Of mice and men

November 2 2011, By Russell Bonduriansky

(PhysOrg.com) -- How have humans and mice changed since we diverged about 75 million years ago from a small, furry common ancestor? Apart from the obvious, of course.

As a starting point, it's worth noting there's nothing magical about a genome sequence – it's merely a very long string of letters representing the sequence of nucleotides in an organism's DNA.

But for evolutionary biologists, this string of letters is a treasure-trove of information about a species' evolutionary history. The recent development of efficient and affordable tools to sequence and compare genomes of different species – reflected in the rapidly accumulating data-bank of "comparative genomics" – has allowed scientists to tap into this amazing resource on a scale scarcely imaginable just a few years ago.

As usual in science, the basic principles are simple.

Every species can be characterised by the unique sequence of nucleotides in its genome, which is the product of gradual, cumulative changes over millions of years. These changes originate as random mutations, but harmful changes are usually weeded out by natural selection, while beneficial or neutral changes tend to persist.

Since all animals diverged from a common ancestor, it's possible to compare the genomes of any two animal species and identify the changes in their DNA that have taken place since those species diverged.

The brainy branch

A new study by Yong Zhang and colleagues at the University of Chicago, published in the journal PLoS Biology, examined how the genomes of humans and mice have changed since we diverged.

More specifically, they asked how many of the new genes that evolved within each lineage since the human-mouse split play a role in the development or functioning of different bodily organs (hearts, eyes, brains, reproductive systems, etc) and developmental stages.

The analysis revealed some intriguing contrasts. In the mouse lineage, the new genes disproportionately affect the reproductive system (particularly the ovaries), muscle and blood.

By contrast, in human lineage, the new genes are disproportionately expressed in the brain's neocortex (and also, curiously, in the salivary gland).

What's more, a closer look at our lineage revealed a large proportion of new genes were devoted to brain function at multiple stages on the evolutionary path: the old-world primates, the apes, and the branch separating ourselves from our closest living relatives, the chimpanzees.

(Unfortunately, the authors do not report corresponding numbers for the chimp branch. Do the chimps have their own set of new, brain-dedicated genes?)

New genes on the block

Now, few scientists will be knocked off their chairs by the news humans are brainier than mice (and, perhaps, also more likely to enjoy an eclectic diet). We already know primates took the unique evolutionary path of enhanced cognition as a solution to life's challenges. The human branch of the primate lineage merely exploited this strategy to the extreme.

We also know the mouse lineage took a very different turn, evolving efficient strategies for feeding, hiding and, most of all, producing prodigious numbers of offspring.

It is to be expected that – for those who know how to decipher the code – the signature of our unusual evolutionary path will be evident in our genome.

But the study by Zhang and colleagues also reveals some intriguing and unexpected details of how we got to be human.

A question long debated by evolutionary biologists is how evolution modifies existing genetic machinery. Zhang and colleagues found our brain evolution was associated with the appearance of many new genes, rather than the mere tweaking of existing genes for new functions.

They also found most of these new genes are expressed in the brains of embryos and infants rather than adults, suggesting that our brains are unique in their pattern of growth and development.

This study showcases the power of the very new field of comparative genomics. But it also exemplifies the power and relevance of the not-so-new field of evolutionary biology.

It illustrates very clearly why we need Darwin's idea of natural selection, and the fertile research program it engendered, to make any sense of our species.