Identifying Possible Biological Processes Affected By Non-Target Proteins of the SARS-CoV-2

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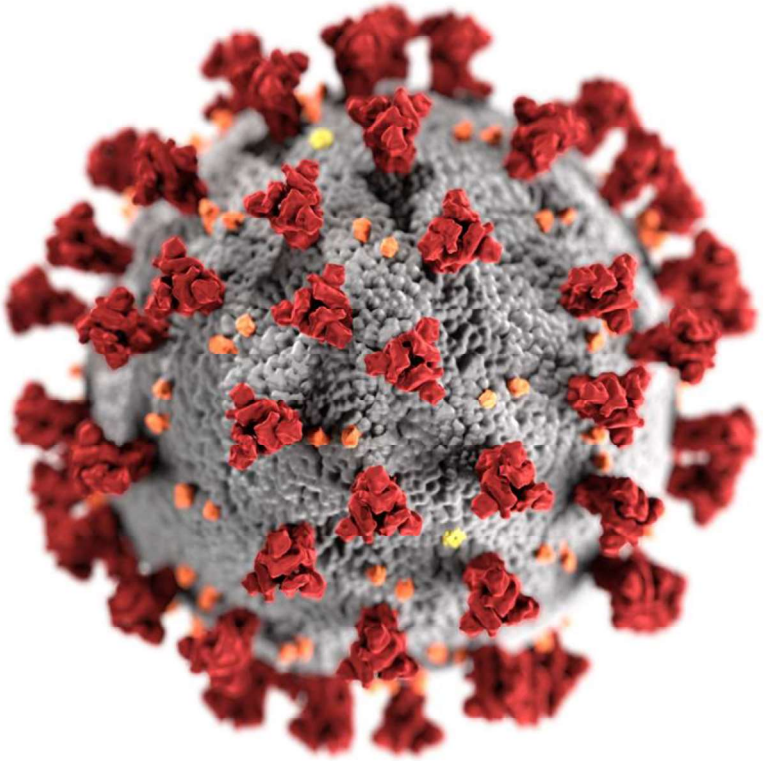
Abstract

SARS-CoV-2 has spurred remarkable interest in vaccine development and our understanding of the virus' enduring effects. My research is aimed at identifying the non-target receptors of SARS-CoV-2 and utilizing comparable proteins to elucidate their impact on organs, potentially contributing to the development of long COVID. The Angiotensin Converting Enzyme 2 (ACE2) receptor was identified as the entry point for SARS-CoV-2 after extensive research. The ACE2 receptor is highly concentrated in the lungs and heart, helping the spread of the virus. The methods involved data collection from the National Center for Biotechnology Information (NCBI), including extensive gene and protein research, following an analysis between the ACE2 receptor and a related protein called Collectrin, which has a 40.87% resemblance. The findings revealed that Collectrin is primarily present in the kidneys, while also showing numerous aspects of gene expression levels of the ACE2 receptor and Collectrin within specific organs. Understanding the presence and functions of Collectrin could contribute to the treatment of long-COVID syndrome, which represents the lingering effects of the SARS-CoV-2 infection. This research provides valuable insights and helps understand the after-effects of the SARS-CoV-2 infection.

Introduction

SARS-CoV-2 struck three years ago, with the pandemic limiting us to our homes until scientists found a vaccine using modern technologies

After seeing people affected by the intensity of symptoms and fatigue of SARS-CoV-2, I aimed for this project to target specific possible non-target proteins of SARS-CoV-2 by identifying their location to provide an explanation for the after-effects. [2]



Background Research: Viruses

Viruses have a fascinating history of discoveries and they come in different forms, replicate through cycles, with notable examples such as SARS-CoV-2, HIV, and Ebola, that present ongoing challenges. [5]

Background Research: SARS-CoV-2

SARS-CoV-2 uses the ACE2-Receptor as an entryway while primarily targeting the lungs and the heart. Afterwards SARS-CoV-2 replicates and this leads to multiple organ failure and sometimes death. [1]

