Instructions for investigating patent US 9587003 B2

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https://patents.google.com/patent/US9587003B2/en

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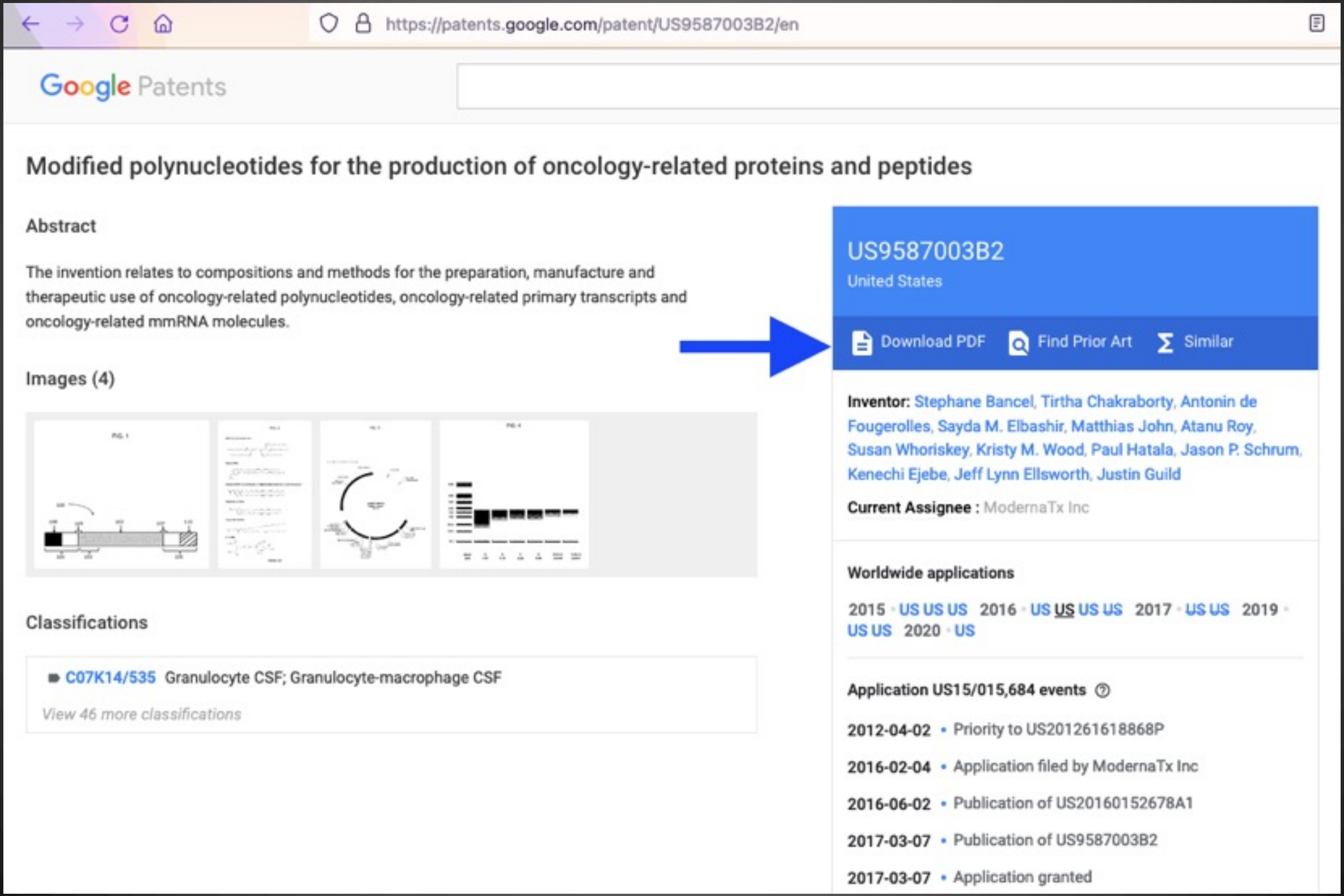


Modified polynucleotides for the production of oncology-related proteins and peptides

Abstract

The invention relates to compositions and methods for the preparation, manufacture and therapeutic use of oncology-related polynucleotides, oncology-related primary transcripts and oncology-related mmRNA molecules.

Images (4)

Classifications

- C07K14/535 Granulocyte CSF; Granulocyte-macrophage CSF

View 46 more classifications

US9587003B2
United States

Inventor: Stephane Bancel, Tirtha Chakraborty, Antonin de Fougerolles, Sayda M. Elbashir, Matthias John, Atanu Roy, Susan Whoriskey, Kristy M. Wood, Paul Hatala, Jason P. Schrum, Kenechi Ejebe, Jeff Lynn Ellsworth, Justin Guild

