Annotating genes and genomes with DNA sequences extracted from biomedical articles

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Which article is analyzing this genomic region?

Which genomic regions are analyzed in this article?

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Identification of *Arx* transcriptional targets in the developing basal forebrain

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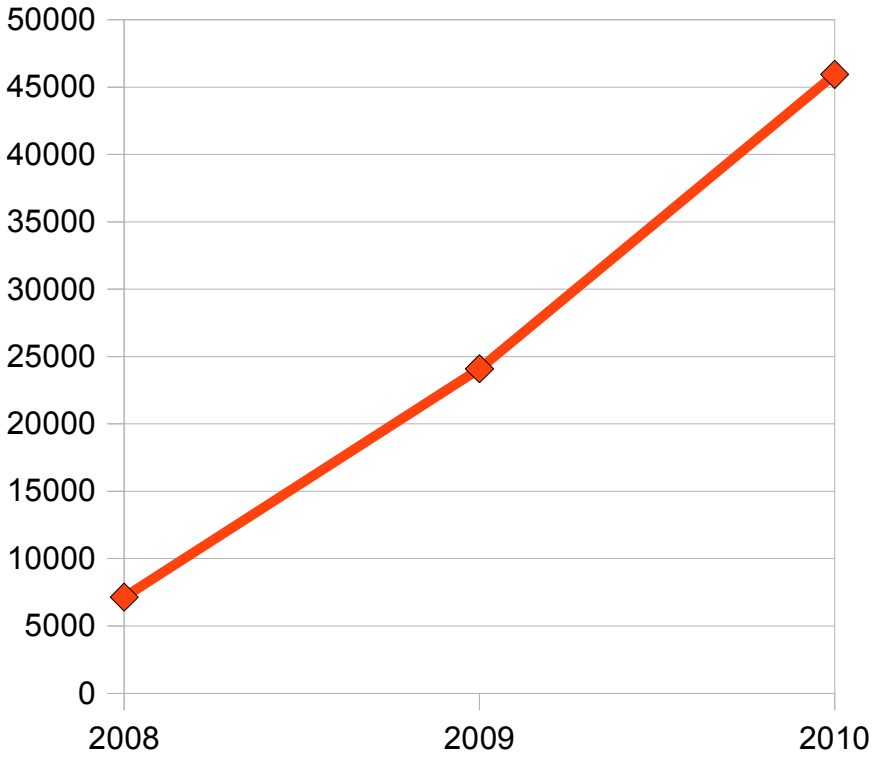
Luciferase reporter assays

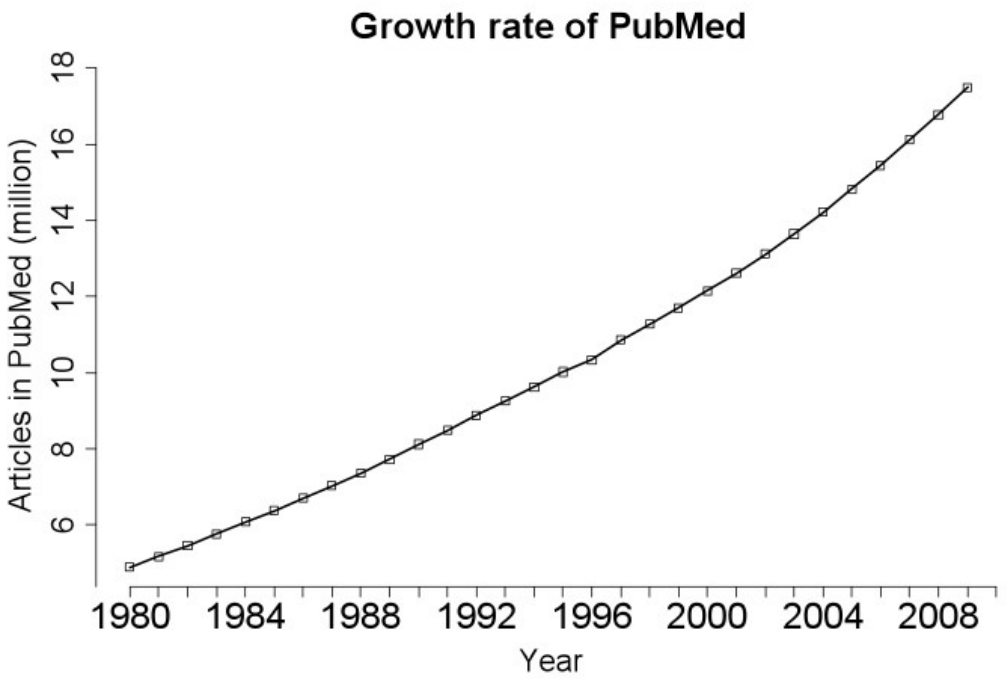
Neuro2a mouse neuroblastoma cells (0.8×10^{-5}) were transfected 24 h after plating with 200 ng of luciferase reporter plasmid DNA, 50 ng of pCDNA3.1-Arx-V5-His (131) or pCDNA3.1-V5-His (Invitrogen) and 50 ng of pRL-TK-*Renilla* luciferase plasmid DNA (Promega) using FuGENE 6 (Roche Diagnostics, Alameda, CA). Forty-eight hours post-transfection, cell lysis and measurement of *firefly* and *Renilla* luciferase activity was performed using the Dual-Glo Luciferase Assay System (Promega) according to the manufacturer's instructions using a Veritus Microplate Luminometer (Turner BioSystems, Sunnyvale, CA). Transfections were performed in quadruplicate, and three independent experiments were performed. The *firefly* luciferase activity was normalized according to the corresponding *Renilla* luciferase activity, and luciferase activity was reported as mean (±SEM) relative to pCDNA3.1-V5-His/luciferase transfection. Luciferase reporter constructs were generated using primer sequences identical to those used for ChIP, modified to include a *Hin*dIII on the 5′ end of the sense primer and a *Bam*HI site on the 3′ end of the antisense primer. These primers were used to PCR amplify product from E14.5 mouse genomic DNA, and the amplified products were cut with *Bam*HI and *Hin*dIII and cloned into the *Bam*HI and *Hin*dIII sites of PPREX3-TK-Luc (Addgene plasmid 1015) (133), which contains the thymidine kinase promoter upstream of luciferase, replacing the PPAR response element.

