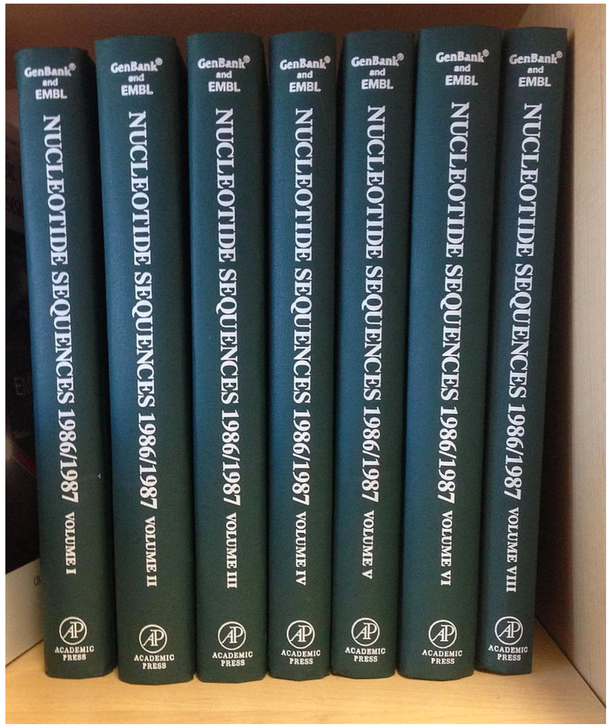
An overview of bioinformatics databases and online resources: what they are and how to access them

Mark Stenglein, GDW

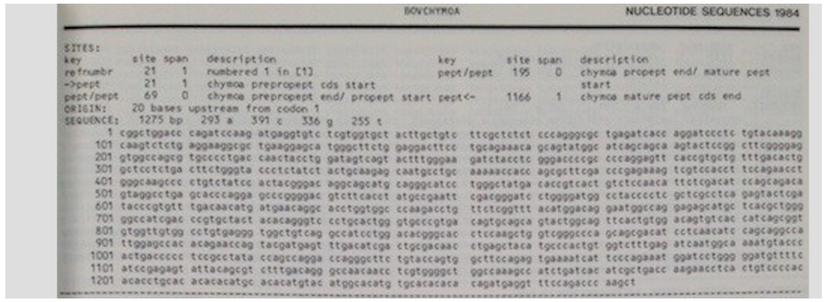
Genomics of Disease in Wildlife

GenBank was one of the earliest sequence databases.

GenBank circa 1987



~10,000 sequences



```
BOVCHYMOA                                                NUCLEOTIDE SEQUENCES 1984

SITES:
key         site span   description                              key         site span   description
refnumbr      21    1   numbered 1 in [1]                        pept/pept    195    0   chymoa propept end/ mature pept
->pept        21    1   chymoa prepropept cds start                                     start
pept/pept     69    0   chymoa prepropept end/ propept start pept<-      1166    1   chymoa mature pept cds end
ORIGIN:   20 bases upstream from codon 1
SEQUENCE:  1275 bp   293 a   391 c   336 g   255 t
       1 cggctggacc cagatccaag atgaggtgtc tcgtggtgct acttgctgtc  ttcgctctct cccagggcgc tgagatcacc aggatccctc tgtacaaagg
     101 caagtctctg aggaaggcgc tgaaggagca tgggcttctg gaggacttcc  tgcagaaaca gcagtatggc atcagcagca agtactccgg cttcgggggag
     201 gtggccagcg tgcccctgac caactacctg gatagtcagt actttgggaa  gatctacctc gggacccccgc cccaggagtt caccgtgctg tttgacactg
     301 gctcctctga cttctgggta ccctctatct actgcaagag caatgcctgc  aaaaaccacc agcgcttcga cccgagaaag tcgtccacct tccagaacct
     401 gggcaagccc ctgtctatcc actacgggac aggcagcatg cagggcatcc  tgggctatga caccgtcact gtctccaaca ttctcgacat ccagcagaca
     501 gtaggcctga gcacccagga gcccgggggac gtcttcacct atgccgaatt  cgacgggatc ctggggatgg cctaccctc gctcgcctca gagtactcga
     601 taccccgtgtt tgacaacatg atgaacaggc acctggtggc ccaagacctg  ttctcggttt acatggacag gaatggccag gagagcatgc tcacgctggg
     701 ggccatcgac ccgtgctact acacagggtc cctgcactgg gtgcccgtga  cagtgcagca gtactggcag ttcactgtgg acagtgtcac catcagcggt
     801 gtggttgtgg cctgtgaggg tggctgtcag gccatcctgg acacgggcac  ctccaagctg gtcgggccca gcagcgacat cctcaacatc cagcaggcca
     901 ttggagccac acagaaccag tacgatgagt ttgacatcga ctgcgacaac  ctgagctaca tgcccactgt ggtctttgag atcaatggca aaatgtaccc
    1001 actgaccccc tccgcctata ccagccagga ccagggcttc tgtaccagtg  gcttccagag tgaaaatcat tcccagaaat ggatcctggg ggatgttttc
    1101 atccgagagt attacagcgt cttttgacagg gccaacaacc tcgtgggggt  ggccaaggcc atctgatcac atcgctgacc aagaacctca ctgtccccac
    1201 acacctgcac acacacatgc acacatgtac atggcacatg tgcacacaca  cagatgaggt ttccagaccc aagct
```

GenBank release 100 (1997)
distributed by CDROM

~1,300,000 sequences

Genbank today

>220,000,000 sequences

First release: 1982: 606 sequences

Today, we'll focus mainly on NCBI databases and resources, and how to access them

Categories of NCBI databases

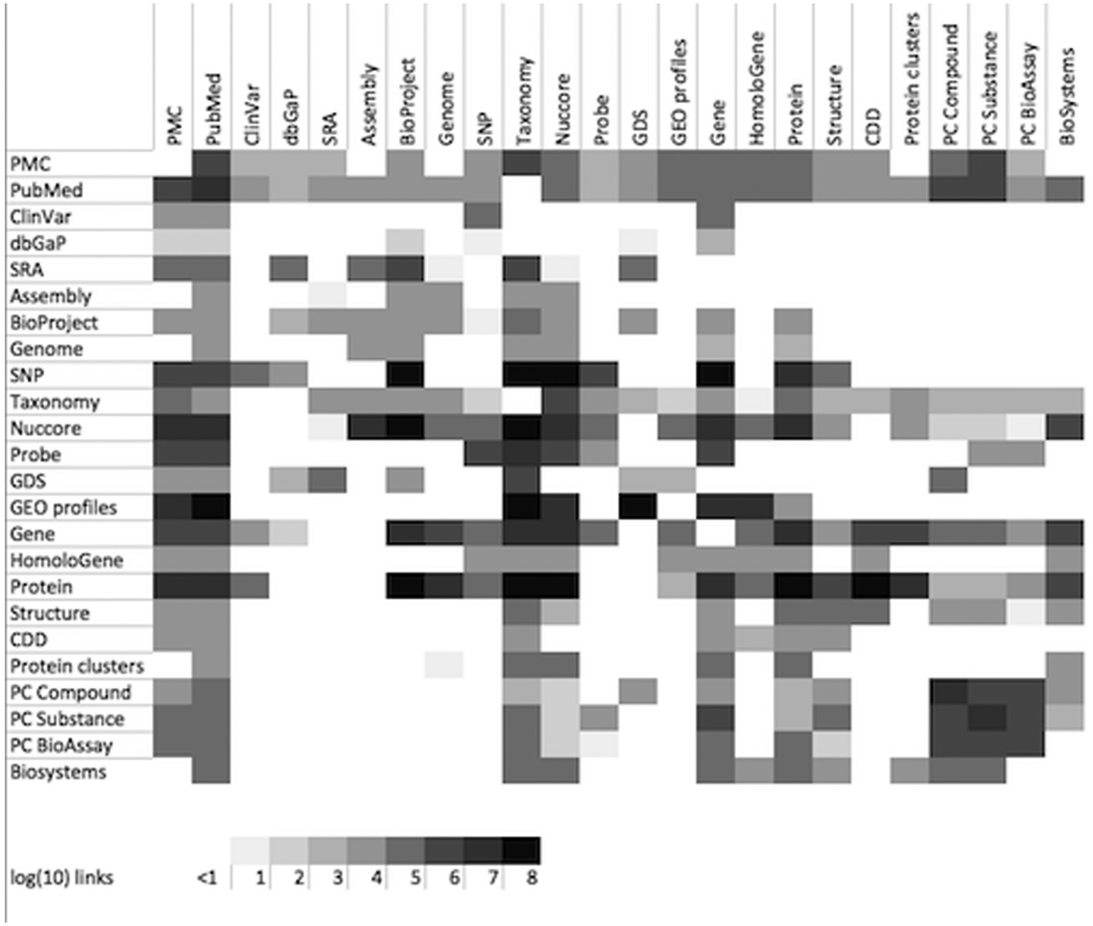
Category	Example NCBI db	Content
Literature	PubMed	Scientific and medical abstracts/ citations
Genomes	Assembly	Genome assembly information
Genes	Gene	Collected information about gene loci
Proteins	Protein	Protein sequences
Chemicals	PubChem Compound	Chemical information with structures, information and links
Health	dbGaP	Genotype/phenotype interaction studies

https://academic.oup.com/nar/issue/45/D1

One really useful feature of NCBI databases is that they link to each other

So, you can, for example:

- get all the nucleotide sequences associated with a taxon of interested
- get all the protein sequences predicted to be encoded by a genome
- get the SRA datasets associated with a particular paper in Pubmed



links from Pubmed to other dbs

links from Taxonomy to other abs

Nucleic Acids Res (2017) 45 (D1): D12-D17

The paper containing the original sequence description of SARS-CoV-2

Article

A new coronavirus associated with human respiratory disease in China

https://doi.org/10.1038/s41586-020-2008-3

Received: 7 January 2020

Accepted: 28 January 2020

Published online: 3 February 2020

Open access

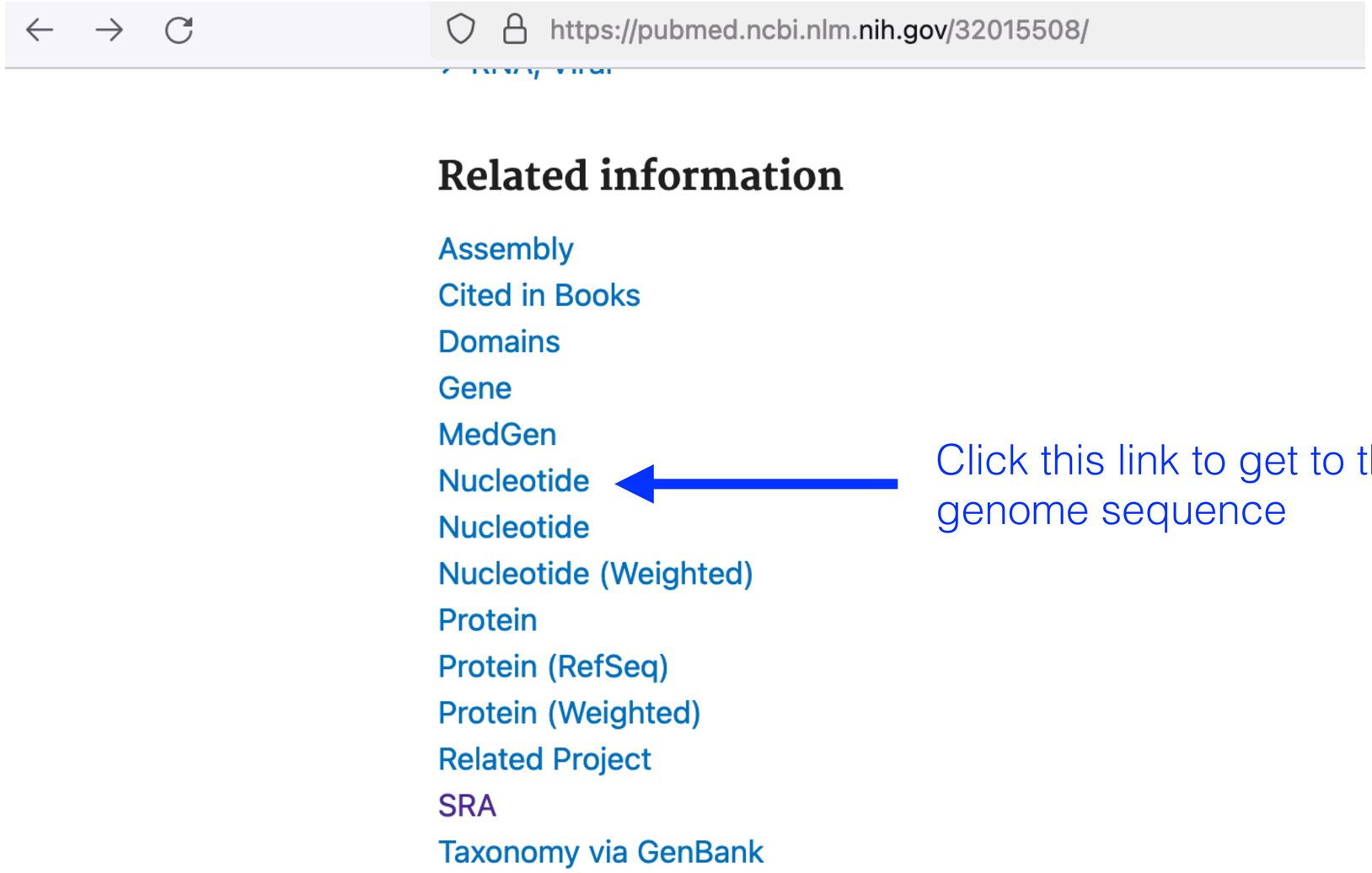
Check for updates

Fan Wu[1,7], Su Zhao[2,7], Bin Yu[3,7], Yan-Mei Chen[1,7], Wen Wang[4,7], Zhi-Gang Song[1,7], Yi Hu[2,7], Zhao-Wu Tao[2], Jun-Hua Tian[3], Yuan-Yuan Pei[1], Ming-Li Yuan[2], Yu-Ling Zhang[1], Fa-Hui Dai[1], Yi Liu[1], Qi-Min Wang[1], Jiao-Jiao Zheng[1], Lin Xu[1], Edward C. Holmes[1,5] & Yong-Zhen Zhang[1,4,6]✉

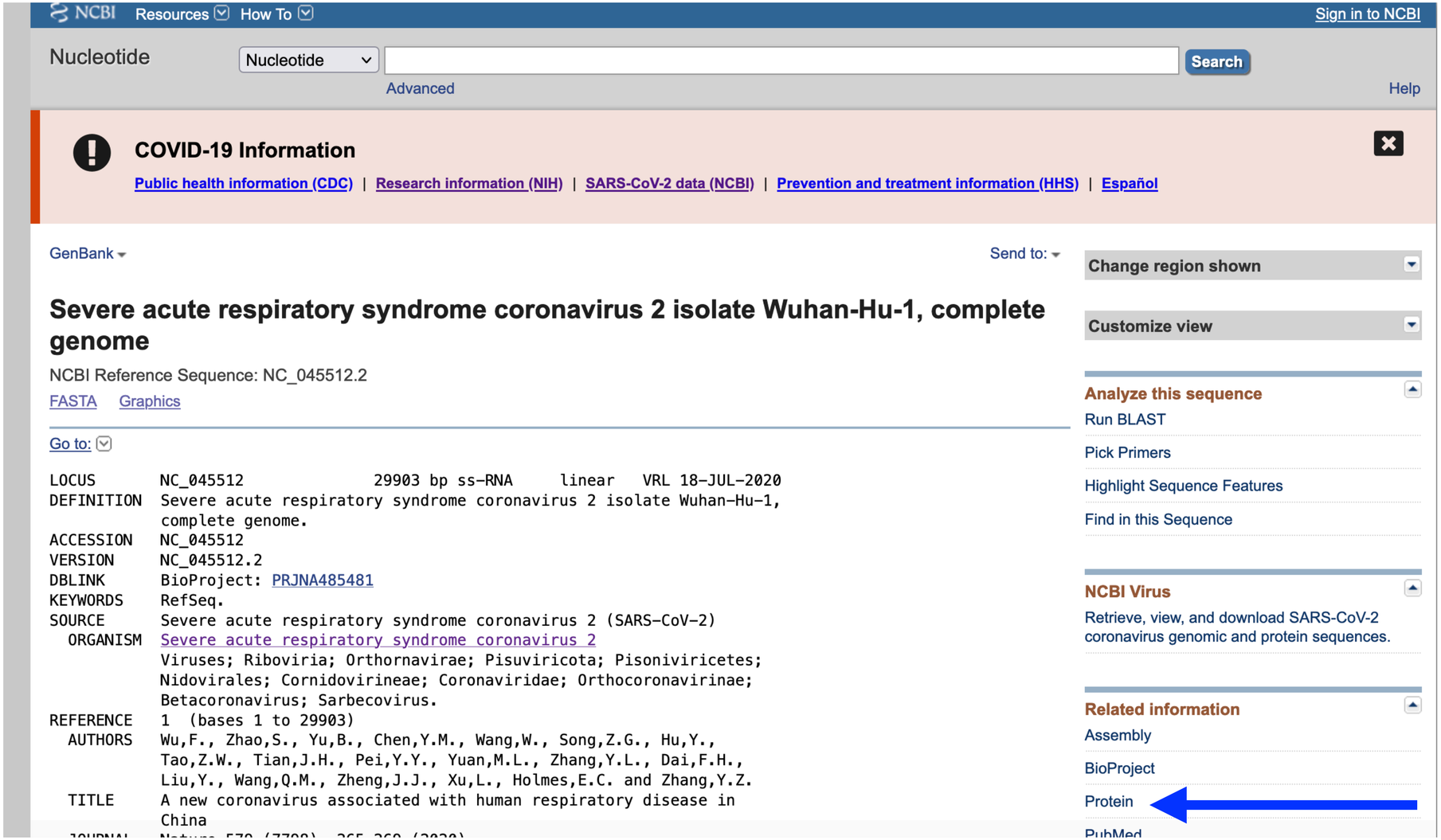
Emerging infectious diseases, such as severe acute respiratory syndrome (SARS) and Zika virus disease, present a major threat to public health[1–3]. Despite intense research efforts, how, when and where new diseases appear are still a source of considerable uncertainty. A severe respiratory disease was recently reported in Wuhan, Hubei province, China. As of 25 January 2020, at least 1,975 cases had been reported since the first patient was hospitalized on 12 December 2019. Epidemiological investigations have suggested that the outbreak was associated with a seafood market in Wuhan. Here we study a single patient who was a worker at the market and who was admitted to the Central Hospital of Wuhan on 26 December 2019 while experiencing a severe respiratory syndrome that included fever, dizziness and a cough. Metagenomic RNA sequencing[4] of a sample of bronchoalveolar lavage fluid from the patient identified a new RNA virus strain from the family *Coronaviridae*, which is designated here 'WH-Human 1' coronavirus (and has also been referred to as '2019-nCoV'). Phylogenetic analysis of the complete viral genome (29,903 nucleotides) revealed that the virus was most closely related (89.1% nucleotide similarity) to a group of