Current Assignee : ModernaTx Inc

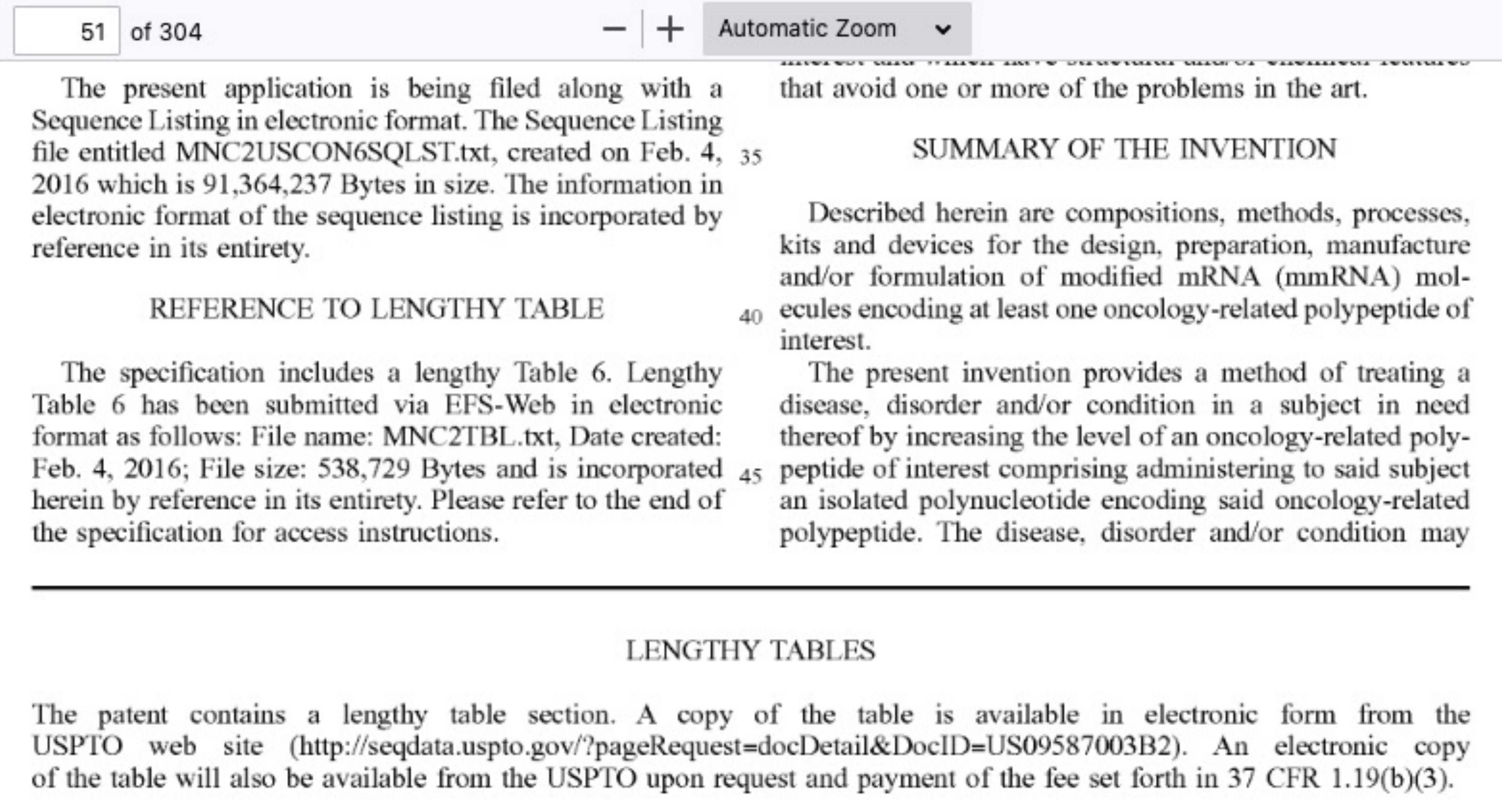
Worldwide applications

2015 · US US US 2016 · US US US US 2017 · US US 2019 · US US 2020 · US

Application US15/015,684 events

2012-04-02	Priority to US201261618868P
2016-02-04	Application filed by ModernaTx Inc
2016-06-02	Publication of US20160152678A1
2017-03-07	Publication of US9587003B2
2017-03-07	Application granted

Scroll down to page 51 in the file



The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing file entitled MNC2USCON6SQLST.txt, created on Feb. 4, 2016 which is 91,364,237 Bytes in size. The information in electronic format of the sequence listing is incorporated by reference in its entirety.

REFERENCE TO LENGTHY TABLE

The specification includes a lengthy Table 6. Lengthy Table 6 has been submitted via EFS-Web in electronic format as follows: File name: MNC2TBL.txt, Date created: Feb. 4, 2016; File size: 538,729 Bytes and is incorporated herein by reference in its entirety. Please refer to the end of the specification for access instructions.

that avoid one or more of the problems in the art.

SUMMARY OF THE INVENTION

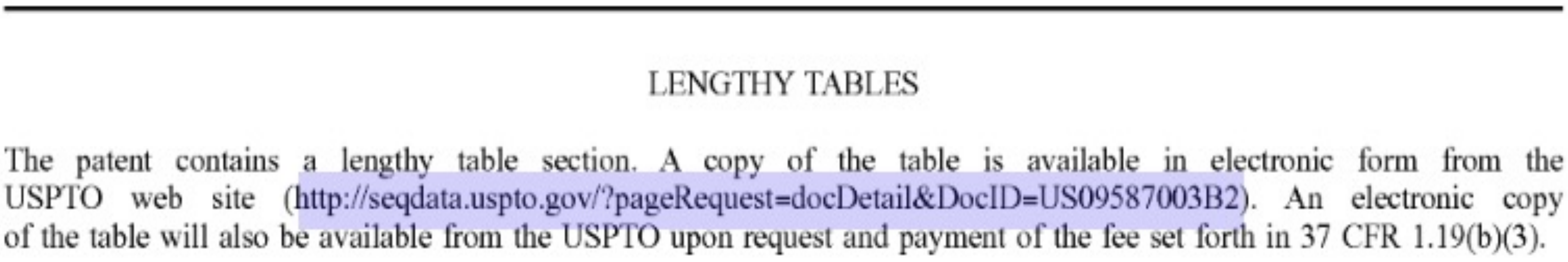
Described herein are compositions, methods, processes, kits and devices for the design, preparation, manufacture and/or formulation of modified mRNA (mmRNA) molecules encoding at least one oncology-related polypeptide of interest.

The present invention provides a method of treating a disease, disorder and/or condition in a subject in need thereof by increasing the level of an oncology-related polypeptide of interest comprising administering to said subject an isolated polynucleotide encoding said oncology-related polypeptide. The disease, disorder and/or condition may

LENGTHY TABLES

The patent contains a lengthy table section. A copy of the table is available in electronic form from the USPTO web site (http://seqdata.uspto.gov/?pageRequest=docDetail&DocID=US09587003B2). An electronic copy of the table will also be available from the USPTO upon request and payment of the fee set forth in 37 CFR 1.19(b)(3).

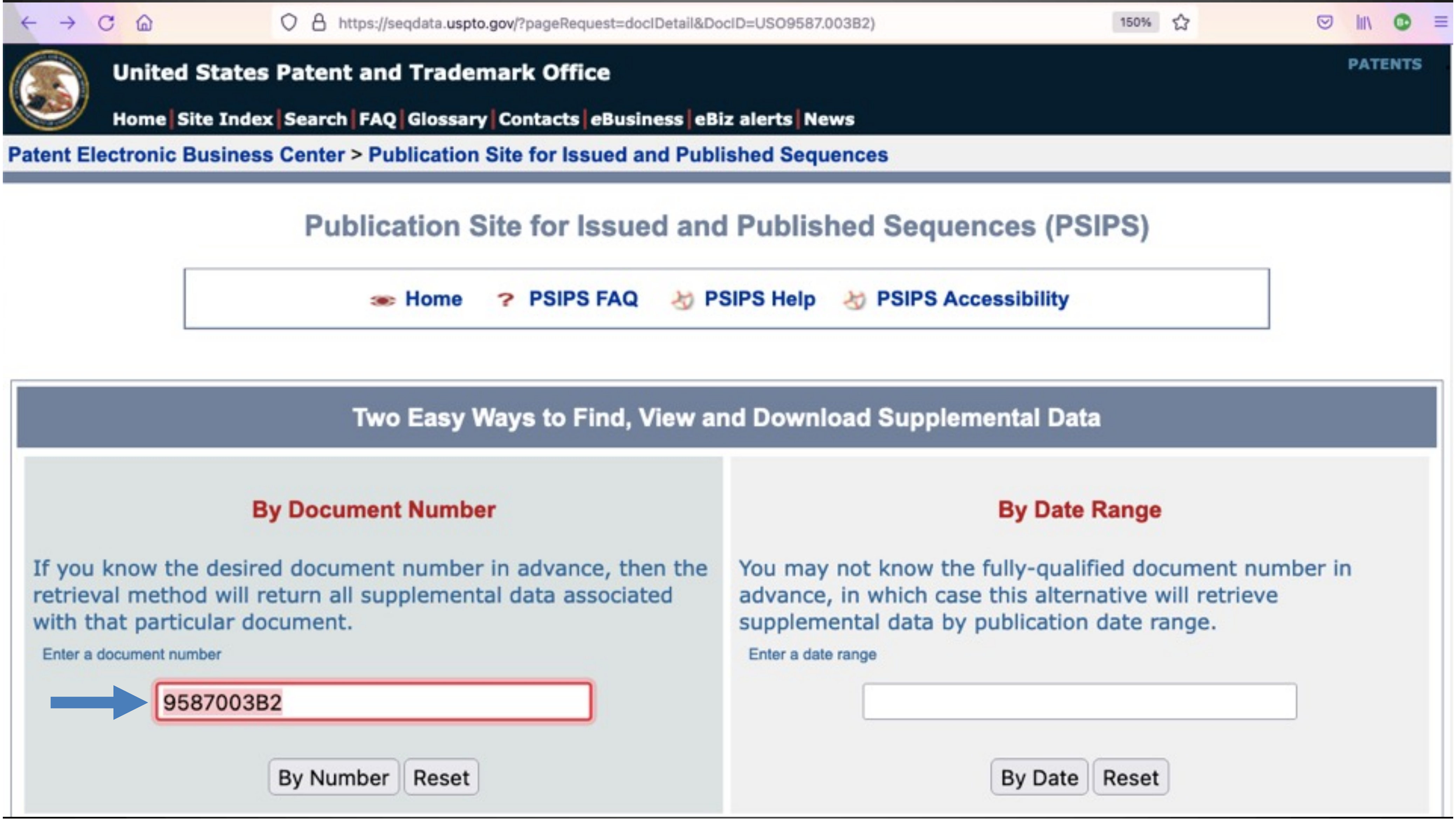
Open the link under the heading that says “LENGTHY TABLES”



LENGTHY TABLES

The patent contains a lengthy table section. A copy of the table is available in electronic form from the USPTO web site (http://seqdata.uspto.gov/?pageRequest=docDetail&DocID=US09587003B2). An electronic copy of the table will also be available from the USPTO upon request and payment of the fee set forth in 37 CFR 1.19(b)(3).

