Novel peptide-based viral inactivation strategy targeting COVID-19

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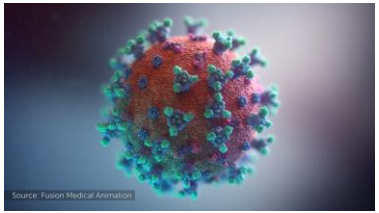
Program: Topic

Jet Propulsion Laboratory
California Institute of Technology

Introduction



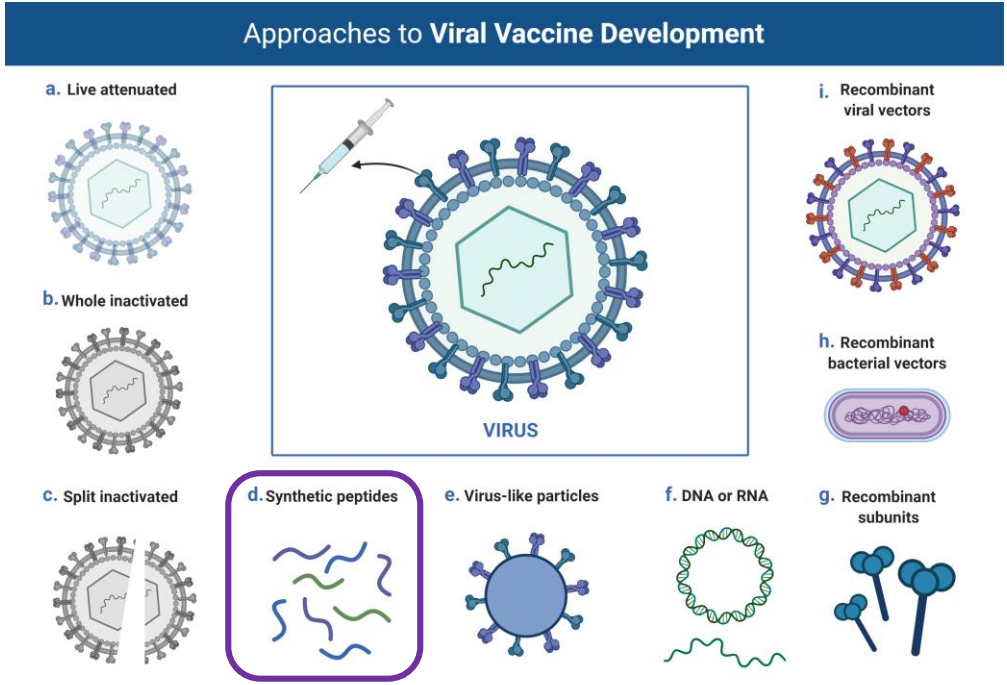
Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV)

A novel coronavirus was first reported in Wuhan on December 29, 2019, that culminated in pneumonia-like symptoms and known as SARS-CoV-2 (COVID-19)(Parker et. al. 2020)

As of September 20, 2019, SARS-CoV-2 has infected more than >31 million people, and the death toll is ~1 million.

Introduction

- New approaches beyond drug repurposing, vaccination, and immunotherapy have to be implemented to cope with outbreak situations like the one we are currently facing.(Madhavan and Mustafa, 2020)
- Peptides are smaller fragments of proteins that can be quickly synthesized and used in the phase of a pandemic (Han and Král, 2020). Advantage of peptide-based drugs are as follow.
  - A short time of production, from prediction to lab testing (1yr or less)
  - Targeted application and quick modification
  - Stable for a longer duration of time compared to the conventional medicine