The pubmed record for that paper

At the bottom of the pubmed page: related information links

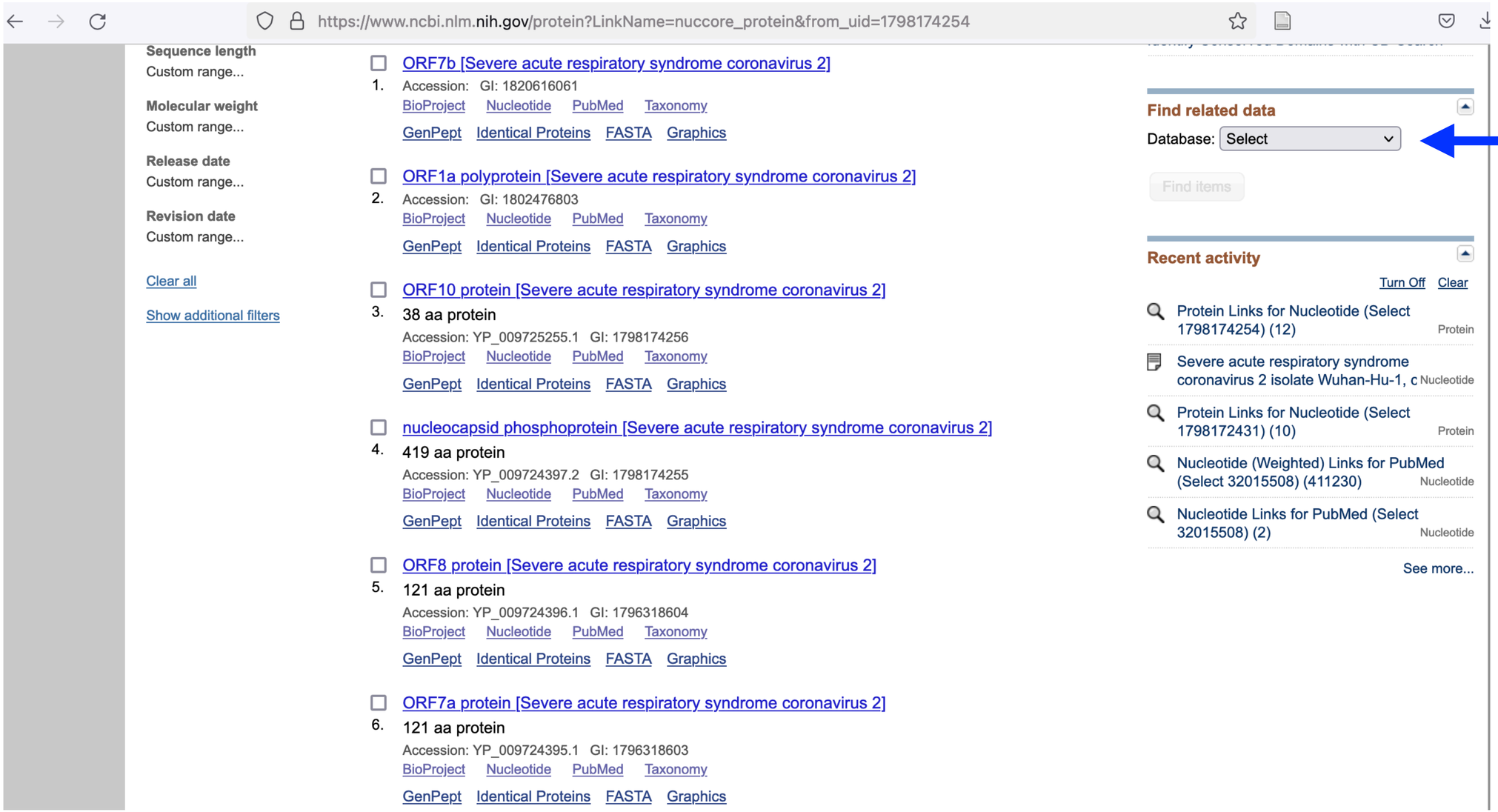


We've jumped to the NCBI nucleotide database (Genbank)