Enter the patent number into this box, then click on "By Number" to access the sequence



https://seqdata.uspto.gov/?pageRequest=docIDetail&DocID=US09587.003B2)

Publication Site for Issued and Published Sequences (PSIPS)

Two Easy Ways to Find, View and Download Supplemental Data

By Document Number

If you know the desired document number in advance, then the retrieval method will return all supplemental data associated with that particular document.

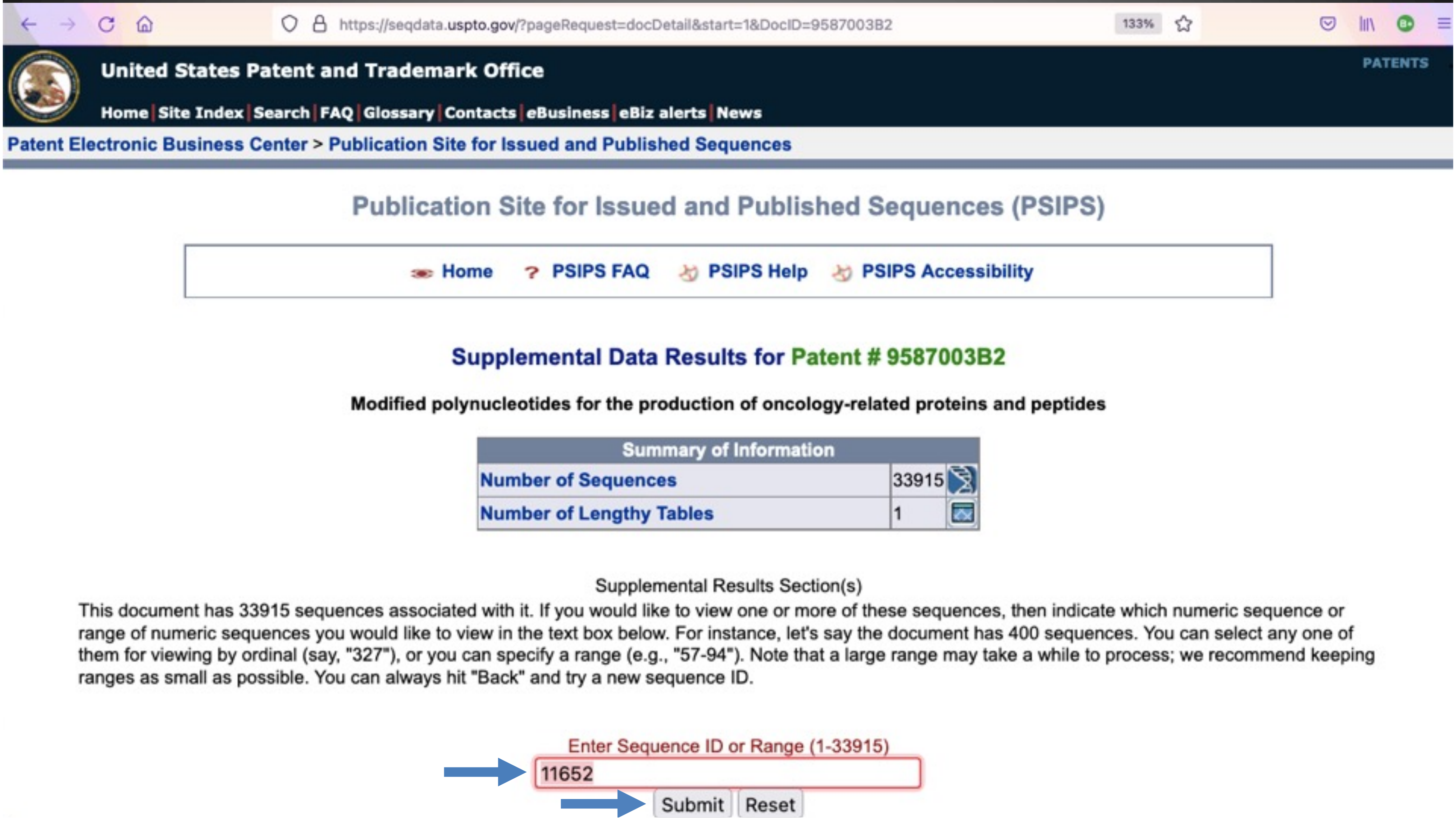
Enter a document number: 9587003B2

By Date Range

You may not know the fully-qualified document number in advance, in which case this alternative will retrieve supplemental data by publication date range.

Enter a date range

Enter sequence number 11652 in this box, then click on “Submit”



Publication Site for Issued and Published Sequences (PSIPS)

Supplemental Data Results for Patent # 9587003B2

Modified polynucleotides for the production of oncology-related proteins and peptides

