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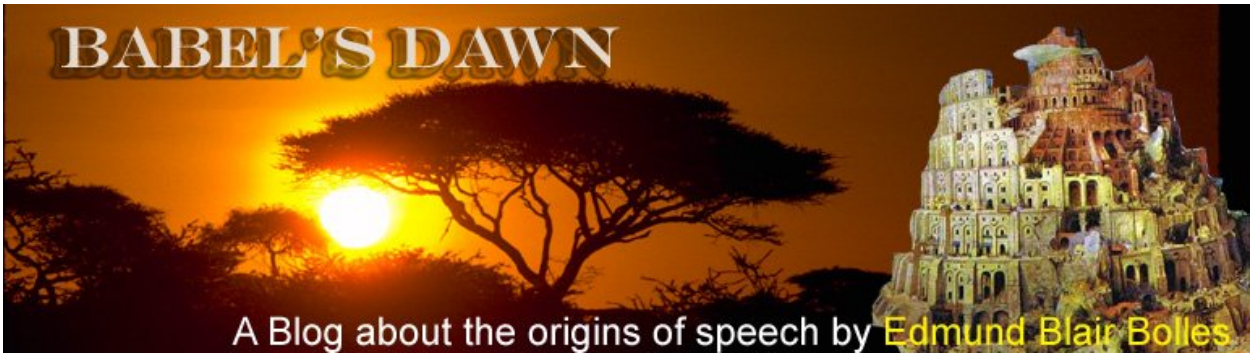
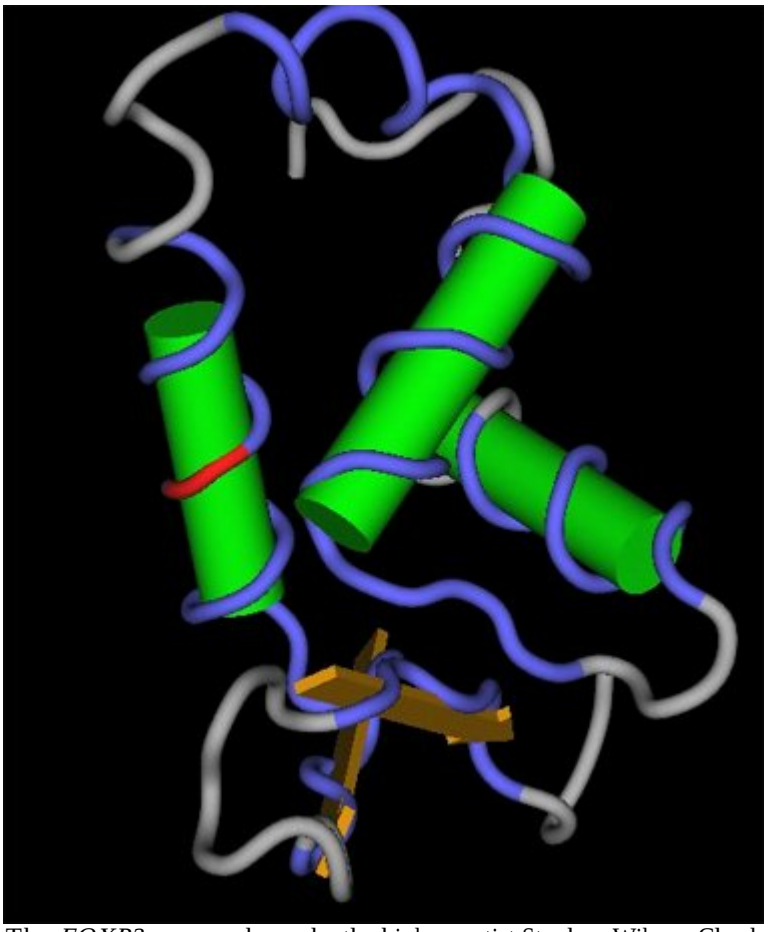


Post of: November 15, 2009

The *FOXP2* Molecular Network Begins Taking Shape



The *FOXP2* gene as shown by the biology artist Stephen Wilson. Check out his work at http://userwww.sfsu.edu/~infoarts/links/isea2006bioartf/art..

A letter to the current issue of *Nature* has caused a stir among those interested in the evolution of language. It looks at the *FOXP2* gene in more detail than any paper has ever done before. It also inspires at least as many questions as it answers, but now at least we have better questions. Also it has dealt yet another blow to the theory that language depends on distinct cognitive modules that permit internal thought and that later interface with motor modules (vocalizing or signing) for "externalizing" what you are thinking. If anything is becoming apparent

from *FOXP2*, it is that language and motor activities are deeply entangled. It also provides more reason to doubt the original recent date ascribe to the gene's mutations.

