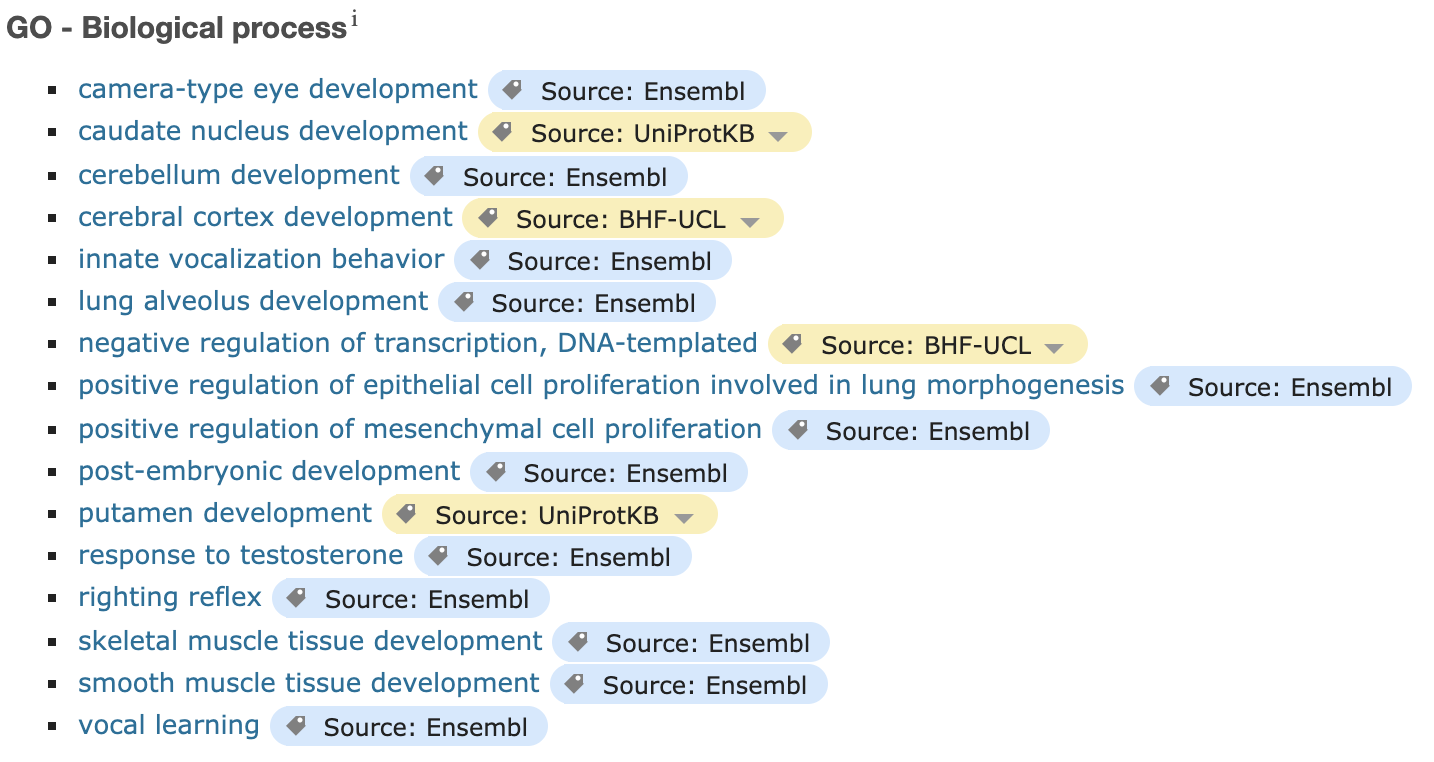
**Report 6 (Foxp2)**

1. **Biological function:**

Transcriptional repressor that may play a role in the specification and differentiation of lung epithelium. May play a role in developing neural, gastrointestinal and cardiovascular tissues. Plays a role in synapse formation by regulating SRPX2 levels. Involved in neural mechanisms mediating the development of speech and language.

**Biological processes where Foxp3 participate:**



1. **Refseq** stands for NCBI Reference Sequence Database. It is a comprehensive, integrated, non-redundant, well-annotated set of reference sequences including genomic, transcript, and protein.