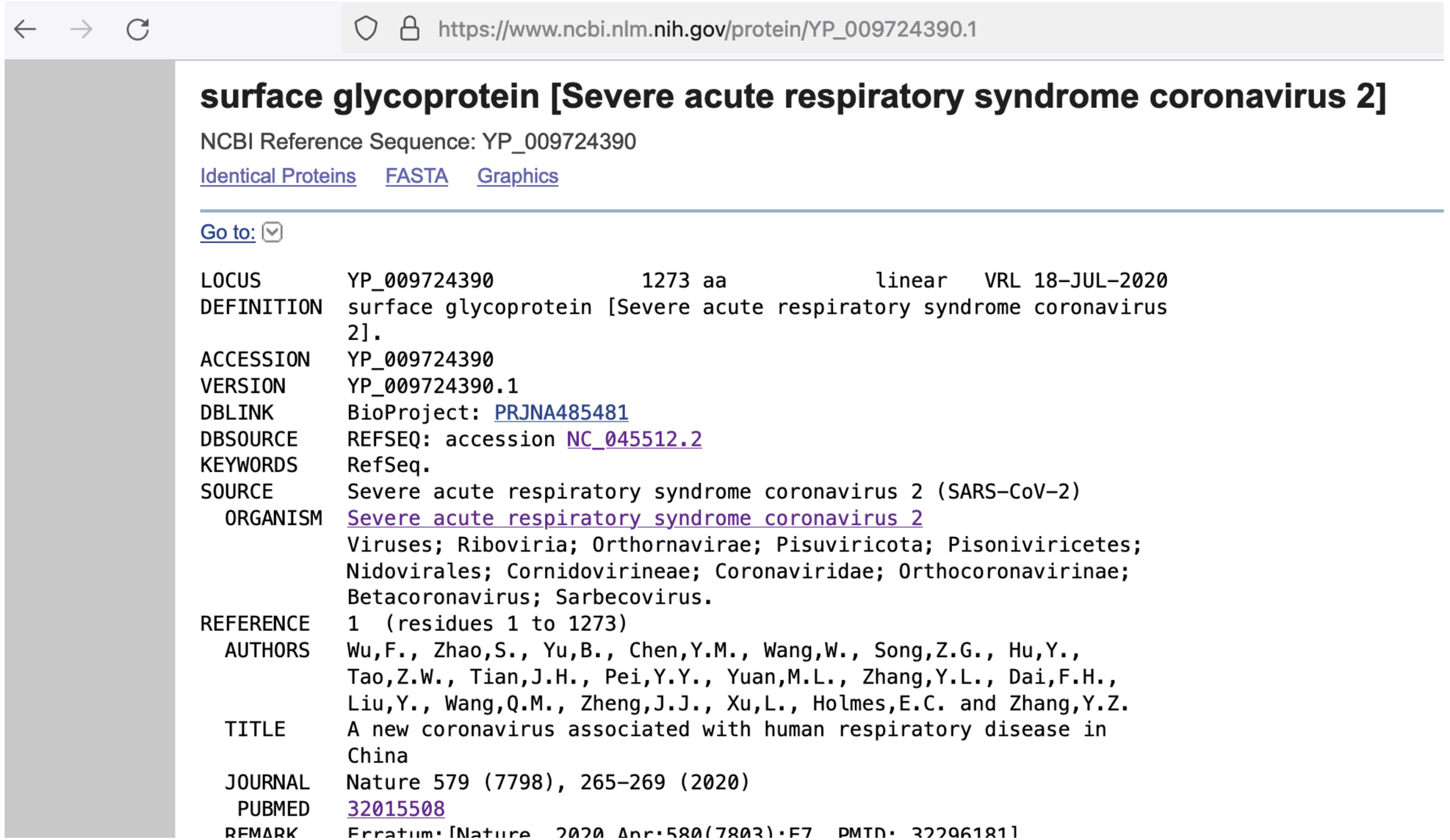


Click this link to get to the protein sequences encoded by this genome

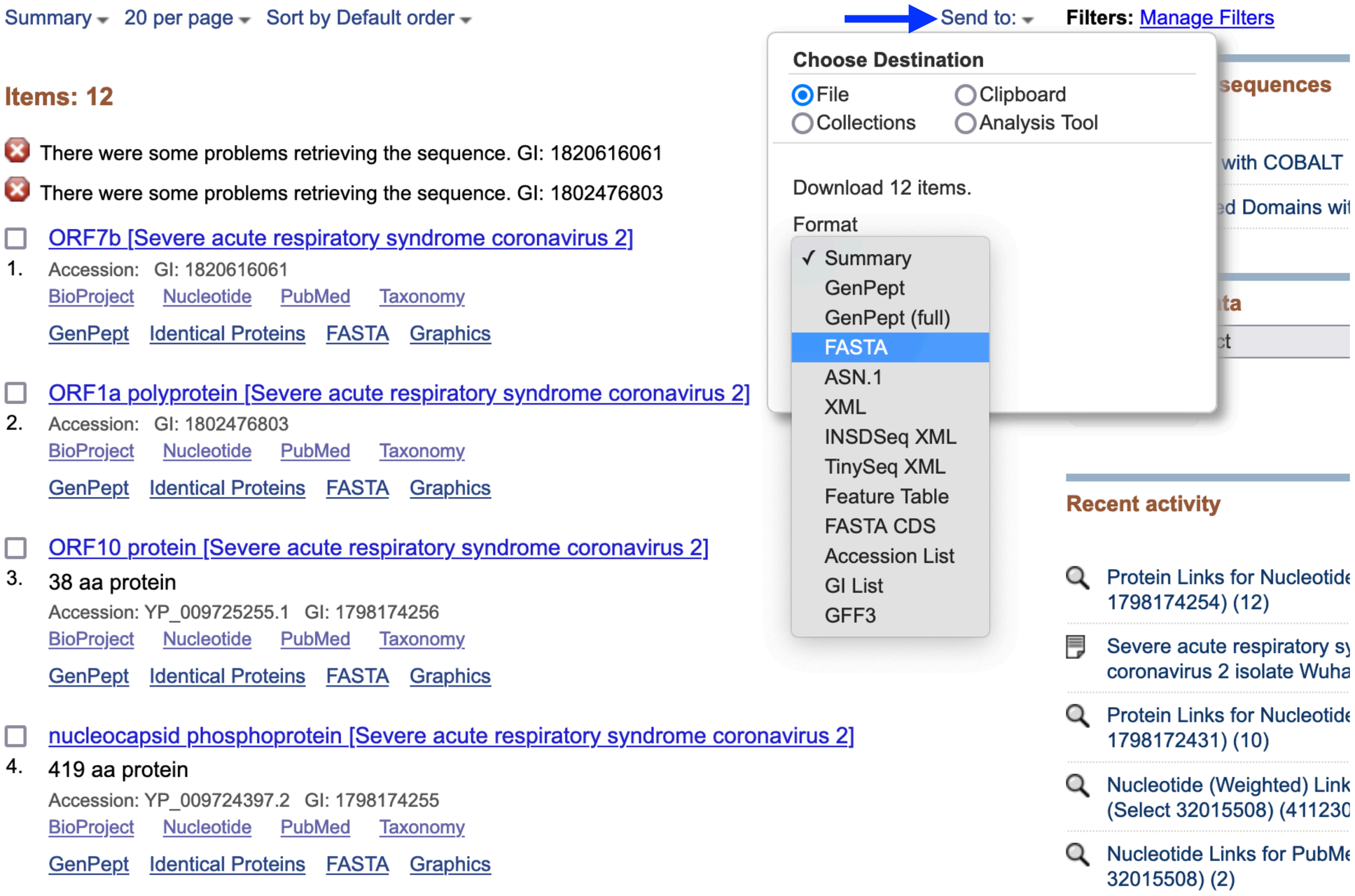
Now we are in the NCBI protein database



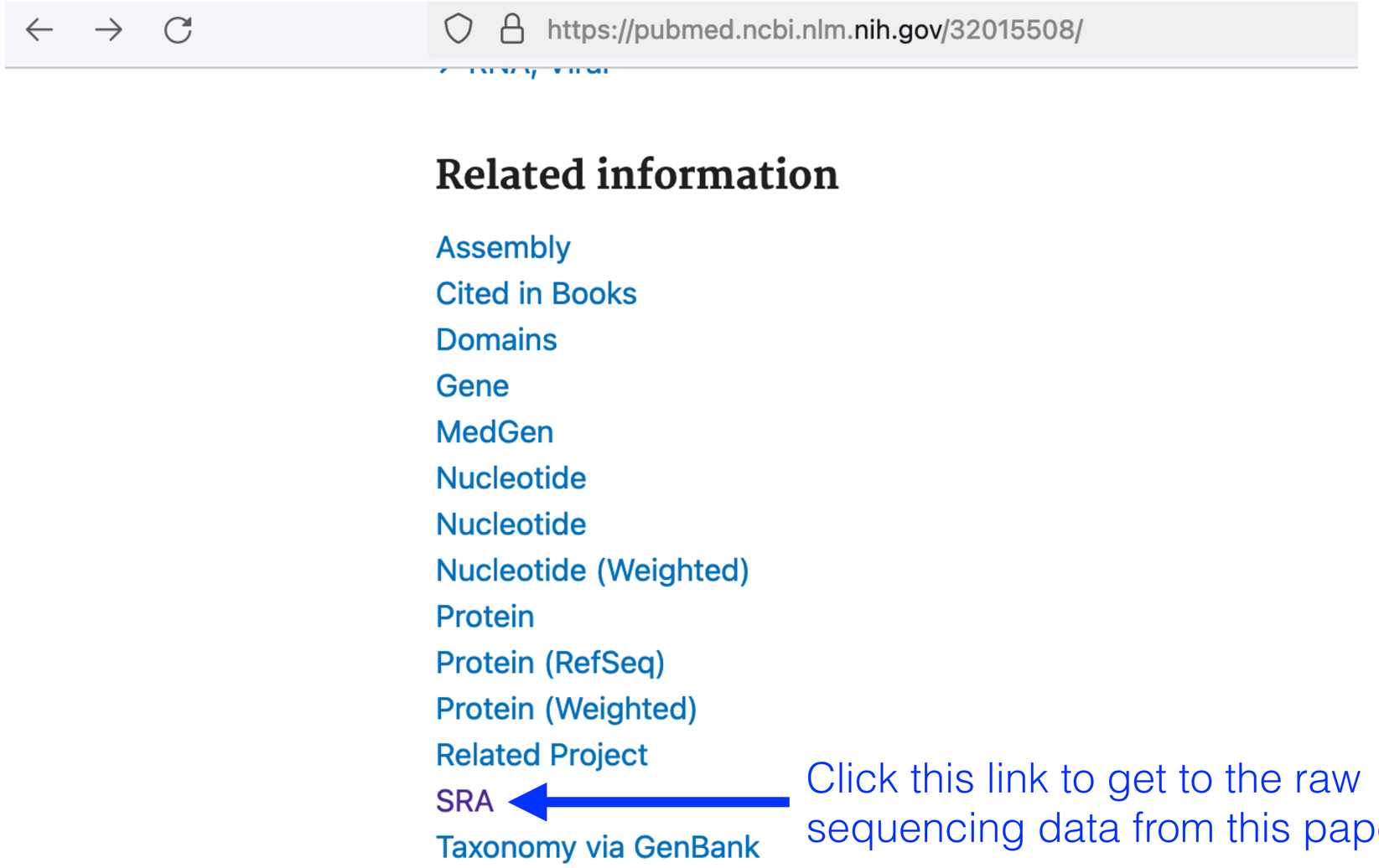
You could click on these sequences one at a time to access them



Or you can download them all at once, in various formats



At the bottom of the pubmed page: related information links



COVID-19 Information

Public health information (CDC) | Research information (NIH) | SARS-CoV-2 data (NCBI) | Prevention and treatment information (HHS) | Español

Full Send to:

Links from PubMed

SRX7636886: Complete genome of a novel coronavirus associated with severe human respiratory disease in Wuhan, China
1 ILLUMINA (Illumina MiniSeq) run: 28.3M spots, 8G bases, 2.6Gb downloads

Design: Total RNA was extracted from the BALF sample of a patient using the RNeasy Plus Universal Mini Kit (Qiagen) following the manufacturers instructions. An RNA library was then constructed using the SMARTer Stranded Total RNA-Seq Kit v2 (TaKaRa, Dalian, China). Ribosomal RNA (rRNA) depletion was performed during library construction following the manufacturers instructions. Paired-end (150 bp) sequencing of the RNA library was performed on the MiniSeq platform (Illumina).