Five hundred nanograms of GST-Arx (286–430) was incubated with 0.1 pmol of labeled-probe in total 20 μl of binding buffer [20 mM HEPES pH 7.4, 50 mM KCl, 1 mM MgCl2, 1 mM DTT, 5% glycerol, 1 μg poly(dI-dC) (Roche)] for 30 min on ice. In competition experiments, 10 pmol cold probes were added. In antibody supershift experiment, 2 μl of anti-GST antibody (Amersham Biosciences) was added. The mixture was loaded on 5% polyacrylamide gel and electrophoresized (constant 33 mA) at 4°C in 1× TBE. Gels were dried and visualized on a phosphorimager (Molecular Dynamics). Oligonucleotides used were as follows: Ebf3: 5′-GCGATTTTCCCGATTAA TTAAAATATTAACGCA-3′ and 5′-GTGCGTTAATATTTT AATTAATCGGGAAAATCG-3′; Ebf3mut1: 5′-GCGATTTT CCCGATT**CC**TTAAAATATTAACGCA-3′ and 5′-GTGCG TTAATATTTTAA**GG**AATCGGGAAAATCG-3′; Ebf3mut2: 5′-GCGAT**CC**TCCCGATTAATTAAAATATTAACGCA-3′ and 5′-GTGCGTTAATATTTTAATTAATCGGGA**GG**ATCG -3′. Lmo1: 5′-GTAATGAATTGATTTAATTAACAGGGGA GTCTGA-3′ and 5′-GTCAGACTCCCCTGTTAATTAAATC AATTCATTA-3′; Lmo1mut1: 5′- GTAATGAATTGATTT**CC** TTAACAGGGGAGTCTGA -3′ and 5′-GTCAGACTCCCCT GTTAA**GG**AAATCAATTCATTA-3′; Lmo1mut2: 5′-GTAA TGAA**CC**GATTTAATTAACAGGGGAGTCTGA-3′ and 5′- GTCAGACTCCCCTGTTAATTAAATC**GG**TTCATTA-3′; Shox2: 5′-GCAAAATCCACGCTTAATTAAATTAATTAGG GA-3′ and 5′-GTCCCTAATTAATTTAATTAAGCGTGGAT TTTG-3′.