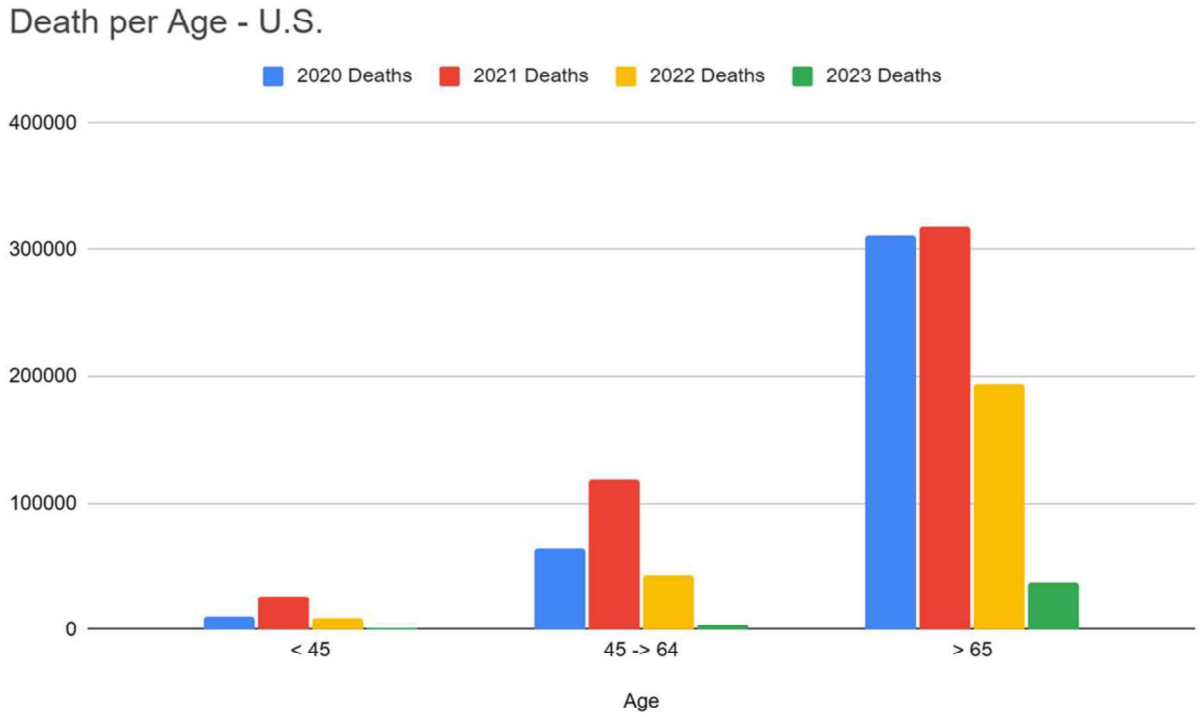
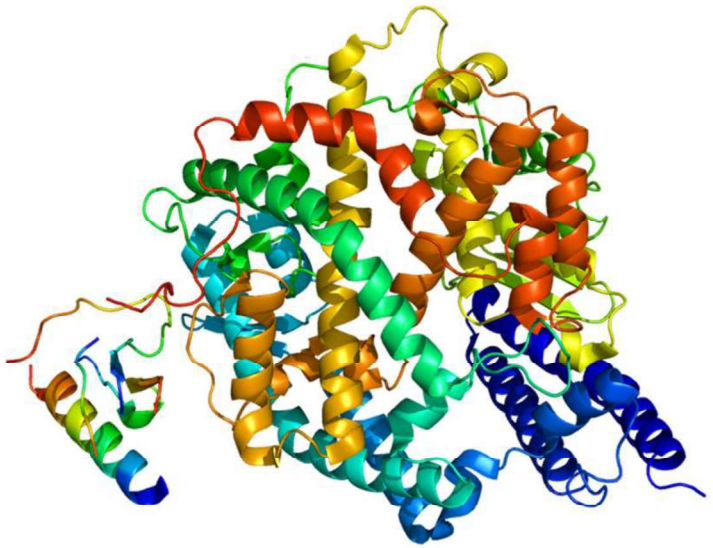