Submitted by: Shanghai Public Health Clinical Center & School of Public Health, Fudan University

Study: Complete genome of a novel coronavirus associated with severe human respiratory disease in Wuhan, China
PRJNA603194 • SRP245409 • All experiments • All runs
show Abstract

Sample:
SAMN13922059 • SRS6067521 • All experiments • All runs
Organism: human lung metagenome

Library:
Name: 1
Instrument: Illumina MiniSeq
Strategy: RNA-Seq
Source: METATRANSCRIPTOMIC
Selection: RANDOM
Layout: PAIRED

Related information

BioProject
BioSample
PMC
PubMed
Taxonomy

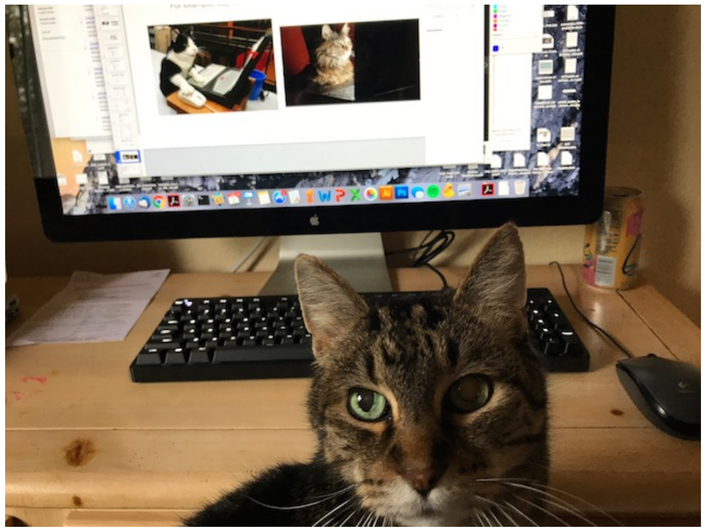
Recent activity

Turn Off Clear

SRA Links for PubMed (Select 32015508) (1) SRA
Protein Links for Nucleotide (Select 1798174254) (12) Protein
Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-1, c Nucleotide
Protein Links for Nucleotide (Select 1798172431) (10) Protein
Nucleotide (Weighted) Links for PubMed (Select 32015508) (411230) Nucleotide

There are often many paths to the same data

For example, say we want to download the cat (*Felis catus*) genome



Kirby

One of my favorite ways to access data in NCBI is via the Taxonomy database

https://www.ncbi.nlm.nih.gov/taxonomy

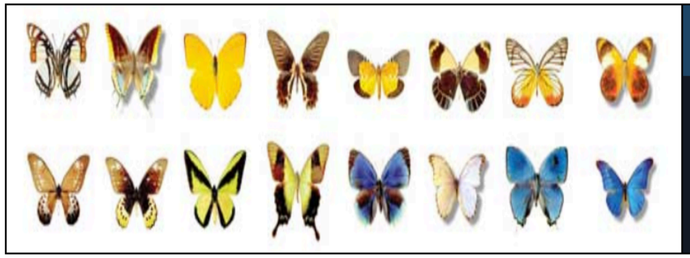
NCBI Resources How To Sign in to NCB

Taxonomy Taxonomy Search

Limits Advanced Hel

COVID-19 Information

Public health information (CDC) | Research information (NIH) | SARS-CoV-2 data (NCBI) | Prevention and treatment information (HHS) | Español



Taxonomy

The Taxonomy Database is a curated classification and nomenclature for all of the organisms in the public sequence databases. This currently represents about 10% of the described species of life on the planet.

Using Taxonomy

- Quick Start Guide
- FAQ
- Handbook
- Taxonomy FTP

Taxonomy Tools

- Browser
- Common Tree
- Statistics
- Name/ID Status
- Genetic Codes
- Linking to Taxonomy
- Extinct Organisms

Other Resources

- GenBank
- LinkOut
- E-Utilities
- Batch Entrez
- INSDC

One of my favorite ways to access data in NCBI is via the Taxonomy database

https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9685

NCBI Taxonomy Browser

Entrez | PubMed | Nucleotide | Protein | Genome | Structure | PMC | Taxonomy | BioCollections

Search for [ ] as [complete name] [lock] Go Clear

Display [3] levels using filter: [none]

Felis catus

Taxonomy ID: 9685 (for references in articles please use NCBI:txid9685)

current name

Felis catus Linnaeus, 1758

homotypic synonym: ***Felis silvestris catus***

includes: ***Korat cats*** L.

Genbank common name: **domestic cat**
NCBI BLAST name: **carnivores**
Rank: **species**
Genetic code: Translation table 1 (Standard)
Mitochondrial genetic code: Translation table 2 (Vertebrate Mitochondrial)
Other names:

heterotypic synonym

Felis domesticus

common name(s)

cat, **cats**

Lineage(*full*)

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria; Carnivora; Feliformia; Felidae; Felinae; Felis

Entrez records

Database name	Direct links
Nucleotide	92,472
Protein	58,274
Structure	21
Genome	1
Popset	207
GEO Datasets	277
PubMed Central	3,386
Gene	46,051
SRA Experiments	2,492
Protein Clusters	12
Identical Protein Groups	45,451
Bio Project	110
Bio Sample	1,649
Bio Systems	495
Assembly	8
Probe	2,877
PubChem BioAssay	1,118
Taxonomy	1

genome

SRA datasets

Felis catus in the NCBI genome database

https://www.ncbi.nlm.nih.gov/genome/?term=txid9685[Organism:noexp]

Genome

Genome | txid9685[Organism:noexp] | Search

Create alert | Limits | Advanced | Help

COVID-19 Information

Public health information (CDC) | Research information (NIH) | SARS-CoV-2 data (NCBI) | Prevention and treatment information (HHS) | Español

Felis catus (domestic cat)
Reference genome: Felis catus (assembly Felis_catus_9.0)
Download sequences in FASTA format for **genome**, **transcript**, **protein**
Download genome annotation in **GFF**, **GenBank** or **tabular** format
BLAST against Felis catus **genome**, **transcript**, **protein**
All 4 genomes for species:
Browse the **list**
Download sequence and annotation from **RefSeq** or **GenBank**
NEW Try **NCBI Datasets** - a new way to download genome sequence and annotation we're testing in NCBI Labs

Display Settings: Overview | Send to:

Organism Overview ; Genome Assembly and Annotation report [4] ; Organelle Annotation Report [1] ID: 78

Felis catus (domestic cat)

domestic cat

Lineage: Eukaryota[7836]; Metazoa[3708]; Chordata[1775]; Craniata[1753]; Vertebrata[1753]; Euteleostomi[1737]; Mammalia[470]; Eutheria[445]; Laurasiatheria[255]; Carnivora[65]; Feliformia[24]; Felidae[16]; Felinae[11]; Felis[2]; Felis catus[1]

Felis catus, the domestic cat, provides several valuable models for infectious disease, including a model for human AIDS. With a large number of recognized breeds, the cat is also a valuable resource for studying phenotypic diversity and evolution. The cat genome will further facilitate research in human medicine as some rare diseases that occur More...