High-throughput versus in-depth analyses

Number of runs submitted to the NCBI short read archive





The identifiers

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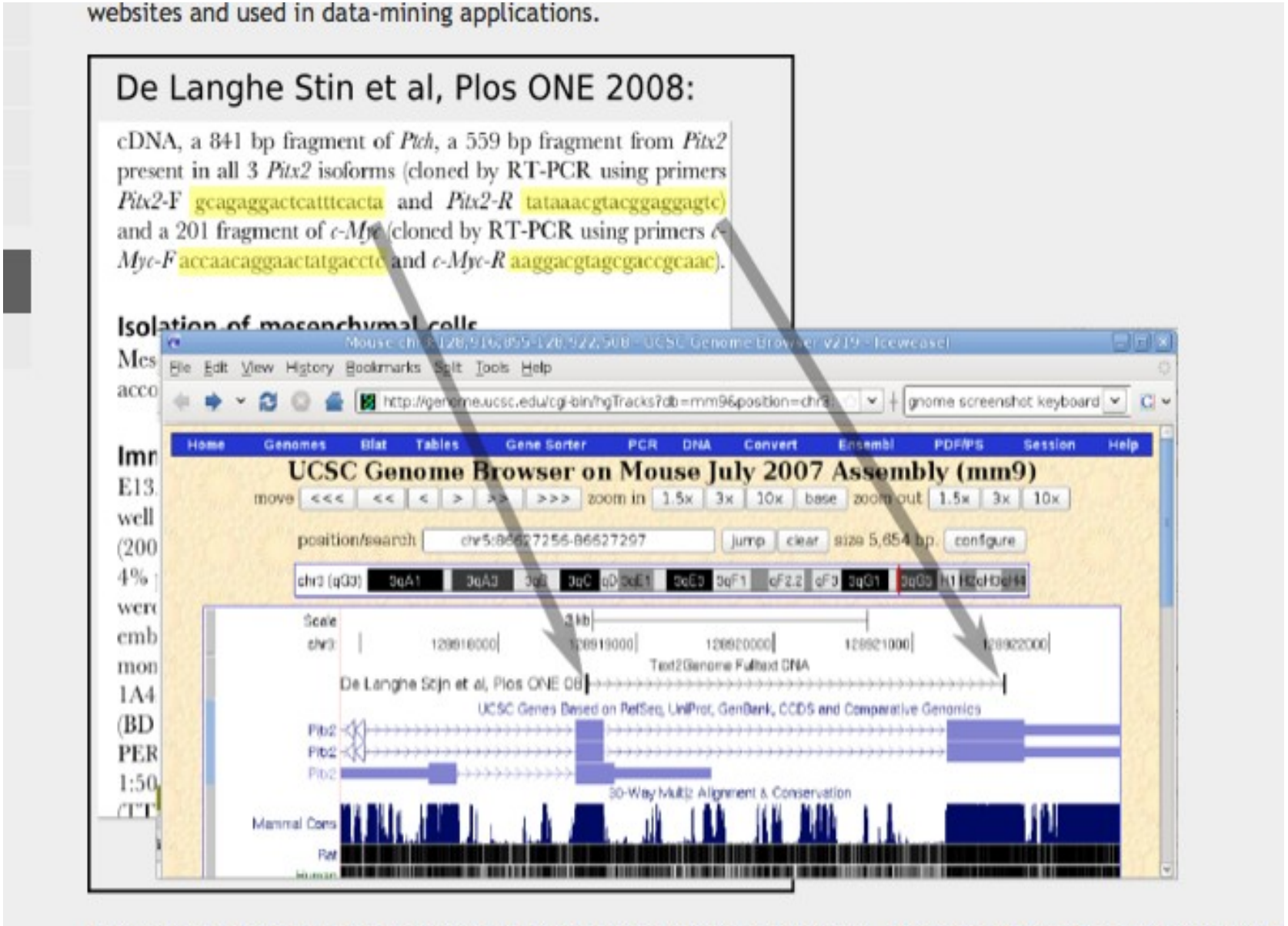
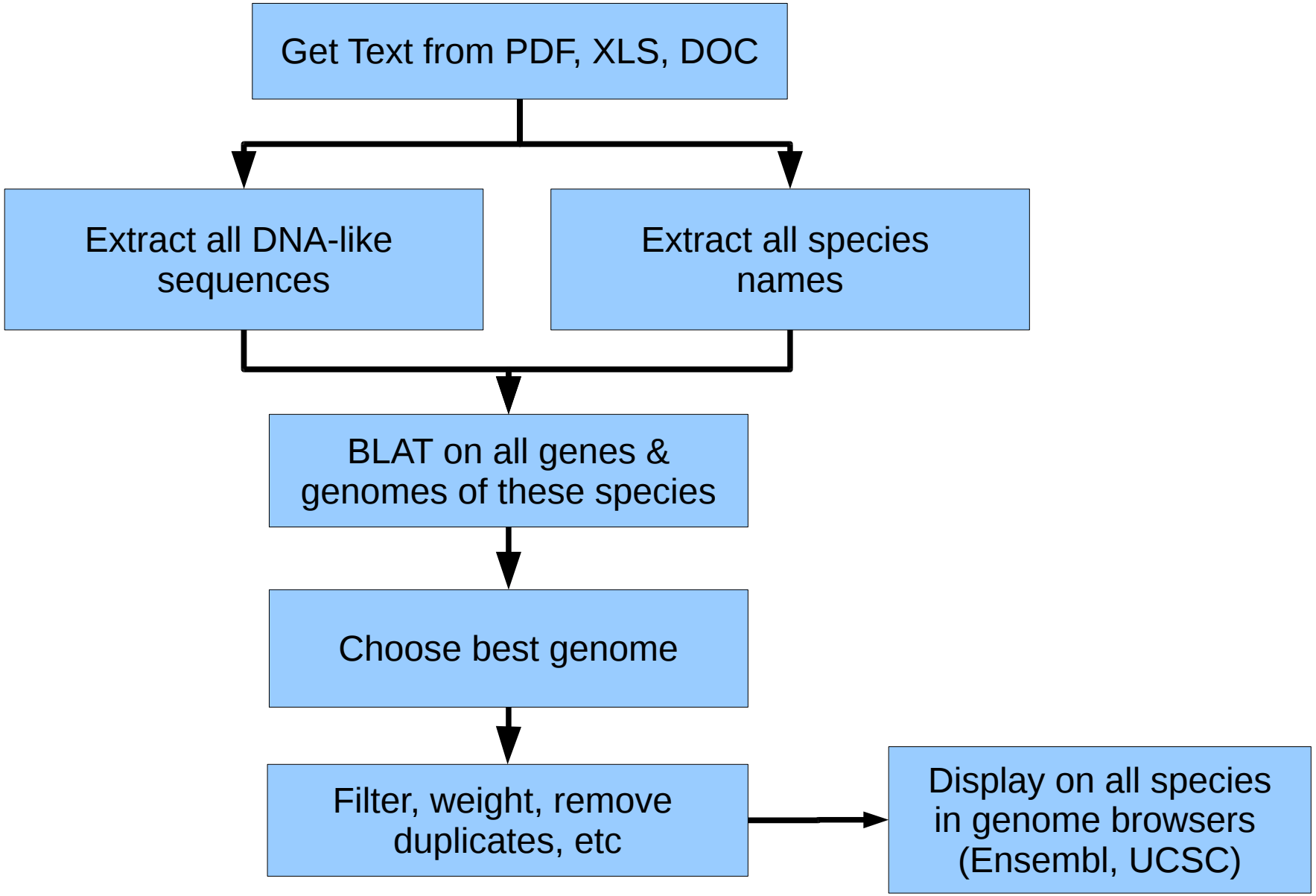
Eight sequences:

1- TCCAGTTCCCCAGTGTTTTACTAAGT
2 - GCTCTTGGCCATTAATCCAGGATT
3- TAAGCTAATGGCGGGCACCT
3 - CTCGCTCTCACCAGAGTGCA
5- CCGTAATGGATTTTGAGATGGGA
6 - TGAATTGGTGGTGTGTGTGC
7- TACTCGCGGCTTTACGGG
8 - TGGAACAGGGAGGAGCAGAGAGCA

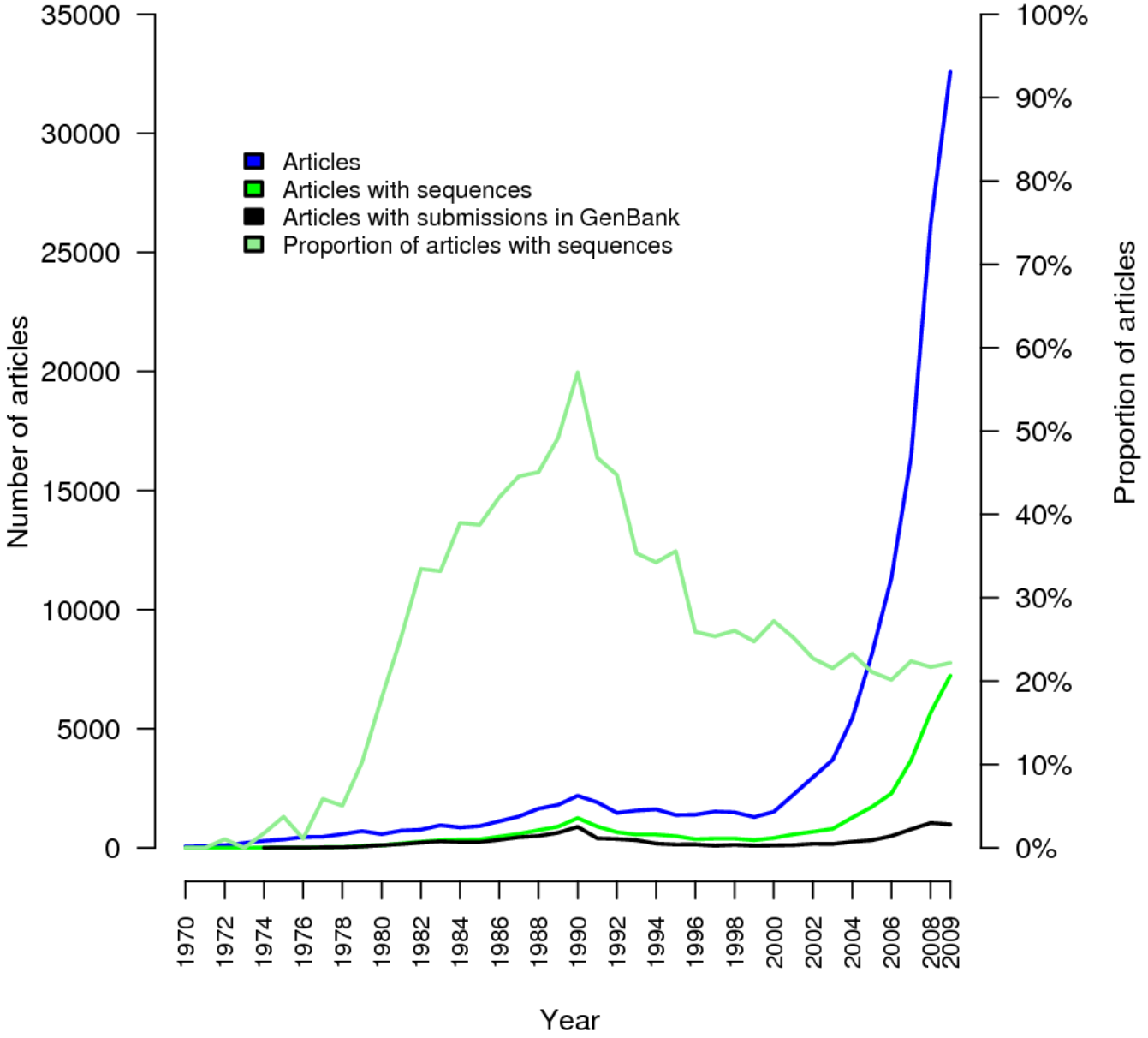
Text2Genome.org



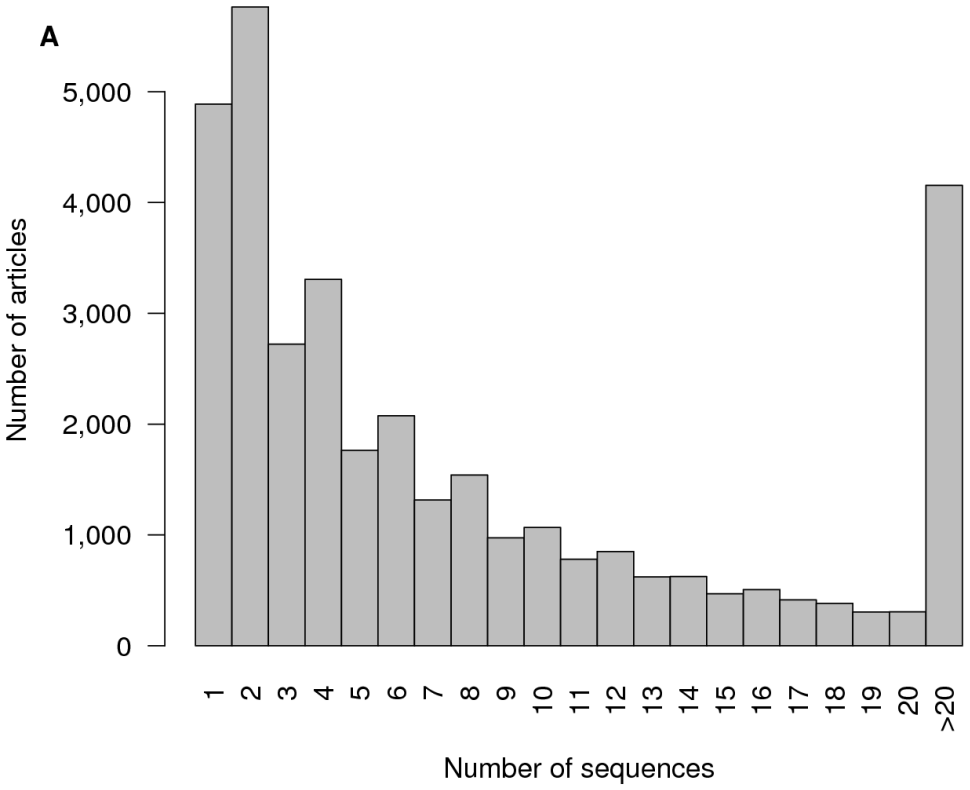
Text2Genome.org Pipeline

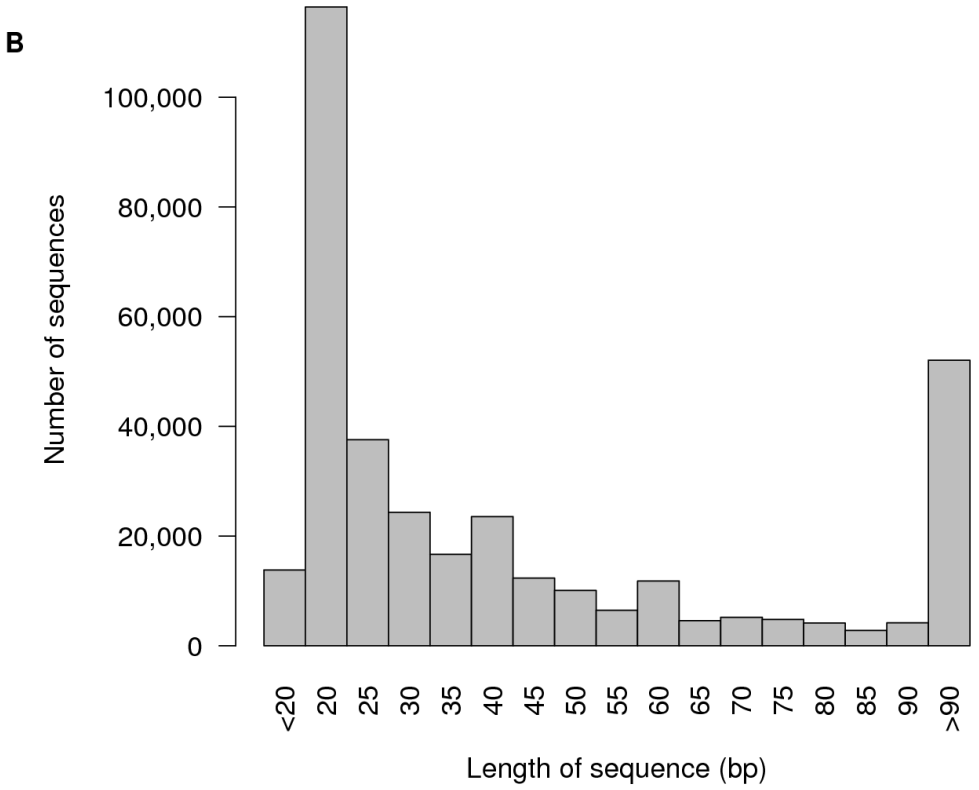


Applied to PubMed Central Open Access Subset (150k articles)