Figure 1.1: *The image above represents the deaths for clusters of ages from 2020 to 2023 for the US. [6]*

Background Research: ACE2-Receptor

The ACE2 Receptor is used by SARS-CoV-2 to enter into the body. [3] The receptor is highly expressed in the lungs and heart. Although, the expression levels for people are different, there is no direct relation between the severity of SARS-CoV-2 and the presence of the ACE2 receptor epithelial cells. [10]



Background Research: Long COVID

Long COVID also known as Post COVID syndrome is a after infection of SARS-CoV-2 which has symptoms such as fatigue, shortness of breath, etc. weeks after the viral diagnosis. Long COVID syndrome affects all ages and affects bodily functions.

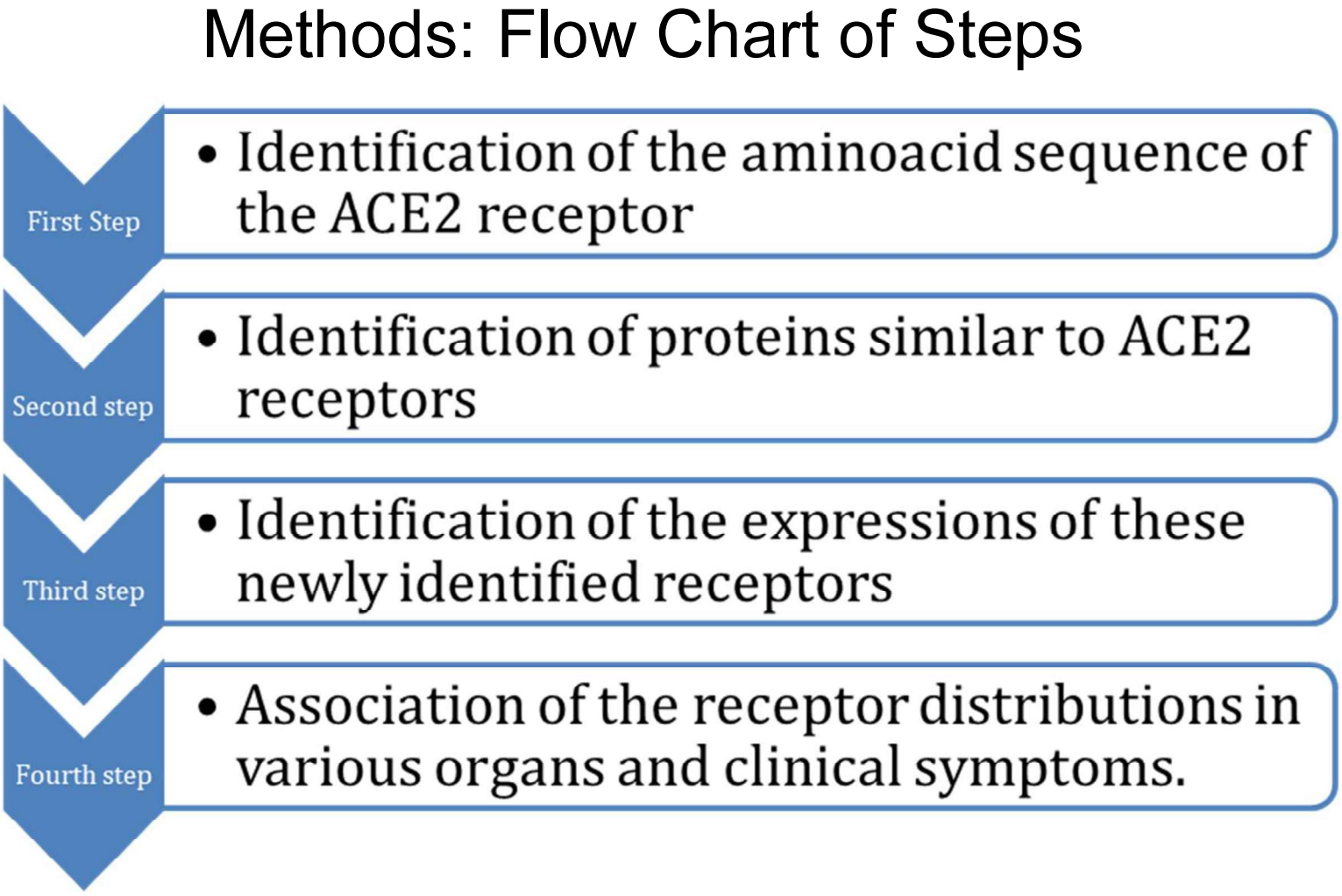


Fig 2.1: *Diagram explaining the steps in the research study.*