Summary

Sequence data: genome assemblies: 4; sequence reads: 2 (See Genome Assembly and Annotation report)
Statistics: median total length (Mb): 2507.5
median protein count: 54726
median GC%: 41.8903
NCBI Annotation Release: 104

NCBI Resources
Genome Data Viewer

Tools
BLAST Genome

Related information
Assembly
BioProject
Gene
Components
Protein
PubMed
Taxonomy

Search details
txid9685[Organism:noexp]

There are actually 4 cat genome assemblies in NCBI

https://www.ncbi.nlm.nih.gov/genome/?term=txid9685[Organism:noexp]

Genome

Genome | txid9685[Organism:noexp] | Search

Create alert | Limits | Advanced | Help

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BLAST Genome

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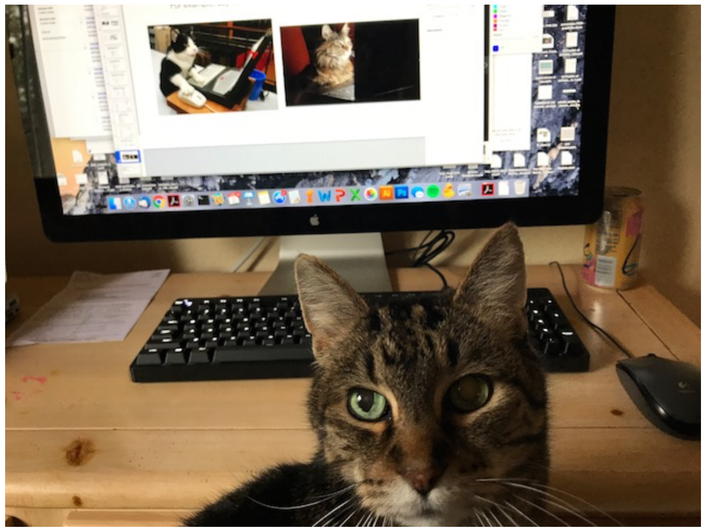
BioProject
Gene
Components
Protein
PubMed
Taxonomy

Search details
txid9685[Organism:noexp]

In reality, there are at least as many cat genomes as their are cats



Kirby

You can go up the taxonomic tree in the Taxonomy db

Felis catus

Taxonomy ID: 9685 (for references in articles please use NCBI:txid9685)

current name

Felis catus Linnaeus, 1758

homotypic synonym: ***Felis silvestris catus***

includes: ***Korat cats*** L.

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heterotypic synonym

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common name(s)

cat, **cats**

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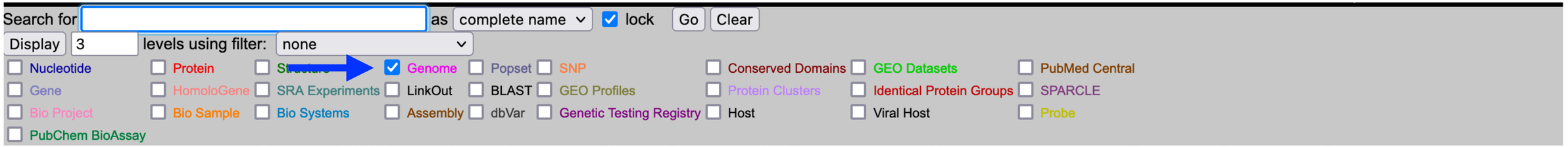
Felidae

You can go up the taxonomic tree in the Taxonomy db

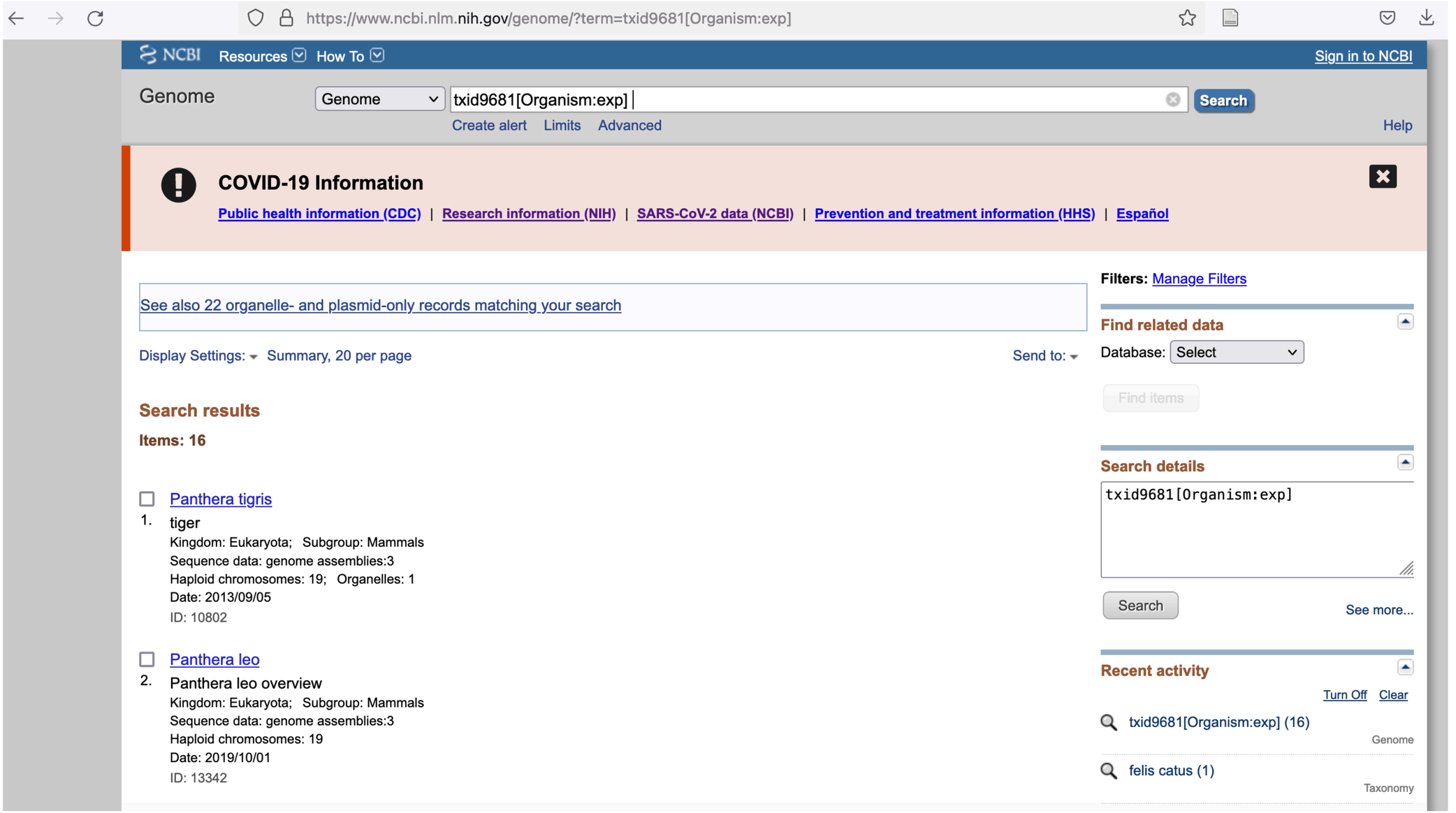


Lineage (full): cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria; Carnivora; Feliformia

- **Felidae** (cat family) 38 *Click on organism name to get more information.*
  - **Acinonychinae** 1
    - **Acinonyx** 1
      - **Acinonyx jubatus** (cheetah) 1
  - **Felinae** 30
    - **Caracal** 1
      - **Caracal caracal** 1
    - **Catopuma** 2
      - **Catopuma badia** (bay cat) 1
      - **Catopuma temminckii** (Asiatic golden cat) 1
    - **Felinae intergeneric hybrids** 1
      - **Felis catus x Leopardis geoffroyi** 1
      - **Felis catus x Prionailurus bengalensis**
      - **Leptailurus serval x Caracal caracal**
    - **Felis** 5
      - **Felis catus** (domestic cat) 1
      - **Felis chaus** (jungle cat) 1
      - **Felis chaus x Felis catus**
      - **Felis margarita** (sand cat) 1
      - **Felis nigripes** (black-footed cat) 1
      - **Felis silvestris** (wild cat) 1
      - **unclassified Felis**
      - **environmental samples**
    - **Leopardus** 7

38 genomes for species in Felidae

Felidae genomes



You can download genome sequences from the genome database

https://www.ncbi.nlm.nih.gov/genome/10802

NCBI Resources How To Sign in to NCBI

Genome Genome Search

Limits Advanced Help

COVID-19 Information

Public health information (CDC) | Research information (NIH) | SARS-CoV-2 data (NCBI) | Prevention and treatment information (HHS) | Español

Panthera tigris (tiger)
Representative genome: Panthera tigris altaica (assembly PanTig1.0)
Download sequences in FASTA format for **genome**, **transcript**, **protein**
Download genome annotation in **GFF**, **GenBank** or **tabular** format
BLAST against Panthera tigris **genome**, **transcript**, **protein**
All 3 genomes for species:
Browse the **list**
Download sequence and annotation from **RefSeq** or **GenBank**
NEW Try **NCBI Datasets** - a new way to download genome sequence and annotation we're testing in NCBI Labs

← Download links

Display Settings: Overview Send to:

Organism Overview ; Genome Assembly and Annotation report [3] ; Organelle Annotation Report [2] ID: 10802

Panthera tigris (tiger)

tiger

Lineage: Eukaryota[7836]; Metazoa[3708]; Chordata[1775]; Craniata[1753]; Vertebrata[1753]; Euteleostomi[1737]; Mammalia[470]; Eutheria[445]; Laurasiatheria[255]; Carnivora[65]; Feliformia[24]; Felidae[16]; Pantherinae[4]; Panthera[4]; Panthera tigris[1]

Tiger is the largest wild cat, and along with other members of the genus *Panthera*, the most endangered species in the world. There are five extant subspecies, namely the Bengal tiger, South China or Amoy tiger, Indochinese tiger, Sumatran tiger and the Siberian tiger. Three subspecies, the Bali tiger, Javan tiger and the Caspian tiger, are extinct.