**Human foxp2**

**RefSeq accession number**: NP\_055306.1

**Sequence in FASTA format:**

>NP\_055306.1 forkhead box protein P2 isoform I [Homo sapiens]

MMQESATETISNSSMNQNGMSTLSSQLDAGSRDGRSSGDTSSEVSTVELLHLQQQQALQAARQLLLQQQTSGLKSPKSSDKQRPLQVPVSVAMMTPQVITPQQMQQILQQQVLSPQQLQALLQQQQAVMLQQQQLQEFYKKQQEQLHLQLLQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQHPGKQAKEQQQQQQQQQQLAAQQLVFQQQLLQMQQLQQQQHLLSLQRQGLISIPPGQAALPVQSLPQAGLSPAEIQQLWKEVTGVHSMEDNGIKHGGLDLTTNNSSSTTSSNTSKASPPITHHSIVNGQSSVLSARRDSSSHEETGASHTLYGHGVCKWPGCESICEDFGQFLKHLNNEHALDDRSTAQCRVQMQVVQQLEIQLSKERERLQAMMTHLHMRPSEPKPSPKPLNLVSSVTMSKNMLETSPQSLPQTPTTPTAPVTPITQGPSVITPASVPNVGAIRRRHSDKYNIPMSSEIAPNYEFYKNADVRPPFTYATLIRQAIMESSDRQLTLNEIYSWFTRTFAYFRRNAATWKNAVRHNLSLHKCFVRVENVKGAVWTVDEVEYQKRRSQKITGSPTLVKNIPTSLGYGAALNASLQAALAESSLPLLSNPGLINNASSGLLQAVHEDLNGSLDHIDSNGNSSPGCSPQPHIHSIHVKEEPVIAEDEDCPMSLVTTANHSPELEDDREIEEEPLSEDLE

1. **Chimpanzee foxp2**

**RefSeq accession number:** NP\_001266127.1

**Sequence in FASTA format:**

>NP\_001266127.1 forkhead box protein P2 [Pan paniscus]

MMQESATETISNSSMNQNGMSTLSSQLDAGSRDGRSSGDTSSEVSTVELLHLQQQQALQAARQLLLQQQTSGLKSPKSSDKQRPLQVPVSVAMMTPQVITPQQMQQILQQQVLSPQQLQALLQQQQAVMLQQQQLQEFYKKQQEQLHLQLLQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQHPGKQAKEQQQQQQQQQQLAAQQLVFQQQLLQMQQLQQQQHLLSLQRQGLISIPPGQAALPVQSLPQAGLSPAEIQQLWKEVTGVHSMEDNGIKHGGLDLTTNNSSSTTSSTTSKASPPITHHSIVNGQSSVLNARRDSSSHEETGASHTLYGHGVCKWPGCESICEDFGQFLKHLNNEHALDDRSTAQCRVQMQVVQQLEIQLSKERERLQAMMTHLHMRPSEPKPSPKPLNLVSSVTMSKNMLETSPQSLPQTPTTPTAPVTPITQGPSVITPASVPNVGAIRRRHSDKYNIPMSSEIAPNYEFYKNADVRPPFTYATLIRQAIMESSDRQLTLNEIYSWFTRTFAYFRRNAATWKNAVRHNLSLHKCFVRVENVKGAVWTVDEVEYQKRRSQKITGSPTLVKNIPTSLGYGAALNASLQAALAESSLPLLSNPGLINNASSGLLQAVHEDLNGSLDHIDSNGNSSPGCSPQPHIHSIHVKEEPVIAEDEDCPMSLVTTANHSPELEDDREIEEEPLSEDLE

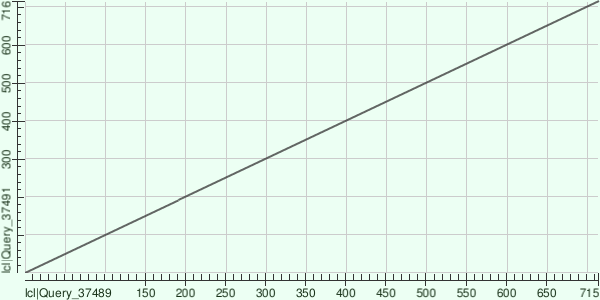
1. **BLAST result (human vs Chimpanzee)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Score | Length | Query coverage | Identity | Positives | Gaps | E-value |
| 1431 | 716 | 100% | 713/716(99%) | 714/716(99%) | 1/716(0%) | 0.0 |

E-value is a parameter that describes the number of hits one can "expect" to see by chance when searching a database of a particular size.