Summary of Information	
Number of Sequences	33915
Number of Lengthy Tables	1

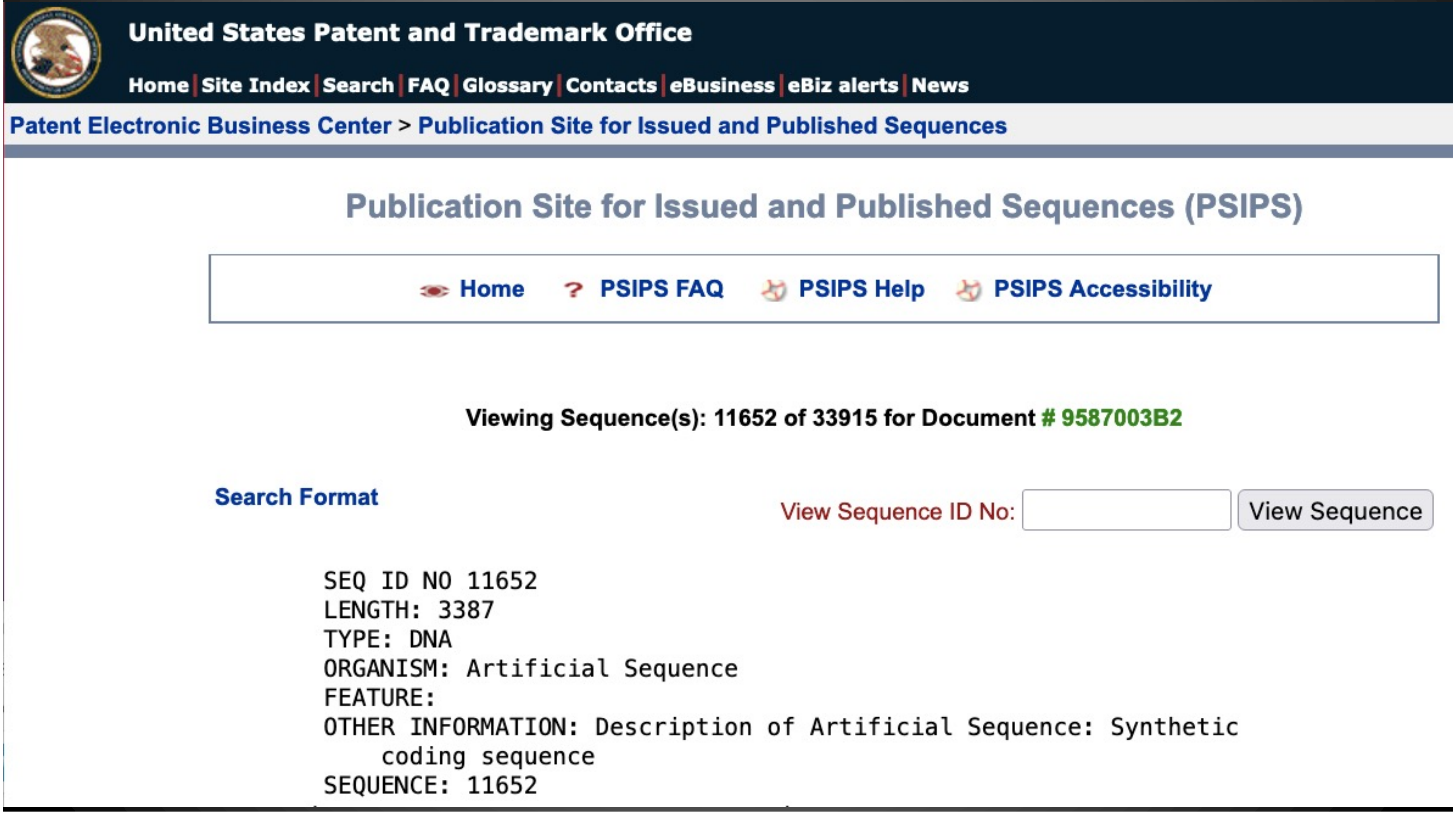
Supplemental Results Section(s)

This document has 33915 sequences associated with it. If you would like to view one or more of these sequences, then indicate which numeric sequence or range of numeric sequences you would like to view in the text box below. For instance, let's say the document has 400 sequences. You can select any one of them for viewing by ordinal (say, "327"), or you can specify a range (e.g., "57-94"). Note that a large range may take a while to process; we recommend keeping ranges as small as possible. You can always hit "Back" and try a new sequence ID.

Enter Sequence ID or Range (1-33915)

11652

Your screen will display this sequence



Publication Site for Issued and Published Sequences (PSIPS)

Viewing Sequence(s): 11652 of 33915 for Document # 9587003B2

View Sequence ID No: ______

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SEQ ID NO 11652
LENGTH: 3387
TYPE: DNA
ORGANISM: Artificial Sequence
FEATURE:
OTHER INFORMATION: Description of Artificial Sequence: Synthetic
    coding sequence
SEQUENCE: 11652
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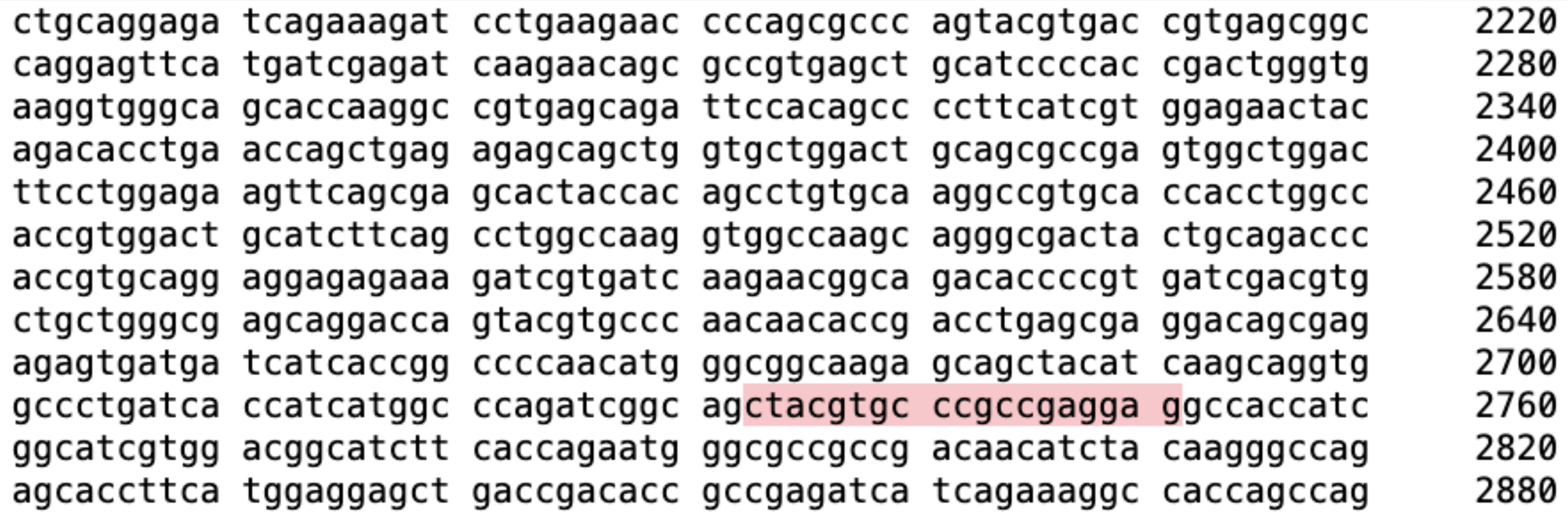
Highlight then copy this 19-letter sequence found in the 2760 region