Summary

Sequence data: genome assemblies: 3; sequence reads: 3 (See Genome Assembly and Annotation report)
Statistics: median total length (Mb): 2424.64

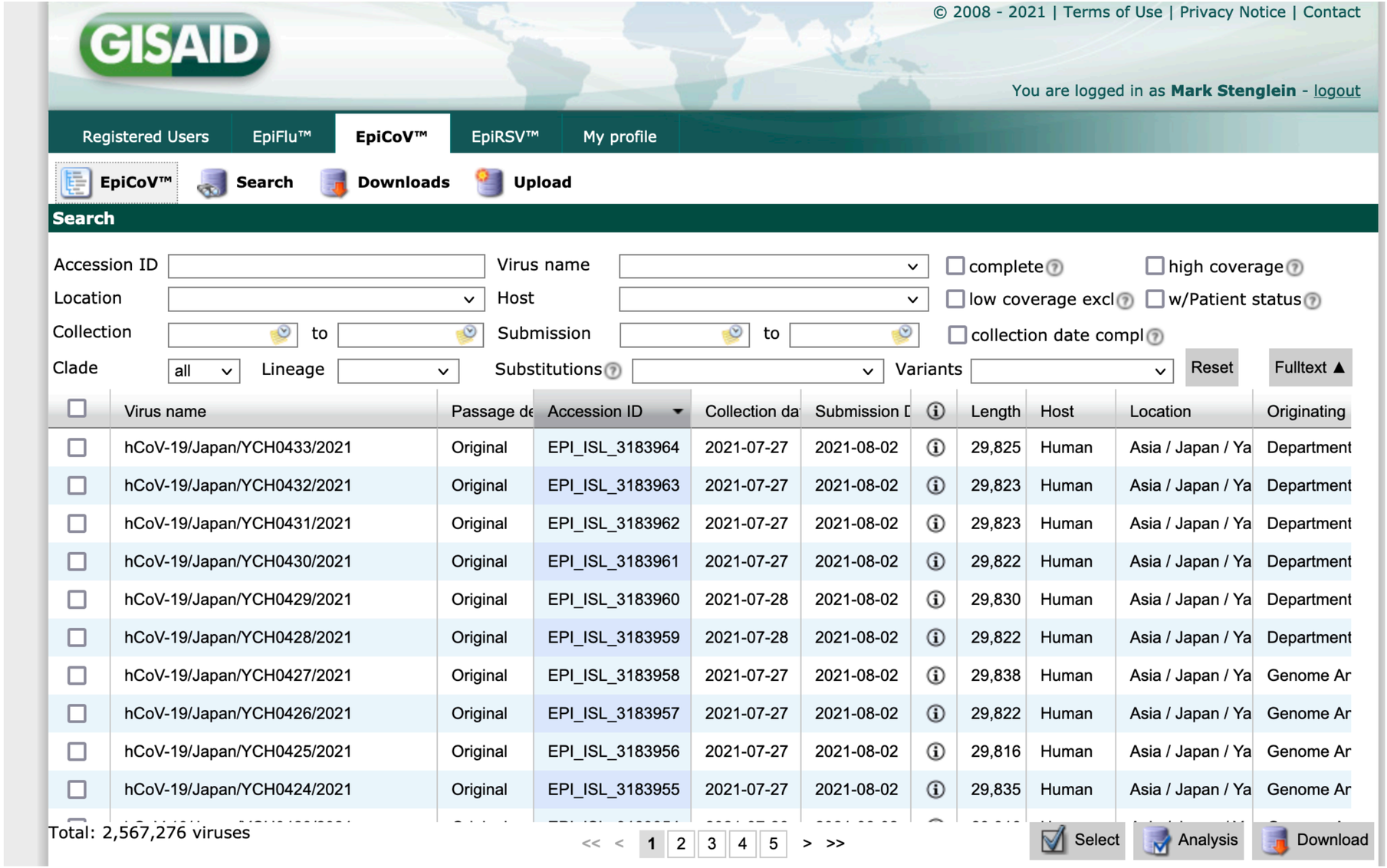
NCBI Resources
Genome Data Viewer

Tools
BLAST Genome

Related information
Assembly
BioProject
Gene
Components
Protein
PubMed
Taxonomy

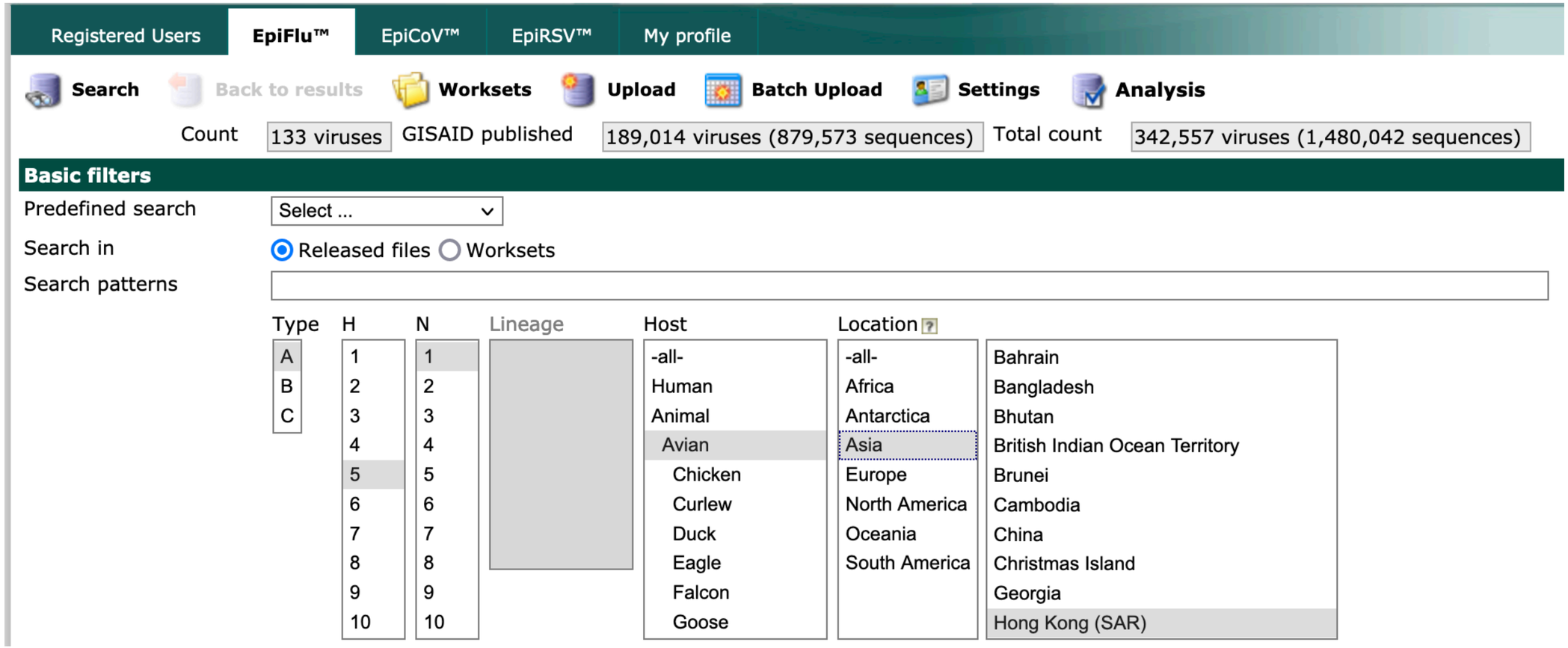
Recent activity
Turn Off Clear

Non-NCBI databases include GISAID: a repository for virus sequences



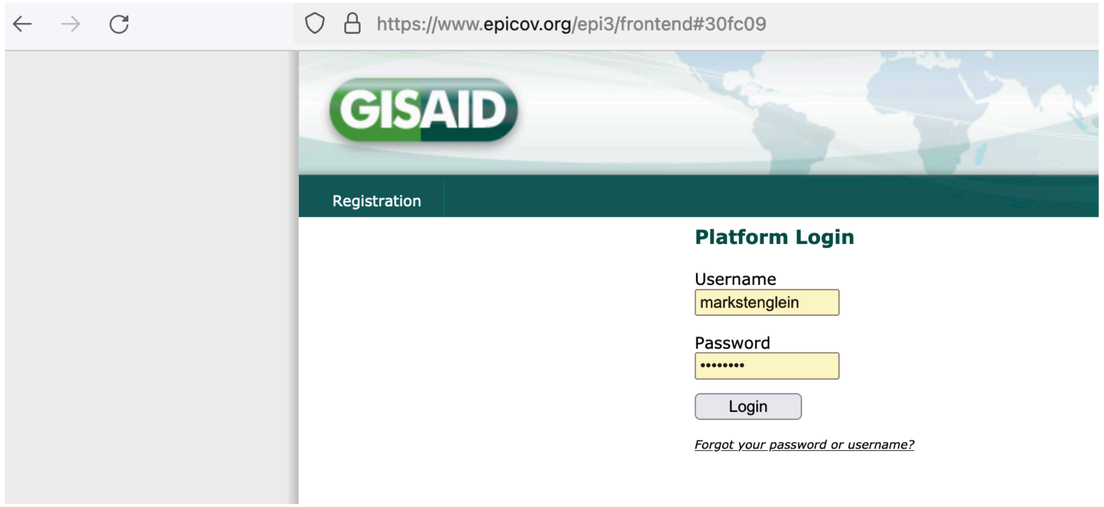
2.5 million SARS-CoV-2 sequences!!

GISAID has some nice features, but is limited to a few pathogens



Download all the IAV H5N1 sequences from birds in Hong Kong (133 viruses)

GISAID requires approval to access data and has restrictive terms of use



GISAID EPIFLU™ DATABASE ACCESS AGREEMENT

Effective: March 16, 2011

WHEREAS Freunde von GISAID e.V. ("**GISAID**") maintains a global database for influenza gene sequences along with associated data, including virological, clinical, epidemiological and demographic information (if available) for all influenza viruses, including but not limited to H5N1 sequences, (the "**GISAID EpiFlu™ Database**") for the purpose of facilitating the sharing, research and investigation of such sequences and associated data.

NOW, therefore, this Database Access Agreement (the "**Agreement**") is entered into by and between the undersigned ("You") and GISAID.

1. **Access to the GISAID EpiFlu™ Database, Data.** Access to, and use of, the GISAID EpiFlu™ Database and Data, as defined herein, is governed by this Agreement. By accessing or otherwise using the GISAID EpiFlu™ Database, whether as a provider or user of Data, You accept and agree to be bound by the terms of this Agreement. For purposes of this Agreement, the term "**Data**" means any and all (i) sequence data and other associated data and information contained in the GISAID EpiFlu™ Database pertaining to influenza viruses, (ii) any annotations, corrections, updates, modifications, improvements, derivatives or other enhancements to any such data contained in the GISAID EpiFlu™ Database, and (iii) any safety information relevant to use of the data or to regulatory approval of vaccines or other therapies that embody or utilize the data contained in the GISAID EpiFlu™ Database.