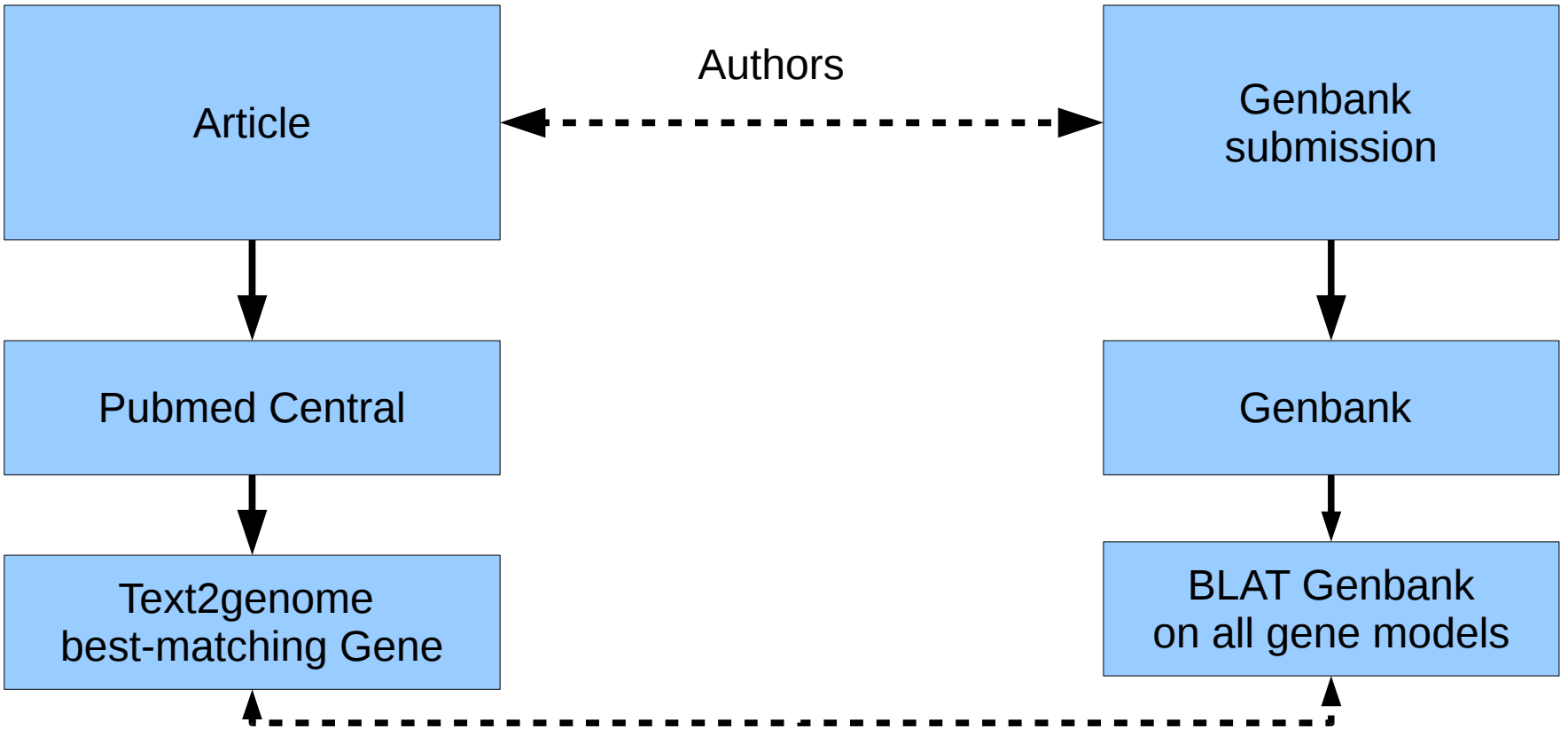


Most sequences are primers





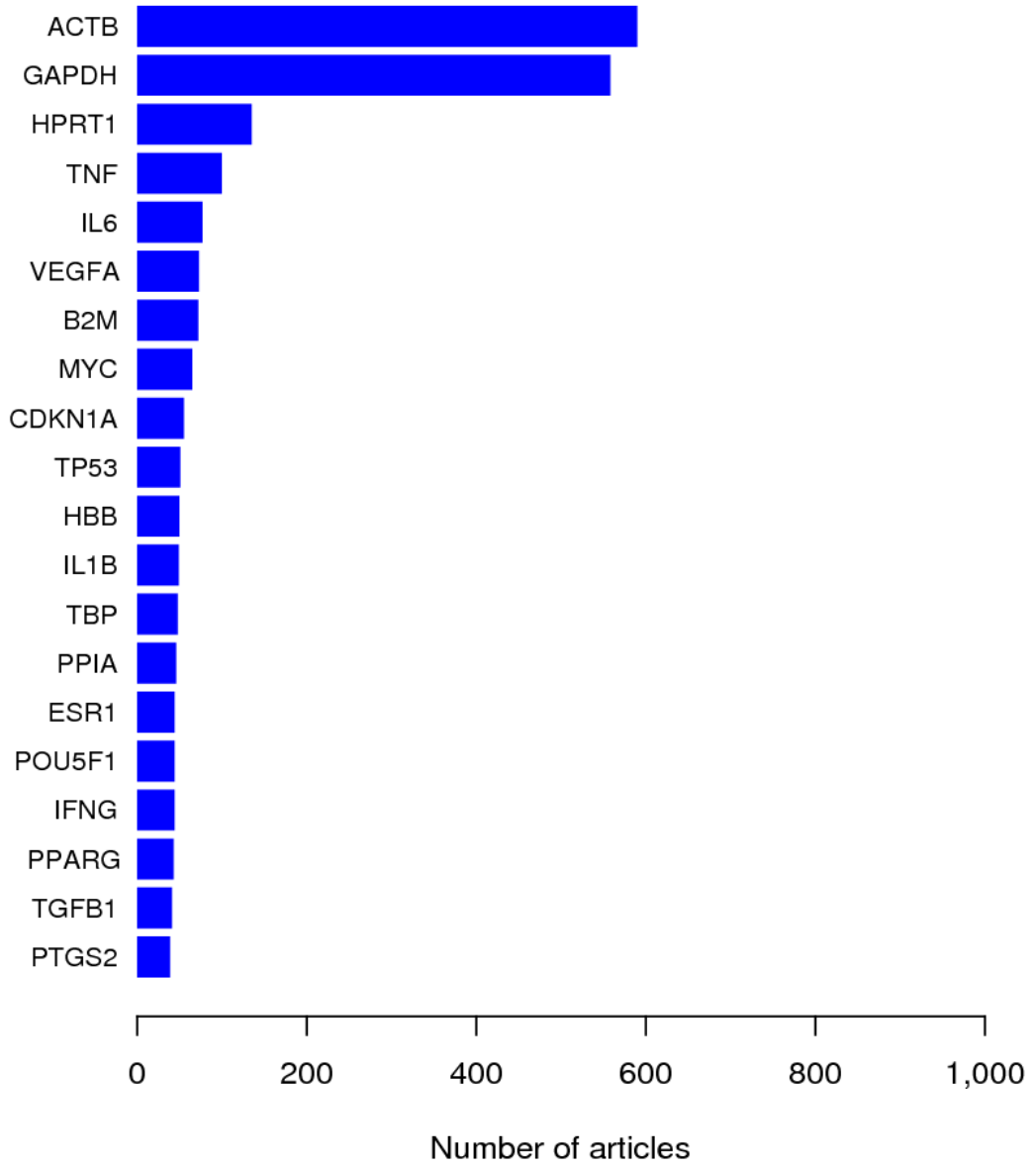
Estimate Precision vs. Genbank



Predict correct species: 95%

Predict correct gene: 88%

Most frequent genes with sequences in articles are RT-PCR loci



Technical details

- Parsing from PDF/XML/TXT
- And supplemental files (XLS/DOC/...)!
- DNA sequences look like...?
- How do you quickly search for 150k species names?
- Short sequences
- 100GB of genome data
- Display: Ensembl DAS Server, UCSC custom tracks