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aaggtgggca gcaccaaggc cgtgagcaga ttccacagcc ccttcatcgt ggagaactac     2340
agacacctga accagctgag agagcagctg gtgctggact gcagcgccga gtggctggac     2400
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ctgctgggcg agcaggacca gtacgtgccc aacaacaccg acctgagcga ggacagcgag     2640
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ggcatcgtgg acggcatctt caccagaatg ggcgccgccg acaacatcta caagggccag     2820
agcaccttca tggaggagct gaccgacacc gccgagatca tcagaaaggc caccagccag     2880
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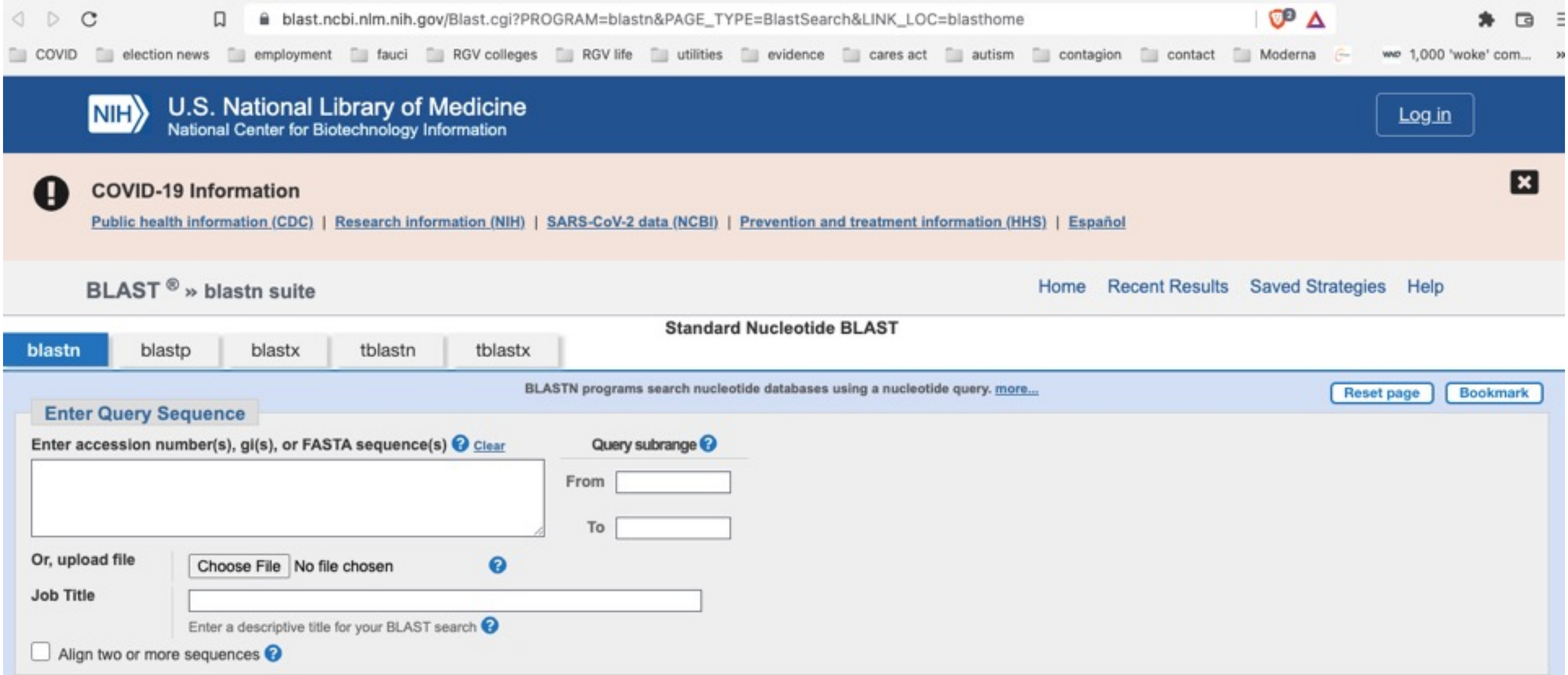
Open a new browser instance, then proceed to open NIH’s database of gene sequences

https://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastn&PAGE_TYPE=BlastSearch&LINK_LOC=blasthome

Your page will appear like this



BLASTN programs search nucleotide databases using a nucleotide query. more...

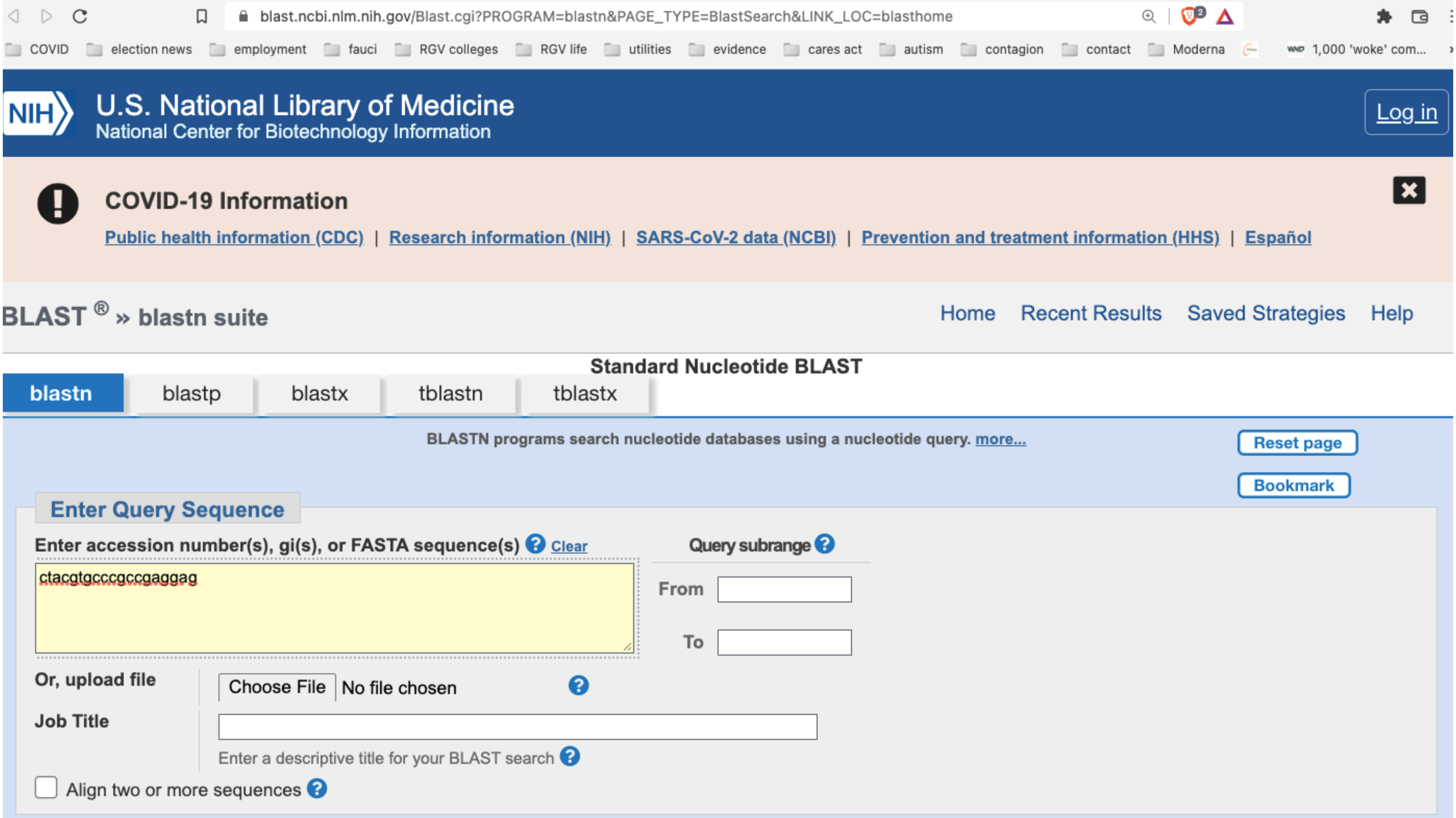
Enter accession number(s), gi(s), or FASTA sequence(s)

Or, upload file: No file chosen

Enter a descriptive title for your BLAST search

☐ Align two or more sequences

Place cursor in the "Enter Query Sequence" box indicated and paste copied sequence



blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastn&PAGE_TYPE=BlastSearch&LINK_LOC=blasthome

COVID | election news | employment | fauci | RGV colleges | RGV life | utilities | evidence | cares act | autism | contagion | contact | Moderna | 1,000 'woke' com...

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Standard Nucleotide BLAST

blastn | blastp | blastx | tblastn | tblastx

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Enter Query Sequence

Enter accession number(s), gi(s), or FASTA sequence(s) ? Clear

ctacgtgcccgccgaggag

Query subrange ?