Methods: Sites Used

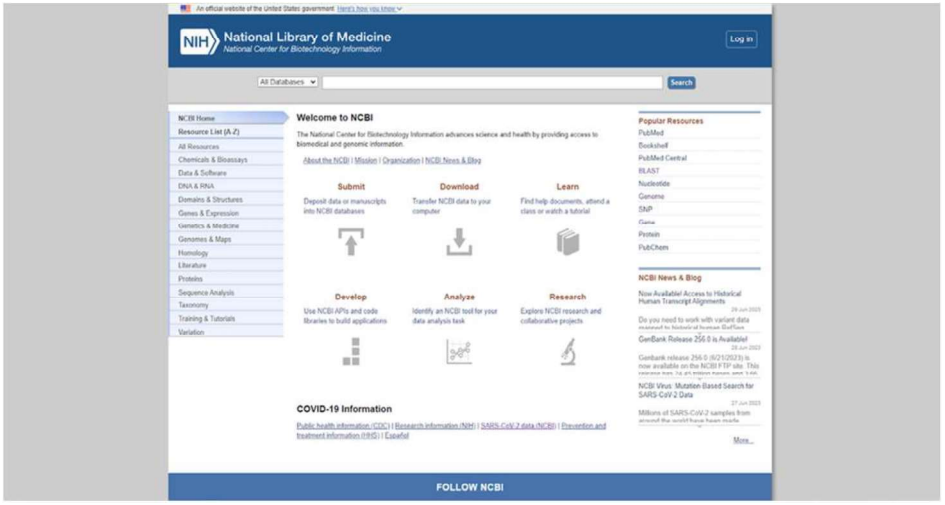


Figure 3.1: *The above shows NIH the National Library of Medicine*

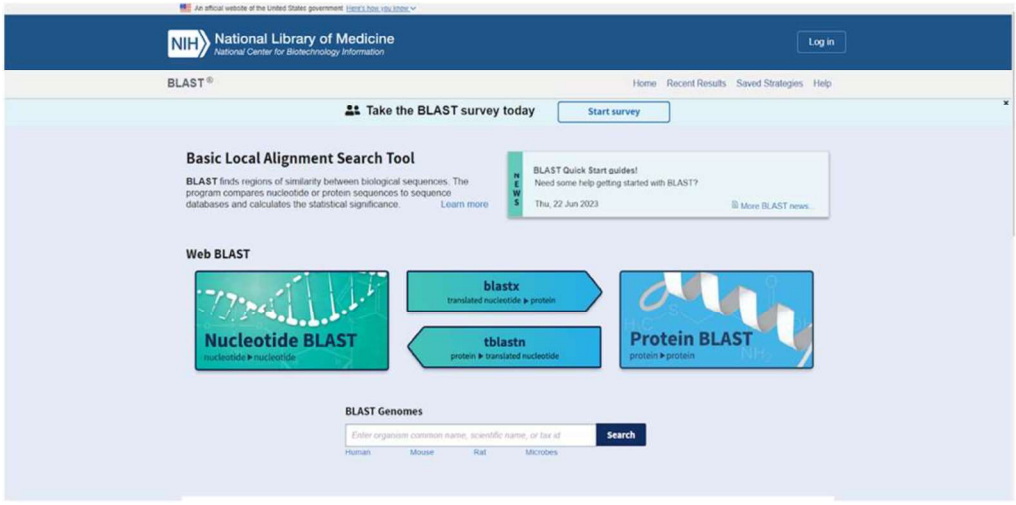


Figure 3.2: *The BLAST page by the NIH is shown above [4]*

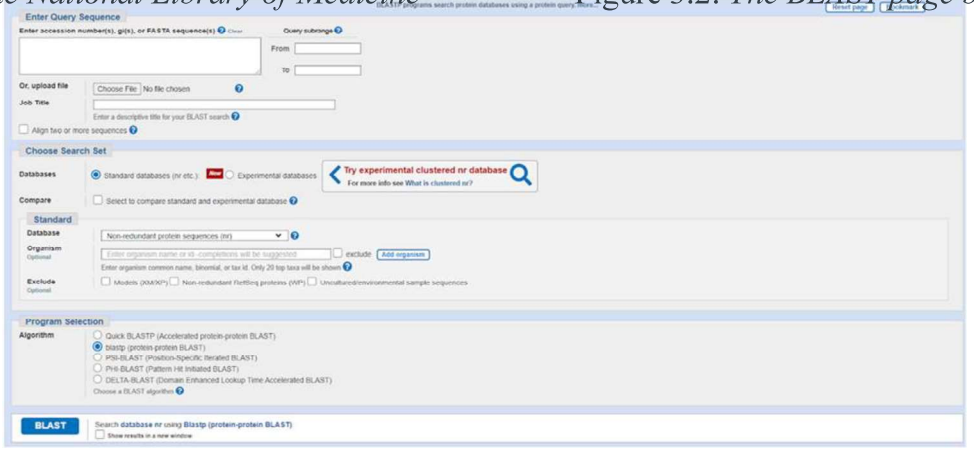


Figure 3.3: *The above request form from the Protein BLAST*

Findings: ‘Distance Tree of Results’