www.text2genome.org

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doi:10.1093/hmg/ddn271
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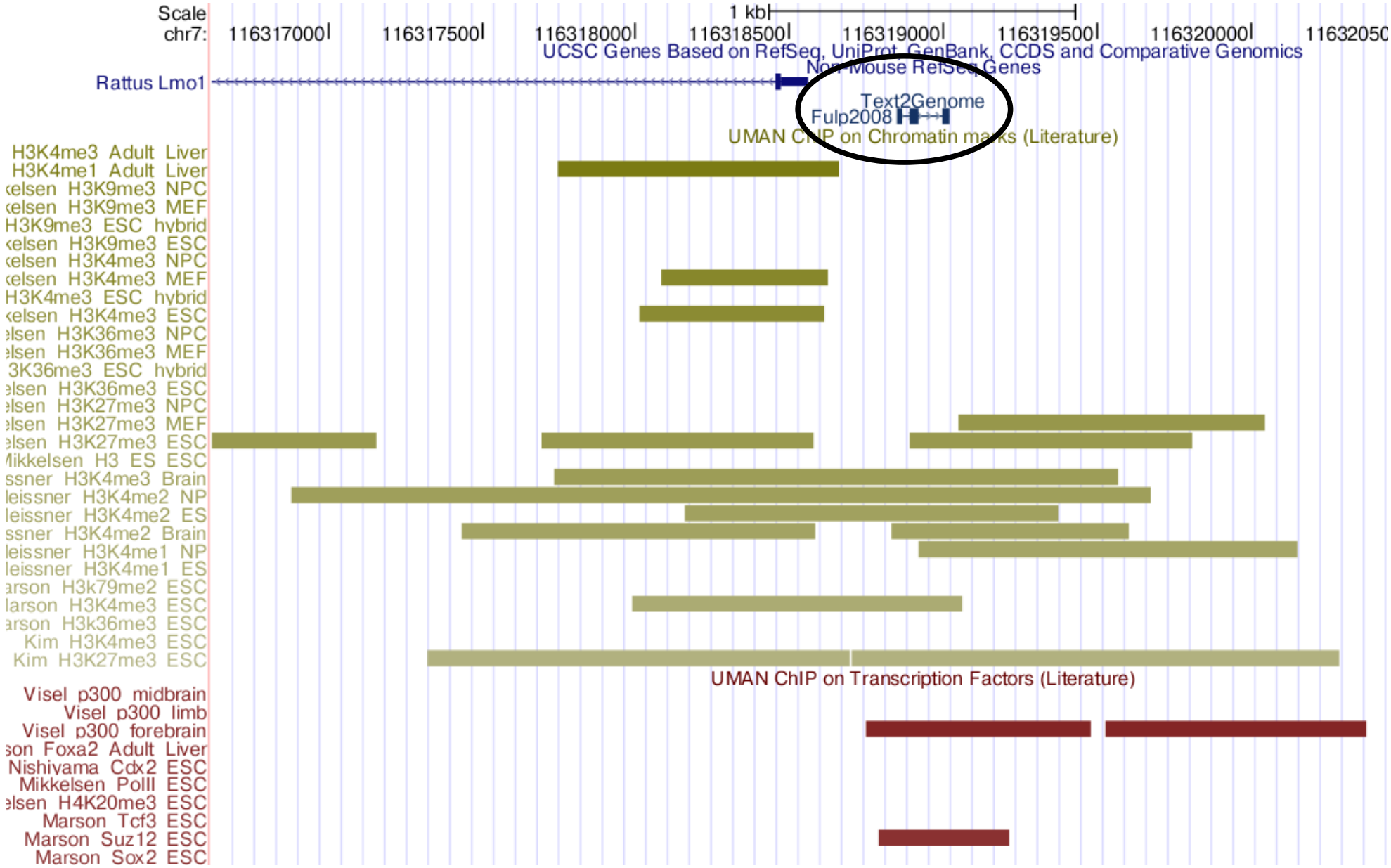
Genome Annotation: Links to best and chained genome matches

SeqNo	Coordinate Range
7, 8, 28, 29	chr3:66786225-66786328
9, 10, 22, 23, 26, 27	chr7:116318846-116319016
31	chr7:69524512-69524547
13	chr6:125115600-125115624
4, 5	chrY:1917607-1920436
0, 1	chrX:90533156-90535654
13	chr12:5597479-5597862
13	chr18:55998656-55998680
11, 12, 16, 17, 18, 19, 20, 21	chr7:144507440-144507660

Recognized sequences in fulltext

SeqNo	file name	Recognized DNA
0	PMC2581427.pdf	TGGAGCGGGGACAGGGGTGAGGTT
1	PMC2581427.pdf	GGCCGGTCTCTTTCTTTCTACTCA
2	PMC2581427.pdf	CAATGCTGTTTCACTGGTTATG
3	PMC2581427.pdf	CATTGCCCCTGTTTCACTATC
4	PMC2581427.pdf	CAGAAATGAACTACTGCATCCC
5	PMC2581427.pdf	AACTTGTGCCTCTCACCACG
6	PMC2581427.pdf	AAGAACCCCAAAAGCTAAG
7	PMC2581427.pdf	TCCAGTTCCCCAGTGTTTTACTAAGT
8	PMC2581427.pdf	GCTCTTGGCCATTAATCCAGGATT

Is there any literature analyzing this genomic region?



Future directions

- Standard UCSC genome browser track
- More articles to come:
  - Elsevier (30 % of Pubmed-abstracts)
  - Nature Publishing
  - **...your journal... ?**

MANCHESTER 1824
The University of Manchester

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  - Motivation & support for an idea which sounded crazy some years ago and took some time to realize
- Martin Gerner (Manchester):
  - Fast species name recognizer: http://linnaeus.sourceforge.net
- Hiram Clawson (UCSC):
  - Integration into UCSC browser (coming soon)
- Funding: EU 7th Framework Project CISSTEM (www.cisstem.eu), BBSRC Project “pubmed2ensembl” (www.pubmed2ensembl.org)