From

To

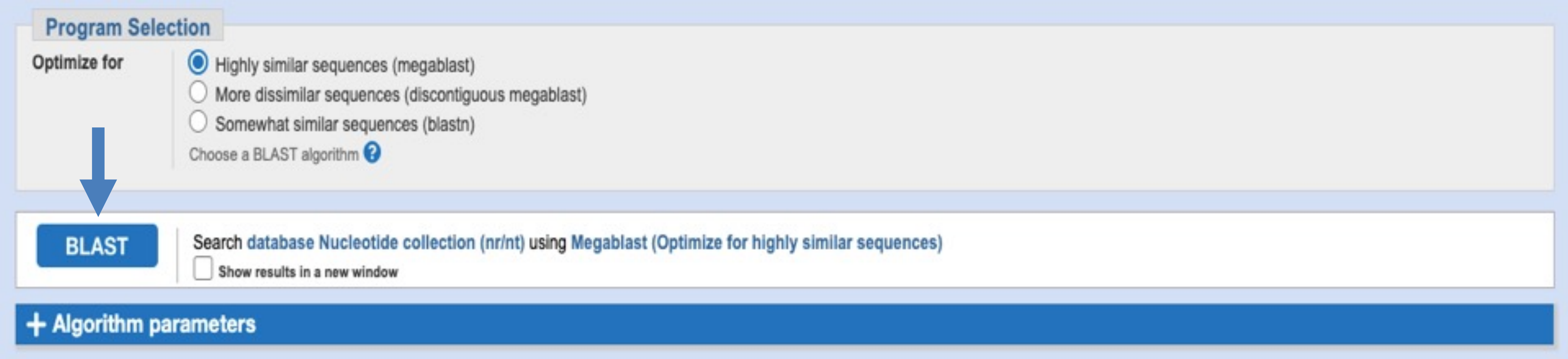
Or, upload file: Choose File No file chosen ?

Job Title

Enter a descriptive title for your BLAST search ?

☐ Align two or more sequences ?

Scroll down to the bottom and then click on "BLAST"



Program Selection

Optimize for

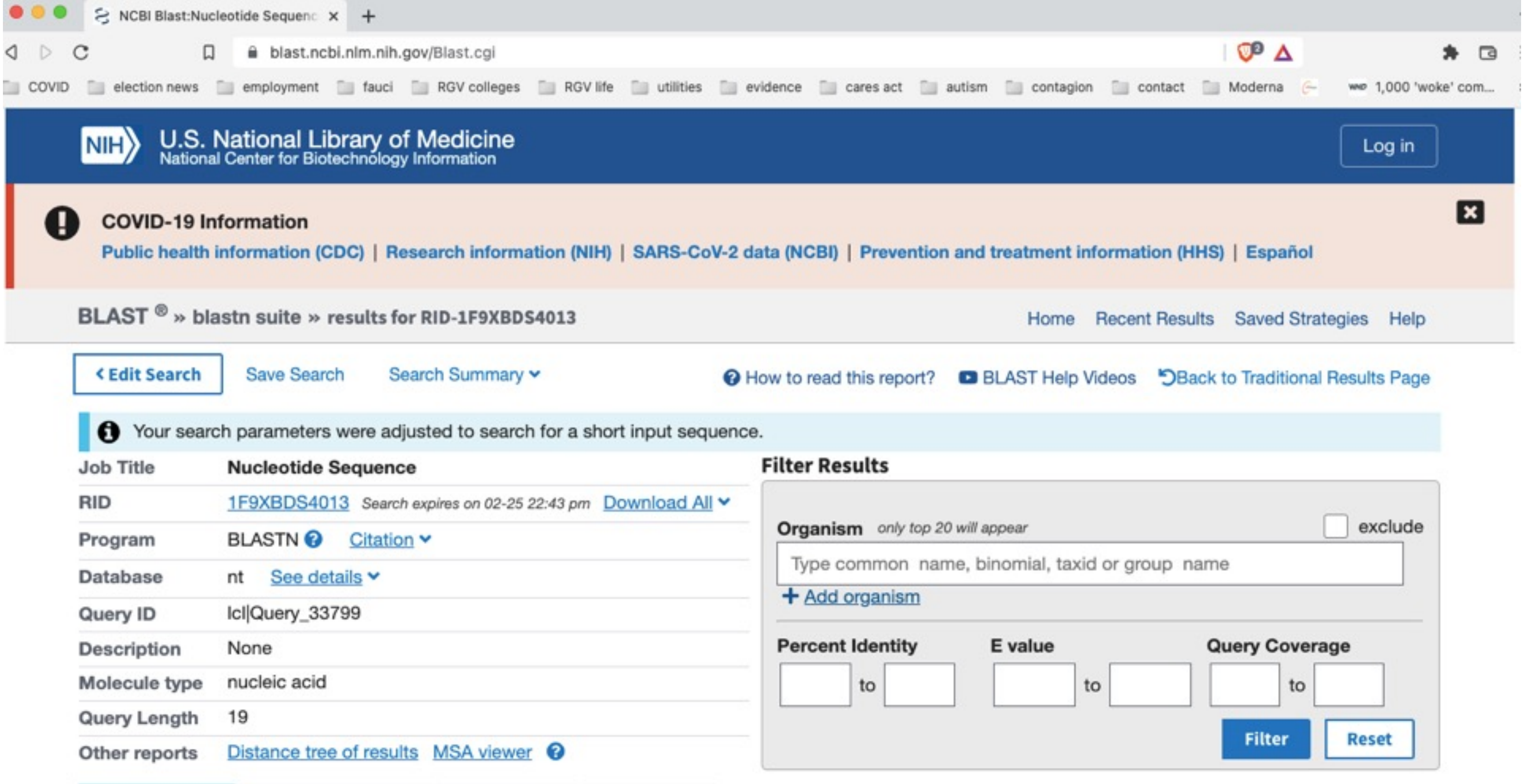
● Highly similar sequences (megablast)
○ More dissimilar sequences (discontiguous megablast)
○ Somewhat similar sequences (blastn)

Choose a BLAST algorithm

Search database Nucleotide collection (nr/nt) using Megablast (Optimize for highly similar sequences)

☐ Show results in a new window

The search may take 5 minutes. Be patient!



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COVID-19 Information

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

BLAST ® » blastn suite » results for RID-1F9XBDS4013

Your search parameters were adjusted to search for a short input sequence.

Job Title	Nucleotide Sequence
RID	1F9XBDS4013 *Search expires on 02-25 22:43 pm* Download All
Program	BLASTN Citation
Database	nt See details
Query ID	lcl|Query_33799
Description	None
Molecule type	nucleic acid
Query Length	19
Other reports	Distance tree of results MSA viewer