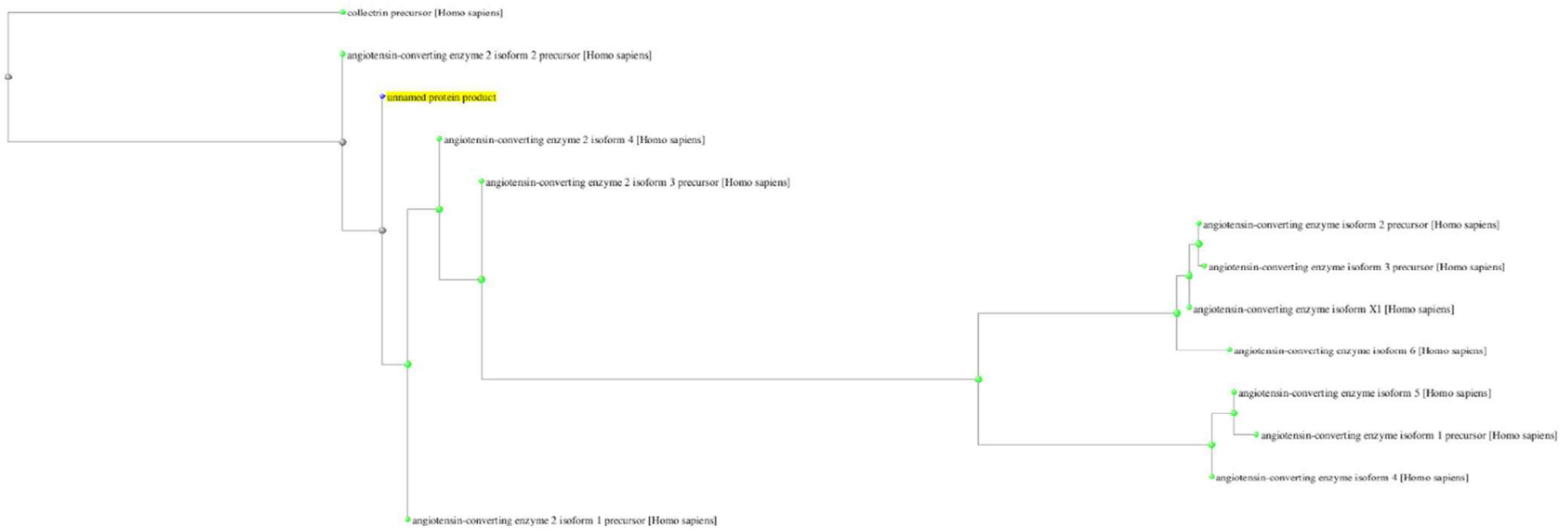


Figure 5.1: *The ‘distance tree of results’ helps show the related proteins with the ACE2 receptor. The ‘distance tree of results’ is always changing with more information on related proteins and the highlighted protein or the unnamed one is Collectrin, which is the similar protein to ACE2.*

Findings: Resemblance

Sequences producing significant alignments Download Select columns Show 100

select all *5 sequences selected* GenPept Graphics Distance tree of results Multiple alignment MSA Viewer

	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
☐	angiotensin-converting enzyme 2 isoform 1 precursor [Homo sapiens]	Homo sapiens	1685	1685	100%	0.0	100.00%	805	NP_001358344.1
☐	angiotensin-converting enzyme 2 isoform 2 precursor [Homo sapiens]	Homo sapiens	1611	1611	95%	0.0	100.00%	786	NP_001373188.1
☐	angiotensin-converting enzyme 2 isoform 3 precursor [Homo sapiens]	Homo sapiens	1172	1459	90%	0.0	95.41%	694	NP_001373189.1
☐	angiotensin-converting enzyme 2 isoform 4 [Homo sapiens]	Homo sapiens	942	942	57%	0.0	98.47%	459	NP_001375381.1
☐	angiotensin-converting enzyme isoform 2 precursor [Homo sapiens]	Homo sapiens	512	512	74%	6e-171	41.83%	732	NP_690043.1
☐	angiotensin-converting enzyme isoform 5 [Homo sapiens]	Homo sapiens	509	859	74%	4e-166	41.79%	1022	NP_001369630.1
☐	angiotensin-converting enzyme isoform 4 [Homo sapiens]	Homo sapiens	510	770	74%	2e-165	41.79%	1117	NP_001369629.1
☐	angiotensin-converting enzyme isoform 1 precursor [Homo sapiens]	Homo sapiens	509	1007	74%	4e-163	41.79%	1306	NP_000780.1
☐	angiotensin-converting enzyme isoform X1 [Homo sapiens]	Homo sapiens	488	488	67%	6e-163	43.59%	616	XP_006721800.3
☐	angiotensin-converting enzyme isoform 3 precursor [Homo sapiens]	Homo sapiens	433	433	74%	7e-141	37.42%	691	NP_001171528.1
☐	angiotensin-converting enzyme isoform 6 [Homo sapiens]	Homo sapiens	300	300	67%	4e-92	32.66%	511	NP_001369631.1
☑	collectrin precursor [Homo sapiens]	Homo sapiens	135	135	23%	3e-35	40.87%	222	NP_065716.1
☐	collectrin isoform X1 [Homo sapiens]	Homo sapiens	92.8	92.8	19%	5e-21	38.24%	170	XP_016885169.1
☐	collectrin isoform X2 [Homo sapiens]	Homo sapiens	57.4	57.4	5%	3e-09	54.76%	119	XP_016885170.1

Figure 5.2: *The resemblance or the percent of identity between Collectrin and ACE2 is shown above, with a 40.87%*

