpress* 25 July 2002 (DOI: 10.1126/science.1072104) | Gregory, S. G. *et al.* A physical map of the mouse genome. *Nature* 31 July 2002 (DOI: 10.1038/nature00957)

WEB SITES

Fugubase: http://www.fugubase.org

***Fugu rubripes* web sites:** http://genome.jgi-psf.org/fugu3/fugu3.home.html | http://fugu.hgmp.mrc.ac.uk

Mouse map: http://www.ncbi.nlm.nih.gov/genome/guide/mouse

ETHICS WATCH

Genetics, 'family consent' and the law

Genetic information is inherently familial. As such, a person's decision to have a genetic test might raise privacy, confidentiality and stigmatization issues for their entire family or for the cultural group to which they belong. Indeed, the familial nature of genetic information has been identified as one of the characteristics that makes genetic information different from other forms of health information. This biological reality can cause a variety of unique consent dilemmas (Wadman 2000). For example, what if one family member chooses to forego genetic testing, whereas another wants to know his or her genetic risks? The autonomous decision by one family member will inevitably affect that of the other.

As a result, it has been suggested that biological relatives should participate in the consent process in clinical and research settings. For example, Canada's primary research ethics policy, the Tri-Council Policy Statement on *Ethical Conduct for Research Involving Humans*, suggests that, in the context of genetic research, "free and informed consent shall also involve [the participation of biological relatives] as far as is practical and possible."

Given the potential medical and social ramifications of the disclosure of genetic information, it is understandable why this 'family consent' approach has emerged. A 'familial' trait can, for instance, affect the granting of insurance and, rightly or not, individual perceptions of risk and health. However, the idea of 'family consent' conflicts with well-established legal norms, most notably the idea of autonomous consent. In fact, in many jurisdictions, existing legal norms make it very difficult to adopt a 'family consent' approach.

Consent law is a manifestation of Western culture's deep respect for the principle of autonomy. Although exceptions exist (such as in health care emergencies), consent law has continued to reinforce the right and necessity of individual consent before the provision of any health care procedure or participation in a research protocol. From the law's perspective, the interests of third parties, even family members, are not considered. In fact, in most jurisdictions, current consent law suggests that health care providers should follow the informed decision of the competent patient regardless of third-party wishes to the contrary.

As noted above, there are sound reasons for health care providers and researchers to encourage a more inclusive approach to consent. But, unless there is a radical shift away from the autonomy-driven conception of legal consent, clinicians and researchers might find themselves in a legal/ethical bind. On the one hand, they are being asked to include family members in the consent process, while on the other hand, the law focuses on individual consent. Without changes to the overall consent process, it will remain the purview of the individual, not the family.

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REFERENCES Wadman, M. Geneticists oppose consent ruling. *Nature* **404**, 114–115 (2000) | Canadian Tri-Council Policy Statement on *Ethical Conduct for Research Involving Humans* (Medical Research Council, Ottawa, 1998)

WEB SITE

Ethics Watch advisors: http://www.nature.com/nrg/info/ethicswatch.html