Filter Results

Organism *only top 20 will appear* ☐ exclude

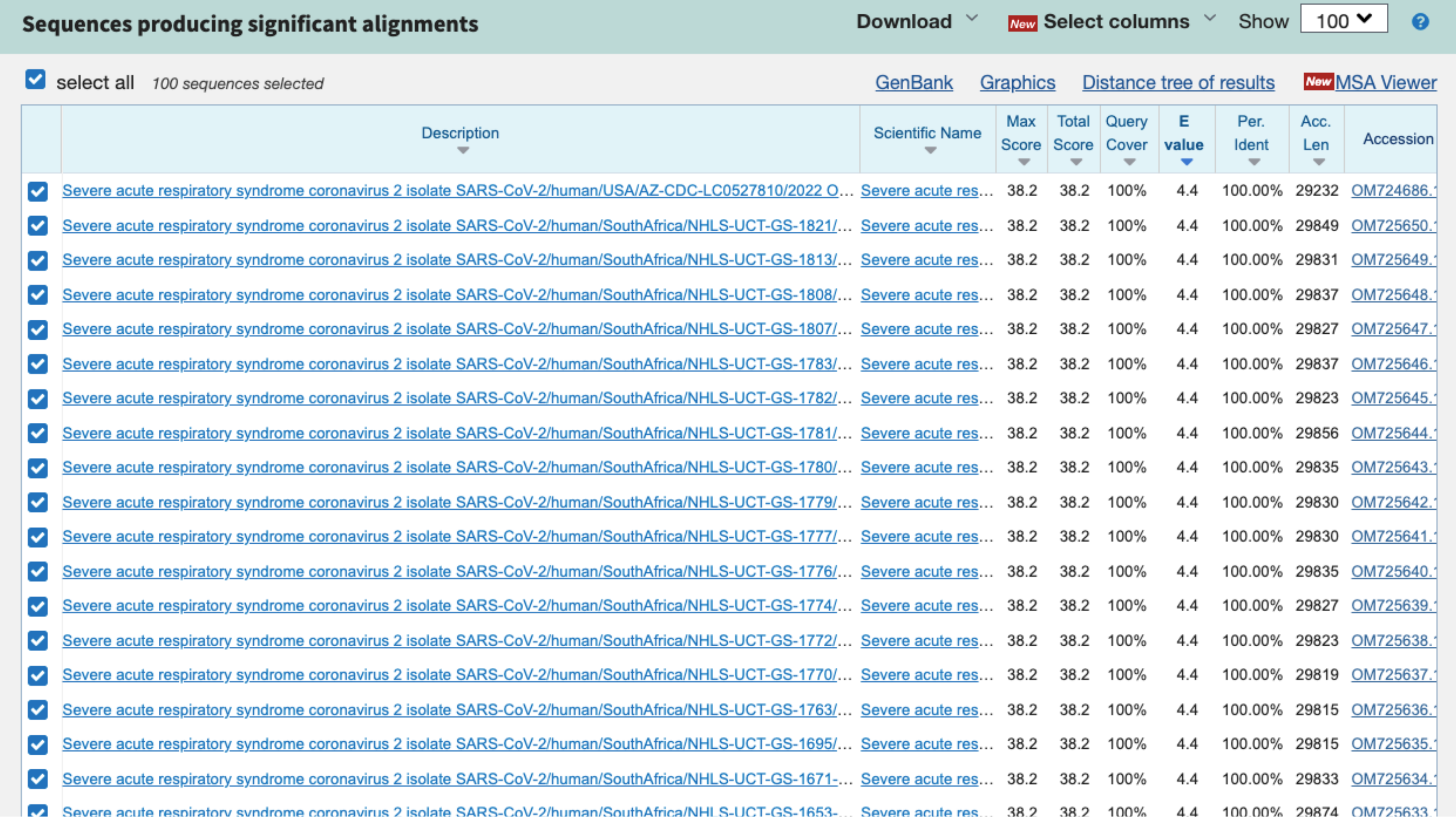
Type common name, binomial, taxid or group name

+ Add organism

Percent Identity ☐ to ☐ **E value** ☐ to ☐ **Query Coverage** ☐ to ☐

Your page will eventually appear like this

Scroll down and you will find links to all nucleotide sequences uploaded to NIH



Sequences producing significant alignments

☑ select all *100 sequences selected*

	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/AZ-CDC-LC0527810/2022 O…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29232	OM724686.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1821/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29849	OM725650.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1813/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29831	OM725649.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1808/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29837	OM725648.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1807/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29827	OM725647.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1783/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29837	OM725646.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1782/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29823	OM725645.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1781/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29856	OM725644.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1780/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29835	OM725643.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1779/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29830	OM725642.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1777/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29830	OM725641.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1776/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29835	OM725640.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1774/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29827	OM725639.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1772/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29823	OM725638.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1770/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29819	OM725637.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1763/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29815	OM725636.
☑	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/SouthAfrica/NHLS-UCT-GS-1695/…	Severe acute res…	38.2	38.2	100%	4.4	100.00%	29815	OM725635.
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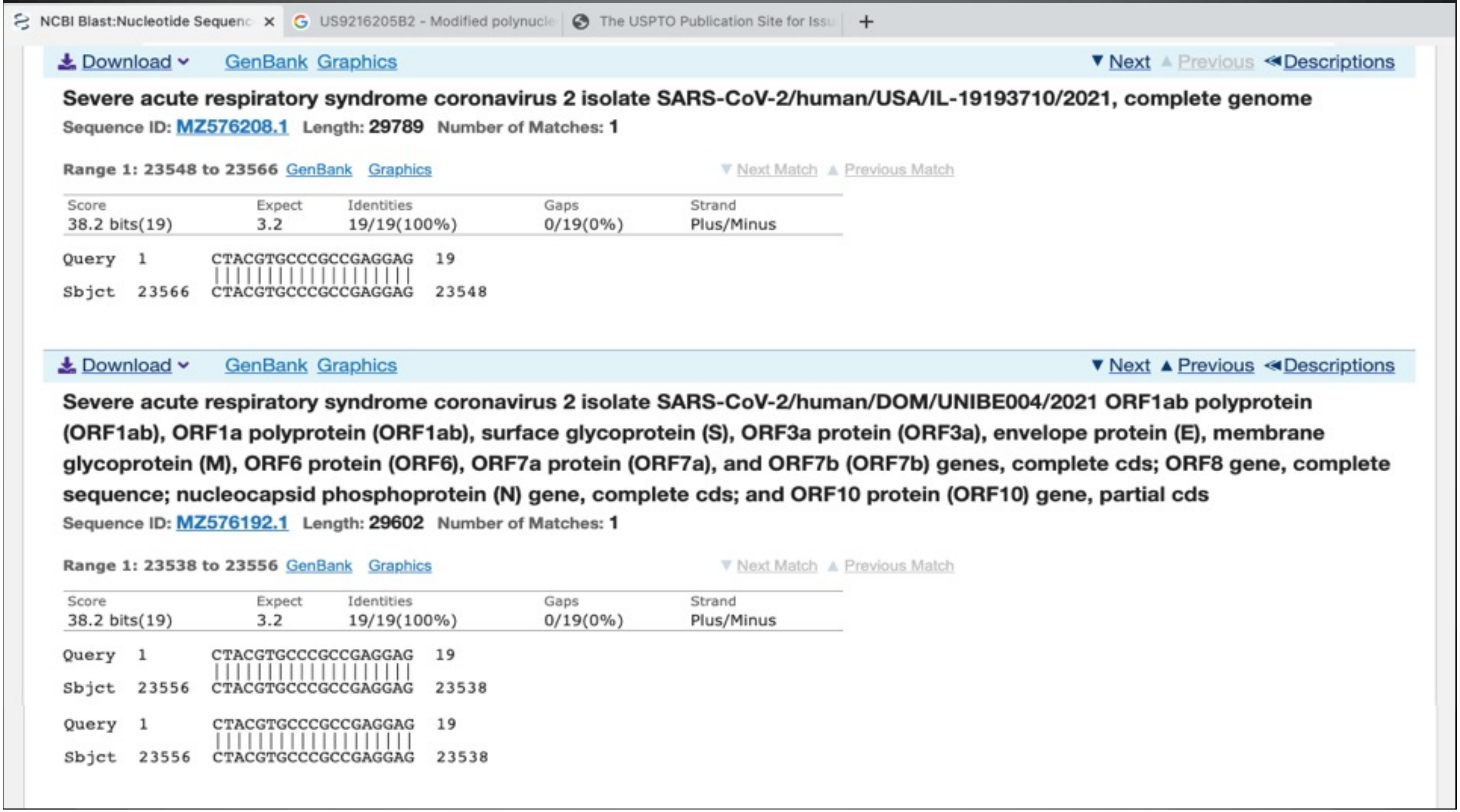
This is a sample of what you might see if you open one of these sequence links



Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/USA/IL-19193710/2021, complete genome

Sequence ID: MZ576208.1 Length: **29789** Number of Matches: **1**

Range 1: 23548 to 23566 GenBank Graphics

Score	Expect	Identities	Gaps	Strand
38.2 bits(19)	3.2	19/19(100%)	0/19(0%)	Plus/Minus

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Query  1      CTACGTGCCCGCCGAGGAG  19
              |||||||||||||||||||
Sbjct  23566  CTACGTGCCCGCCGAGGAG  23548
```

Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/human/DOM/UNIBE004/2021 ORF1ab polyprotein (ORF1ab), ORF1a polyprotein (ORF1ab), surface glycoprotein (S), ORF3a protein (ORF3a), envelope protein (E), membrane glycoprotein (M), ORF6 protein (ORF6), ORF7a protein (ORF7a), and ORF7b (ORF7b) genes, complete cds; ORF8 gene, complete sequence; nucleocapsid phosphoprotein (N) gene, complete cds; and ORF10 protein (ORF10) gene, partial cds

Sequence ID: MZ576192.1 Length: **29602** Number of Matches: **1**

Range 1: 23538 to 23556 GenBank Graphics

Score	Expect	Identities	Gaps	Strand
38.2 bits(19)	3.2	19/19(100%)	0/19(0%)	Plus/Minus

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              |||||||||||||||||||
Sbjct  23556  CTACGTGCCCGCCGAGGAG  23538

Query  1      CTACGTGCCCGCCGAGGAG  19
              |||||||||||||||||||
Sbjct  23556  CTACGTGCCCGCCGAGGAG  23538
```
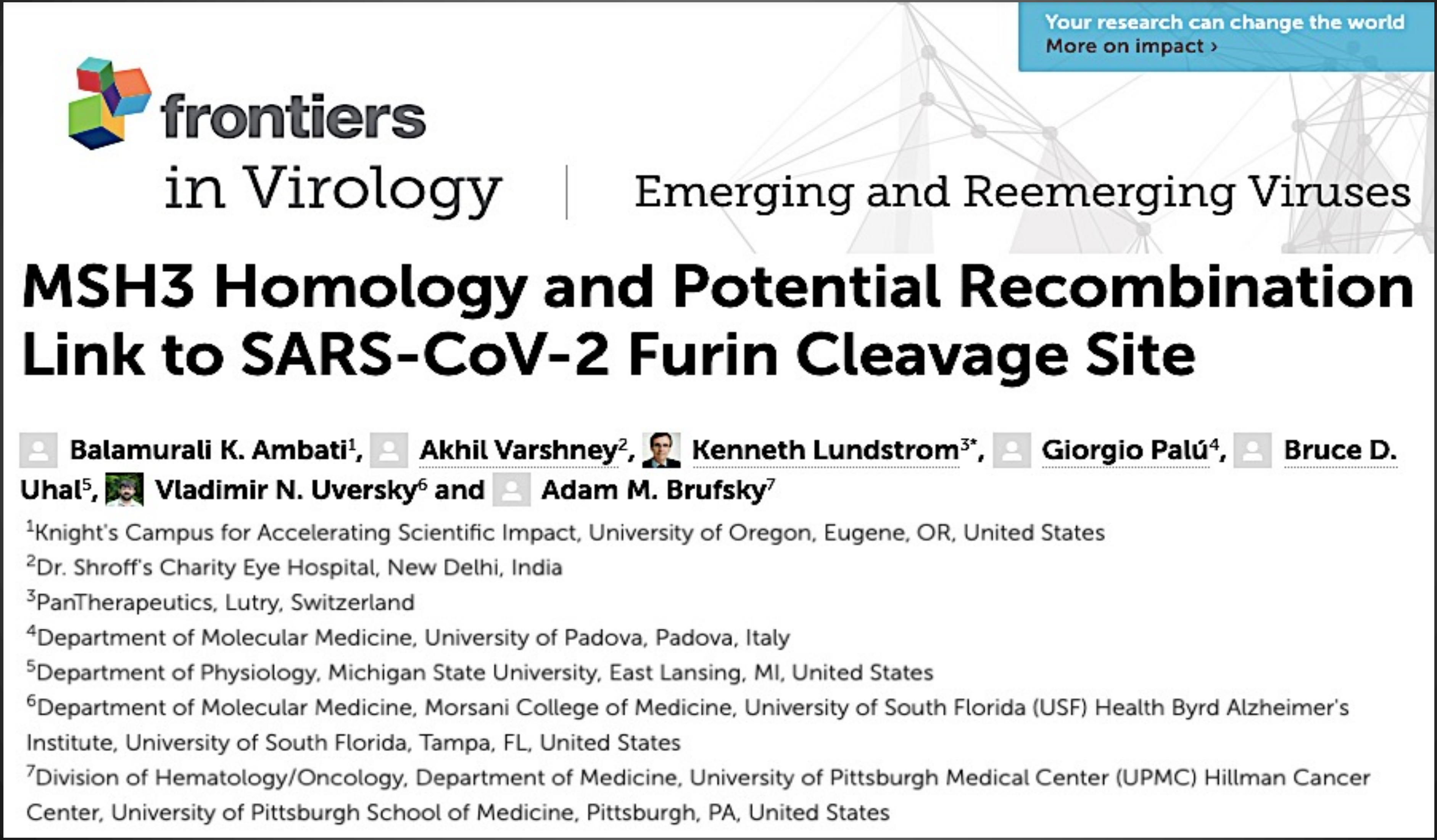

What is the significance of these results?

1. In 2013 Moderna applied to patent a “modified polynucleotide” that contains a 19-base sequence that is the reverse compliment of a 19-base sequence in the COVID-19 virus.
2. This 19-base sequence does not occur in any other virus listed in the NIH database
3. This 19-base sequence contains the “furin cleavage site”(PRRAR)
4. The furin cleavage site plays a key role facilitating entry of the COVID-19 virus into human cells
5. The probability that the same 19-base sequence appeared in the virus by means of natural selection is 1 out of 3.6 trillion.

ACKNOWLEDGMENTS:

The power point is based on information provided in the following article:



frontiers in Virology | Emerging and Reemerging Viruses

MSH3 Homology and Potential Recombination Link to SARS-CoV-2 Furin Cleavage Site

Balamurali K. Ambati[1], **Akhil Varshney**[2], **Kenneth Lundstrom**[3]*, **Giorgio Palú**[4], **Bruce D. Uhal**[5], **Vladimir N. Uversky**[6] and **Adam M. Brufsky**[7]

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[5]Department of Physiology, Michigan State University, East Lansing, MI, United States
[6]Department of Molecular Medicine, Morsani College of Medicine, University of South Florida (USF) Health Byrd Alzheimer's Institute, University of South Florida, Tampa, FL, United States
[7]Division of Hematology/Oncology, Department of Medicine, University of Pittsburgh Medical Center (UPMC) Hillman Cancer Center, University of Pittsburgh School of Medicine, Pittsburgh, PA, United States

https://www.frontiersin.org/articles/10.3389/fviro.2022.834808/full