Findings: RPKM Gene Expression Levels

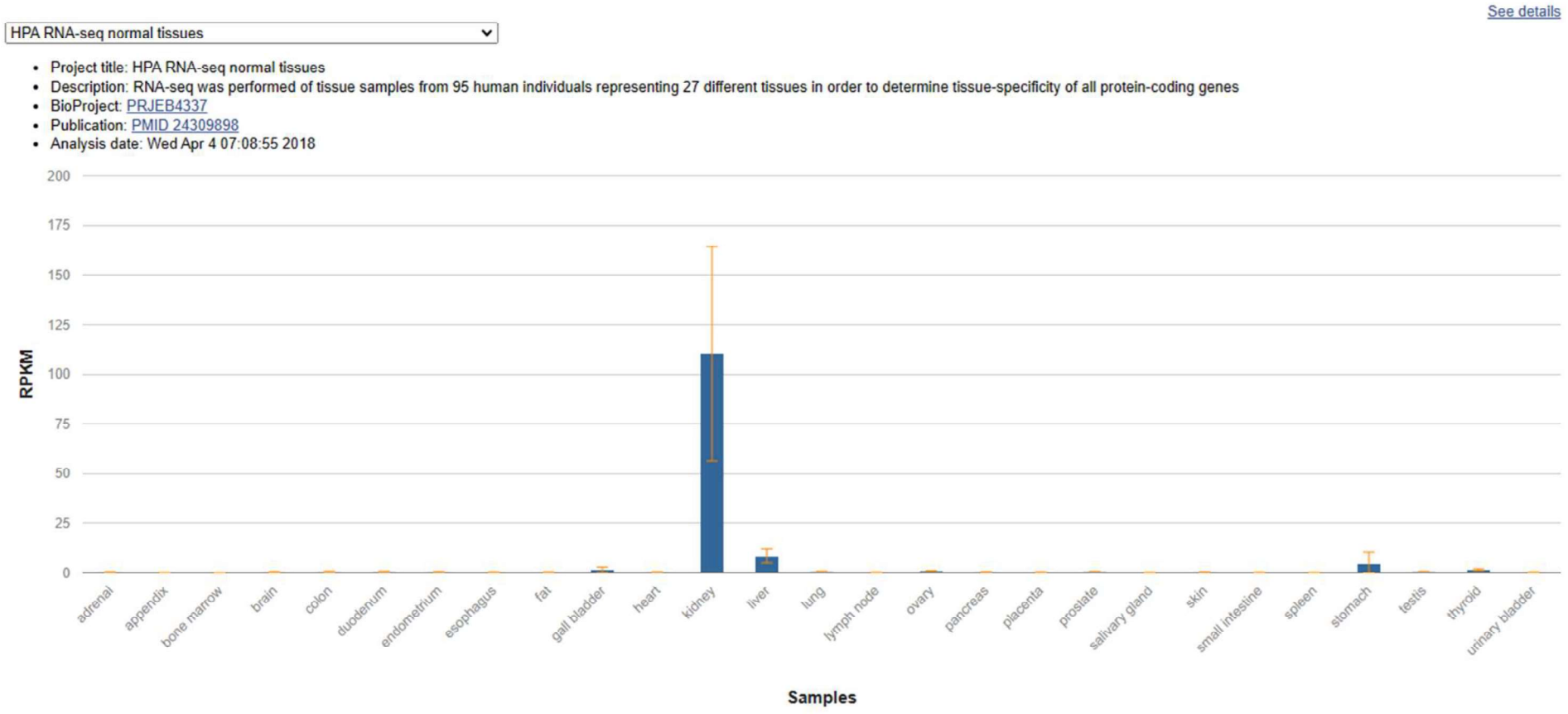


Figure 6.1: *The image above represents the RPKM gene expression levels for Collectrin*