1. **Dot matrix view**

with gap open =11 and gap extension = 1 values



1. **Location in the cell**: Nucleus

**Disease involved**: Speech-language disorder 1 (SPCH1). It is caused by heterozygous mutation in the FOXP2 gene (605317) on chromosome 7q31. The related mutation is p.Arg553His (rs121908377)

1. **Felis catus Foxp2 sequence**

>NP\_001106648.1 forkhead box protein P2 [Felis catus]

MMQESATETISNSSMNQNGMSTLSSQLDAGSRDGRSSGDTSSEVSTVELLHLQQQQALQAARQLLLQQQTSGLKSPKSSDKQRPLQVPVSVAMMTPQVITPQQMQQILQQQVLSPQQLQALLQQQQAVMLQQQQLQEFYKKQQEQLHLQLLQQQQQQQQQQQQQQQQQQQQQQQQQQQQPPPPPPHPGKQAKEQQQQQQQQLAAQQLVFQQQLLQMQQLQQQQHLLSLQRQGLISIPPGQAALPVQSLPQAGLSPAEIQQLWKEVTGVHSMEDNGIKHGGLDLTTNNSSSTTSSTTSKASPPITHHSIVNGQSSVLSARRDSSSHEETGASHTLYGHGVCKWPGCESICEDFGQFLKHLNNEHALDDRSTAQCRVQMQVVQQLEIQLSKERERLQAMMTHLHMRPSEPKPSPKPLNLVSSVTMSKNMLETSPQSLPQTPTTPTAPVTPITQGPSVITPASVPNVGAIRRRHSDKYNIPMSSEIAPNYEFYKNADVRPPFTYATLIRQAIMESSDRQLTLNEIYSWFTRTFAYFRRNAATWKNAVRHNLSLHKCFVRVENVKGAVWTVDEVEYQKRRSQKITGSPTLVKNIPTSLGYGAALNASLQAALAESSLPLLSNPGLINNASSGLLQAVHEDLNGSLDHIDSNGNSSPGCSPQPHIHSIHVKEEPVIAEDEDCPMSLVTTANHSPELEDDREIEEEPLSEDLE

1. **BLAST score (human vs cat)**

|  |  |  |
| --- | --- | --- |
| Open=11, extension=1 | Open=8, extension=2 | Open=7, extension=2 |
| 1396 | 1379 | 948 |

Gap Opening Penalty: The penalty for opening a gap in the alignment. Increasing this value makes the gaps less frequent.

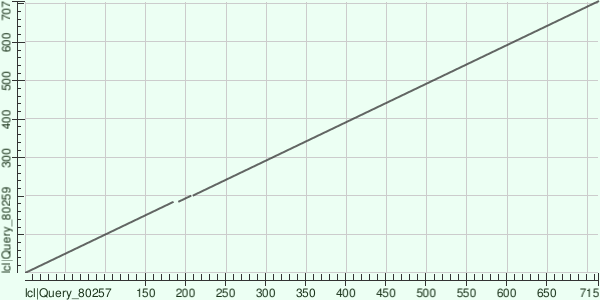
Gap Extension Penalty: The penalty for extending a gap by one residue. Increasing this value will make the gaps shorter. Terminal gaps are not penalized