The letter, titled, "Human-specific transcriptional regulation of C[entral] N[ervous] S[ystem] development genes by FOXP2," was written by a large team represented by Genevieve Konopka and Daniel Geschwind (abstract here). The journal also had a summary article on the study, "The Importance of Being Human," by Martin H. Dominguez and Pasko Rakic (abstract here).

The story so far: The *FOXP2* gene is a highly stable gene, changing very little over millions of years, but it has changed twice since the last common ancestor with chimpanzees and bonobos, and it turns out to be important to the proper development of language. It cannot be directly responsible for speech, however, because it works by regulating the activity of other genes. (See: The Human FOXP2 Gene) The gene's role in vocalization has been strengthened by evidence that FOXP2 is crucial in songbirds for enabling young birds to learn how to imitate the songs of their elders, (see: Birds Also Use FOXP2) and making echolocation sounds in bats (see: The Latest on the FOXP2 Gene). A year ago British researchers identified a "downstream" gene (*CNTNAP2*) regulated by *FOXP2*. Their report ended by saying that their work was a first step in understanding molecular networks affecting language. (See: A Second Gene Supports Language). Now it is time for another step.

What's new: The letter reports a series of experiments. One set (*in vitro*) used human neurons in lab dishes. Their normal *FOXP2* genes were replaced by chimpanzee versions of the gene. The other set of experiments (*in vivo*) used living mice who had their mouse FOXP2 replaced with human genes. The great difficulty of *FOXP2* is that it regulates the operation of other genes. A full understanding of the gene thus requires learning what those downstream genes are, how they are regulated by *FOXP2*, how the changes to human *FOXP2* have altered their operation, and how the downstream genes themselves have changed.

Briefly, the *in vitro* experiments established that chimp and human versions of *FOXP2* have distinguishable downstream effects; the human gene makes some other genes react more strongly, others less strongly, while a third set of genes react the same way to both human and chimp versions of the gene. It sounds pretty banal when reduced to a sentence, but of course knowing which genes react in different ways amounts to a mass of valuable technical data. We now have a list of over 100 genes that act differently in response to human *FOXP2* than to the chimp version. This work ends the determined skeptic's argument that although we can see that the human *FOXP2* is slightly different from chimpanzee versions, there is no proof that the differences are functional. The differences are functional, full stop.

The investigators also established that five downstream genes have altered in the human version and "met the standard criteria … for positive selection on the human lineage" [p. 216]. In other words, not only has the *FOXP2* gene changed, but so have some of the genes it regulates* and the changes were the result of selection rather than drift.

This co-evolution of *FOXP2* and its downstream genes suggests (to my ears) that the recent date for the human version of the gene that originally given must be wrong. The first attempt at dating the gene placed it at less than 200 thousand years ago, more or less contemporary with *Homo sapiens*, but I have previously reported another study placing it at over 1.5 million years ago. And then there is the controversial finding that Neanderthals also had the human *FOXP2* gene. (See: FOXP2 Gene Over 1.5 Million Years Old). If *FOXP2* was a solitary gene that accomplished many things at once, then a recent date would at least seem possible. But a gene that must co-evolve with many other genes is another story. All that takes time.

The *in vivo* experiments used human *FOXP2* in mouse brains to see which areas were altered. The letter summed up their results:

> this study reveals enrichment of differential FOXP2 targets with known involvement in cerebellar motor function, craniofacial formation, and

> cartilage and connective tissue formation, suggesting an important role for human FOXP2 in establishing both the neural circuitry and physical structures needed for spoken language. [217]

More will be coming for many years..

*For the record, the genes in question are: *AMT*, *C6orf48*, *MAGEA10*, *PHACTRA2*, and *SH3PXD2B*.

Links:
Art page: http://userwww.sfsu.edu/~infoarts/links/isea2006bioartf/art.
Genevieve Konopka: http://geschwindlab.neurology.ucla.edu/index.php/people/post-docs/4-post-docs/44-gena
Daniel Geschwind: http://geschwindlab.neurology.ucla.edu/
Abstract of paper: http://www.nature.com/nature/journal/v462/n7270/abs/nature08549.html
Pasko Rakic: http://rakiclab.med.yale.edu/
Abstract of summary article: http://lib.bioinfo.pl/auid:8457703
The Human FOXP2 Gene: http://ebbolles.typepad.com/babels_dawn/2006/10/the_human_foxp2.html
Birds Also Use FOXP2: http://ebbolles.typepad.com/babels_dawn/2008/01/birds-also-use.html
The Latest on the FOXP2 Gene: http://ebbolles.typepad.com/babels_dawn/2007/09/the-latest-on-t.html
A Second Gene Supports Language: http://www.babelsdawn.com/babels_dawn/2008/11/a-second-gene-supports-language.html
FOXP2 Gene Over 1.5 Million Years Old?: http://www.babelsdawn.com/babels_dawn/2009/03/foxp2-gene-over-15-million-years-old.html