2. **License Terms**. You are hereby granted a non-exclusive, worldwide, royalty-free, non-transferable and revocable license to access and use the GISAID EpiFlu™ Database and Data solely in accordance with this Agreement in all its terms. Without limiting the foregoing, your access to and use of the GISAID

Some data lives in non-standard locations

gigadb.org/dataset/100060

ASSEMBLATHON 2

Assemblathon 2 assemblies.

Dataset type: Genomic
Data released on June 24, 2013

Bradnam KR; Fass JN; Alexandrov A; Baranay P; Bechner M; Birol I; Boisvert S; Chapman JA; Chapuis G; Chikhi R; Chitsaz H; Chou W; Corbeil J; Del Fabbro C; Docking TRR; Durbin R; Earl D; Emrich S; Fedotov P; Fonseca NA; Ganapathy G; Gibbs RA; Gnerre S; Godzaridis ; Goldstein S; Haimel M; Hall G; Haussler D; Hiatt JB; Ho I; Howard JT; Hunt M; Jackman SD; Jaffe DB; Jarvis ED; Jiang H; Kazakov S; Kersey PJ; Kitzman JO; Knight JR; Koren S; Lam T; Lavenier D; Laviolette F; Li Y; Li Z; Liu B; Liu Y; Luo R; MacCallum I; MacManes MD; Maillet N; Melnikov S; Naquin D; Ning Z; Otto TD; Paten B; Paulo OS; Phillippy AM; Pina-Martins F; Place M; Przybylski D; Qin X; Qu C; Ribeiro FJ; Richards S; Rokhsar DS; Ruby JG; Scalabrin S; Schatz MC; Schwartz DC; Sergushichev A; Sharpe T; Shaw TI; Shendure J; Shi Y; Simpson JT; Song H; Tsarev F; Vezzi F; Vicedomini R; Vieira BM; Wang J; Worley KC; Yin S; Yiu S; Yuan J; Zhang G; Zhang H; Zhou S; Korf IF (2013): Assemblathon 2 assemblies. GigaScience Database. http://dx.doi.org/10.5524/100060

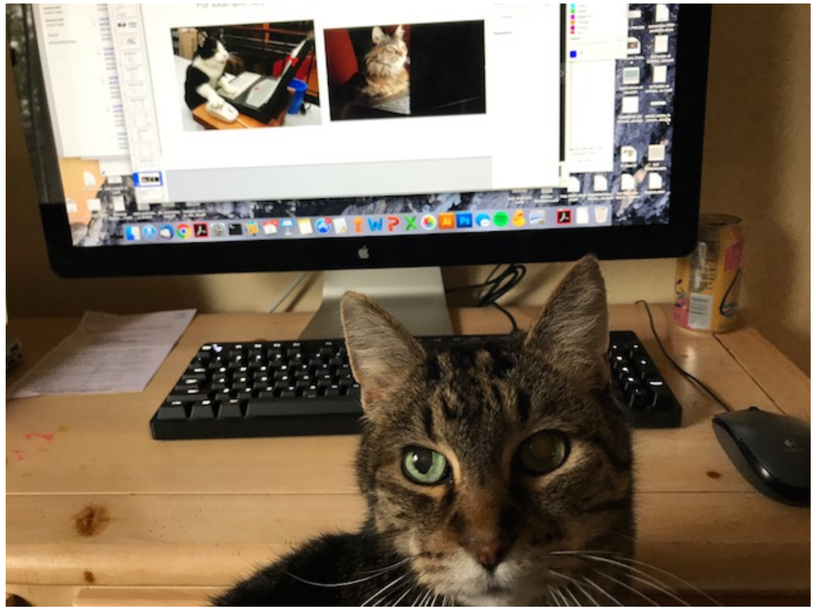
DOI 10.5524/100060

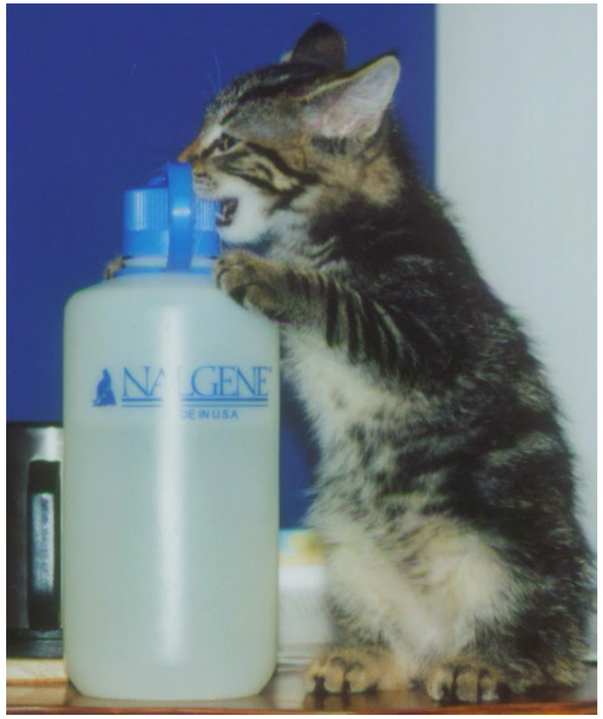
Table Settings

Sample ID	Taxonomic ID	Common Name	Genbank Name	Scientific Name	Sample Attributes
ERS218597	499168	Boa constrictor constrictor		Boa constrictor constrictor	
ERS222880	13146	Melopsittacus undulatus	budgerigar	Melopsittacus undulatus	Cell type:blood Sex:male [PATO:0000384] Common name:budgerigar
SRS140425	106582	Maylandia zebra	zebra mbuna	Maylandia zebra	Sex:male [PATO:0000384] Tissue:muscle and heart Common name:zebra mbuna fish ... +

Displaying 1-3 of 3 Sample(s).

Questions?





Kirby in 2000, wondering where his GenBank CDROMs are