1. **The default value in BLAST**: gap open 11 gap extension 1

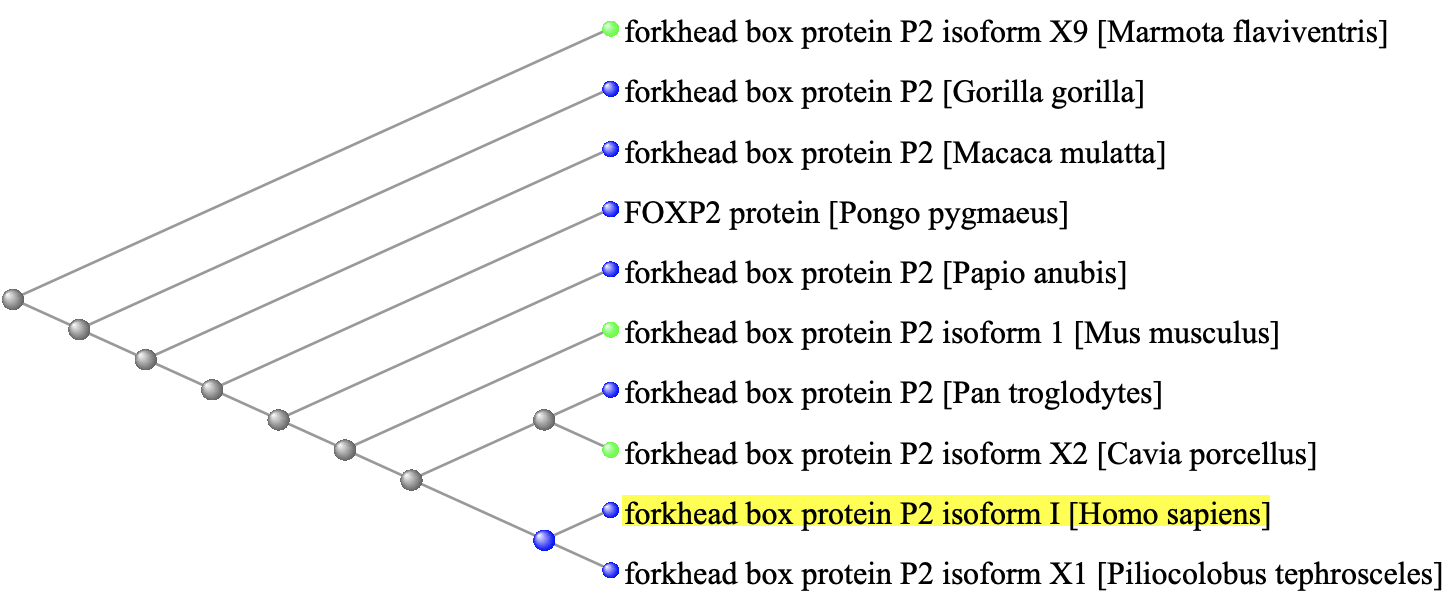
**The BLAST result using the default value**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Score | Length | Query coverage | Identity | Positives | Gaps | E-value |
| 1396 | 707 | 100% | 700/715(98%) | 700/715(97%) | 8/715(1%) | 0.0 |

**Dot matrix view**

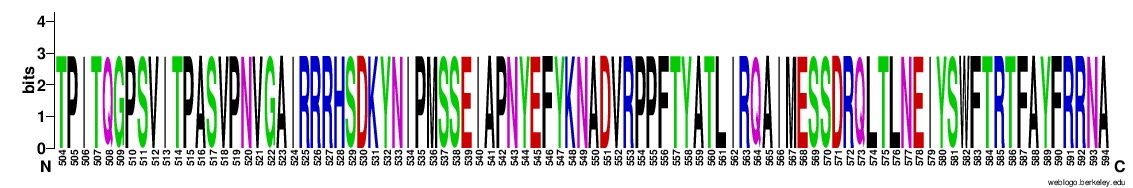


1. **Phylogenetic tree**



For human foxp2, the location of the DNA binding site of is 504-594 (by searching in Uniprot database)

**Logo plot for this site**



The plot shows that this region is highly conserved across the species.

1. The author identified a substitution which is localized in intron 8 of FOXP2 gene and affects a binding site for the transcription factor POU3F2.

This substitution is shared by all or nearly all present-day humans but absent or polymorphic in Neandertals. When exploring the effect of this substation, the author found that the derived allele bound less POU3F2 dimers than POU3F2 monomers compared with the ancestral allele, and performed less efficient than the ancestral allele in driving transcription from the reporter gene. Therefore, the substitution in the POU3F2 binding site is likely to alter the regulation of FOXP2 expression.

Moreover, since it is localized in a region of the gene associated with a previously described signal of positive selection, it is a plausible candidate for having caused a recent selective sweep in the FOXP2 gene. This finding is different from previous studies that at least one of the two amino acid substitutions at positions 303 and 325 in FOXP2 were considered as the cause of the sweep.

1. This paper introduced the amino acid changes that occurred during human evolution into murine Foxp2 and demonstrated the selectivity in the effects of humanized Foxp2 on behavioral learning dynamics as well as on striatal dopamine levels, gene expression levels, and synaptic plasticity. These findings prompt the hypothesis that the humanized Foxp2 phenotype reflects a different tuning of corticostriatal systems involved in declarative and procedural learning.

**One sentence about Foxp2**: highly conserved protein within vertebrates, playing a role in developing speech and language capabilities