Foxp2 lab

Abstract:
The signalling pathways controlling both the evolution and development of language in the human brain remain unknown. So far, the transcription factor FOXP2 (forkhead box P2) is the only gene implicated in Mendelian forms of human speech and language dysfunction1–3. It has been proposed that the amino acid composition in the human variant of FOXP2 has undergone accelerated evolution, and this two-amino-acid change occurred around the time of language emergence in humans. However, this remains controversial, and whether the acquisition of these amino acids in human FOXP2 has any functional consequence in human neurons remains untested. Here we demonstrate that these two human-specific amino acids alter FOXP2 function by conferring differential transcriptional regulation in vitro. We extend these observations in vivo to human and chimpanzee brain, and use network analysis to identify novel relationships among the differentially expressed genes. These data provide experimental support for the functional relevance of changes in FOXP2 that occur on the human lineage, highlighting specific pathways with direct consequences for human brain development and disease in the central nervous system (CNS). Because FOXP2 has an important role in speech and language in humans, the identified targets may have a critical function in the development and evolution of language circuitry in humans.

Classwork:

1. Go to www.uniprot.org. Find out what Foxp2 does. Which biological process does it participate in? Which reaction does it catalyse?
2. Now switch to http://www.ncbi.nlm.nih.gov/refseq/. What does RefSeq stand for and what does it mean? Search for human foxp2. What is the RefSeq accession number? What is the Foxp2 sequence in FASTA format?
3. Find the chimpanzee Foxp2 sequence in FASTA format. What is the RefSeq accession number? You may need to find the scientific name for the species chimpanzee.
4. Use BLAST to align the two sequences. (https://blast.ncbi.nlm.nih.gov/Blast.cgi) Write down the scores (maximum score), lengths of the alignments, query coverage, percent identity, percent positives and percent gaps. What is the e-value? You do not need to show the whole alignment.
5. What does the dot matrix view look like for the alignment with gap open =11 and gap extension = 1 values? Copy the figure.

6. Where is Foxp2 located in the cell? Which diseases is it involved in? How? By a mutation? Which mutation?
7. Find the cat (Felis catus) Foxp2 sequence.
8. Now align the human Foxp2 with the cat (Felis catus) Foxp2. Note the effect of varying gap open and extend penalties on the alignment. What do these penalties mean? You may modify the alignment parameters by hitting "Algorithm Parameters" at the bottom of the page. Report the alignment scores obtained using BLOSUM62 with the following pairs of gap open and gap extend penalties:
   a. 11, 1
   b. 8, 2
   c. 7, 2
9. Use the default values in BLAST for gap open and gap extension penalties (What are the default vales?) Write down the scores, lengths of the alignments, query coverage, percent identity, percent positives and percent gaps. What is the e-value? Do not show the alignment. What does the dot matrix view look like for this alignment?
10. Find 10 Foxp2 sequences from different organisms (Refseqs). Build a phylogenetic tree for the multiple sequence alignment. Build a logo plot for the active site (where is the active site?).
11. An exciting article about the Foxp2 gene came out in Mol Biol Evolution. 2013 Apr;30(4):844-52. doi: 10.1093/molbev/mss271. Epub 2012 Nov 28. "A recent evolutionary change affects a regulatory element in the human FOXP2 gene". Go over this paper and explain the paper in a few sentences. This paper is quite advanced, so I do not expect you to understand every little detail. Tell me about the main contribution of this paper to science.
12. Here is a new article on Foxp2. Schreiweis C Humanized Foxp2 accelerates learning by enhancing transitions from declarative to procedural performance. Proc Natl Acad Sci U S A. 2014 Sep 30;111(39):14253-8. Go over this article. Explain the paper in a few sentences.

What is the one sentence you can write about Foxp2 after having done this homework?