Editorial

Human Genomics has, from its outset, included a great deal of evolutionary analysis. The structure of the Editorial Board includes representation from many evolution-based disciplines, including population and quantitative genetics and, of course, evolutionary genomics. This inclusion is the result of an obvious trend in the field of genomics to incorporate more and more evolutionary analysis, not just as an extra frill, but as a central component of the field. The world now has over one hundred complete bacterial genomes, and with the genomes of human, roundworm, multiple fruitflies, mosquito, rice, *Arabidopsis*, pufferfish, mouse, rat, dog, chimpanzee, chicken and a growing number of other multicellular organisms either sequenced or imminent, comparative genomics is coming into its own. Still, one might argue that a journal of *Human Genomics* should focus on its main target, *Homo sapiens*, and leave aside mucking about with the multitude of other species on the planet, most of which many self-respecting *Homo sapiens* individuals might rather target with the bottom of their shoe rather than with a multimillion dollar sequencing project. As a specialist on evolutionary genomics it seems necessary to provide some explanation and justification.

The short answer is that the sequence of the human genome is, by itself, of relatively little importance. Its value lies in the utility of the sequence data for figuring out what the genome does and how it operates. We can use the sequence in experiments to determine when, where and how much a gene is expressed, how it is regulated to create functional effects via proteins or RNA, what its gene products interact with and also to quickly locate candidate loci affecting functions and traits of interest. But we want more than just a collection of observations, no matter how detailed: we want to understand the genome, to know why it is the way it is and how it came to be. We want to know what it means, at the genomic level, to *be* humans, and for that we need to know what it means to be something else. Because so many differences in sequence do not matter, the listing of 3 billion human base pairs alone is not enough. We need to know which differences matter, and for that we need an evolutionary perspective. We need the chimpanzee (and the bonobo, gorilla and orangutan, please!) to tell us what it means to be human, rather than just another great ape. We also need gibbons and colubines, tarsiers and lemurs to tell us what it means to be a great ape, rather than just another primate, and we need the mouse and rat, dog and cat, cow, rabbit and tree shrew, to tell us what it means to be a primate.

As a result of one of the more recent decisions by the National Human Genome Research Institute, we will soon have a marsupial[1] (*Monodelphis domestica*, the grey, short-tailed opossum) to tell us what it means to be eutherian, and presumably we will soon add a monotreme and perhaps another marsupial to solidify the answer. We will also need birds, snakes, lizards, turtles and crocodiles to tell us what it is about our genome that is critical in making us a mammal. Throughout our evolutionary history, as we have become multicellular, developed vertebrae, learned to walk on land and learned to reproduce away from water, we have made critical physiological, behavioural and biochemical leaps, all of which are reflected in our genome and in the genomes of others that shared the ride to various points of divergence.

From large-scale analyses of chromosome structure and rearrangement[2] to fine-scale comparative analysis of individual repeat elements across the genome,[3] the complete human genome is generating new approaches in evolutionary genomics that help us know what the human genome means. And while complete genomes add an obviously new dimension, evolutionary genomics is also expanding rapidly in its other dimension, the extent of biodiversity being sampled. Rapid increases in taxonomic sampling for large genomic regions are important to allow genetic assessment of the historical rate of evolution and functionality of genes and inter-genic regions.[4] From vertebrates alone, we now have around 300 complete mitochondrial genomes, and laboratories such as that of Eric Green (at the National Human Genome Research Institute) are extending this concept to increase sampling of biodiversity from targeted bacterial artificial chromosomes across the nuclear genome. High taxonomic sampling density from many genes means dramatically more accurate phylogenies and dramatically more accurate models of evolution, and these genetic footprints (phylogenetic shadowing) lead to better functional predictions and annotations for the human genome. Evolutionary genomics provides a deeper understanding of human genomics, so scrape off your shoe and pop the goo in your sequencer: you may learn something about yourself.

References

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