Findings: Collectrin Top 3 Organs RPKM

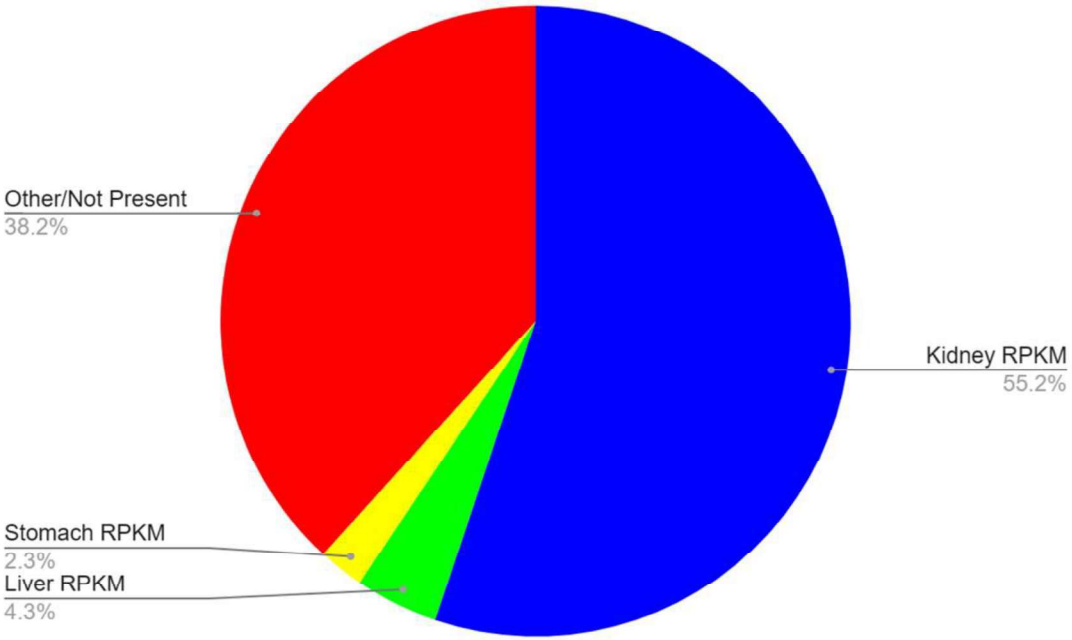


Figure 6.2: *The RPKM gene expression levels for Collectrin in each of its top three organs would be 55.172% for the kidney, 4.26% for the liver, and 2.31% for the stomach. This is the percentage figure of the RPKM gene level expression in* Figure 6.1.

Main Findings:

- Collectrin had a 40.87% resemblance with ACE2
- The probability percentage was 6.16% by using Collectrin's RPKM gene expression levels as well as the resemblance between Collectrin and ACE2

Limitations

- This is not a clinical study but a study that produces a hypothesis with a need for clinical experiments as the next step.
- The extent of the search for ACE2 similar receptors is dependent on the length and breadth of the database which was searched.
- The binding properties to the non-ACE2 receptors would vary depending on the strain of SAR CoV-2; as the virus is prone to frequent mutations.

Conclusion

Collectrin, the newly found protein has a 40.87% similarity with the ACE2 receptor, as a binding site for SARS-CoV-2. Collectrin is expressed in the kidneys, liver, and stomach.

Triggering Collectrin causes…

- Inflammation and kidney dysfunction up to 35% more likely in already recovered patients
- Physiological changes such as unbalanced microbiome, digestive problems, enhanced liver failure [7][8]

With these changes this could explain the following symptoms in Long COVID…

- Diarrhea, bloating, discomfort, fatigue, shortness of breath, swelling, pain, etc.

Future

For the future of this research, it is important to undertake clinical trials and engage in more extensive research. Currently, ACE2 plays a role as the original binding point for SARS-CoV-2. Its interaction with the vaccine's spike proteins is well-established and forms the basis of the vaccine's mechanism of action. [9] The next step of this project is to use understanding of the relation between Collectrin and Long-COVID to make a medication that helps with the prevention of long-term infection.

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