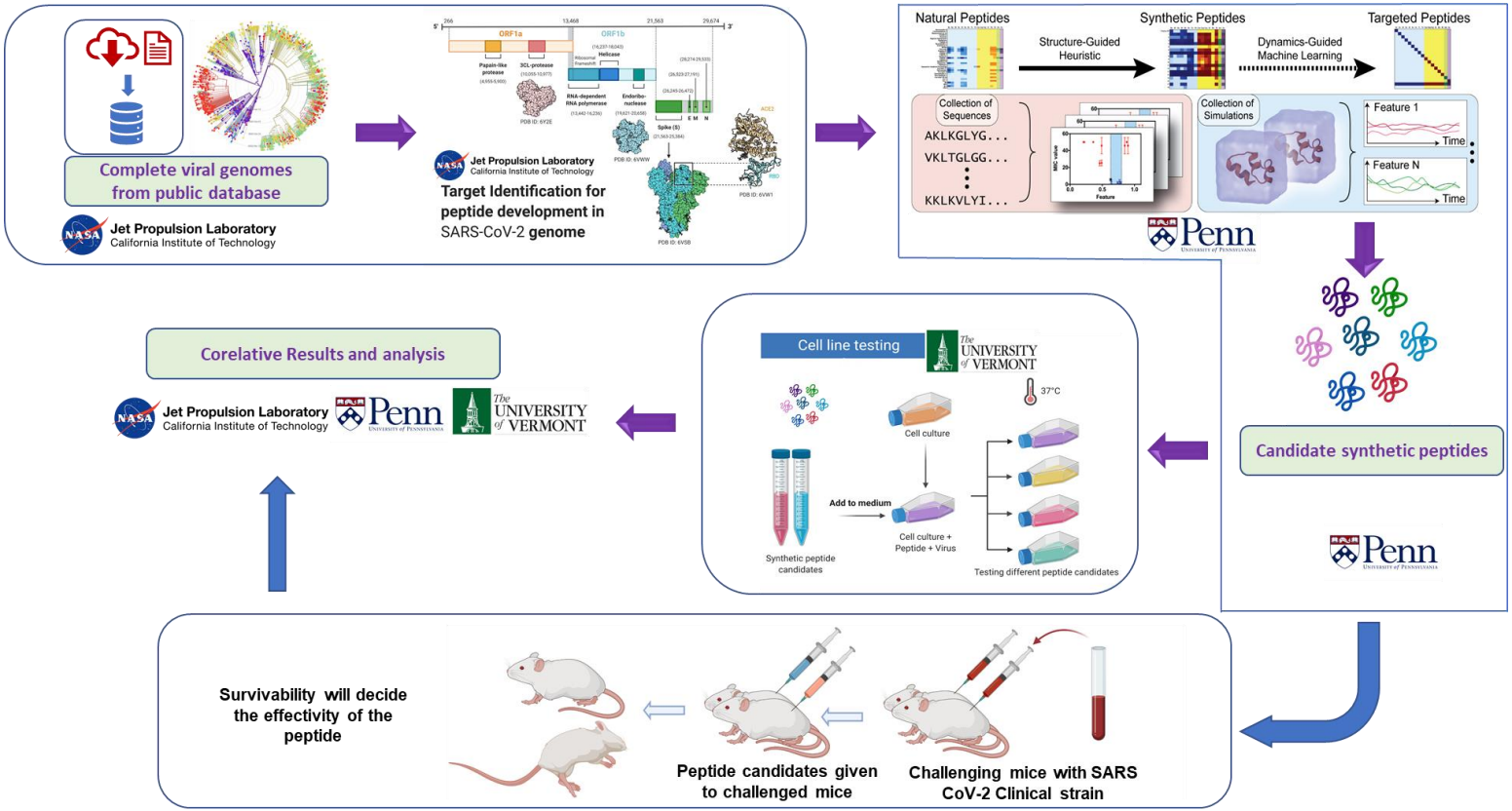
Problem Description

a) During an outbreak situation, traditional drug discovery is not an efficient option as this process is inherently slow to deal with the immense need for timely therapeutic solutions

b) The advantages of peptides as drugs are rapid discovery, specificity and affinity to desired targets, and low toxicity due to the limited possibility for accumulation in the body

c) NASA-JPL has been at the forefront of microbial tracking experiments and is capable of developing strategies for any biological calamities like COVID-19 spread. The proposed work will help create efficient tools for combating microbial infection and help build countermeasures for future similar biological challenges for space missions.

Methodology



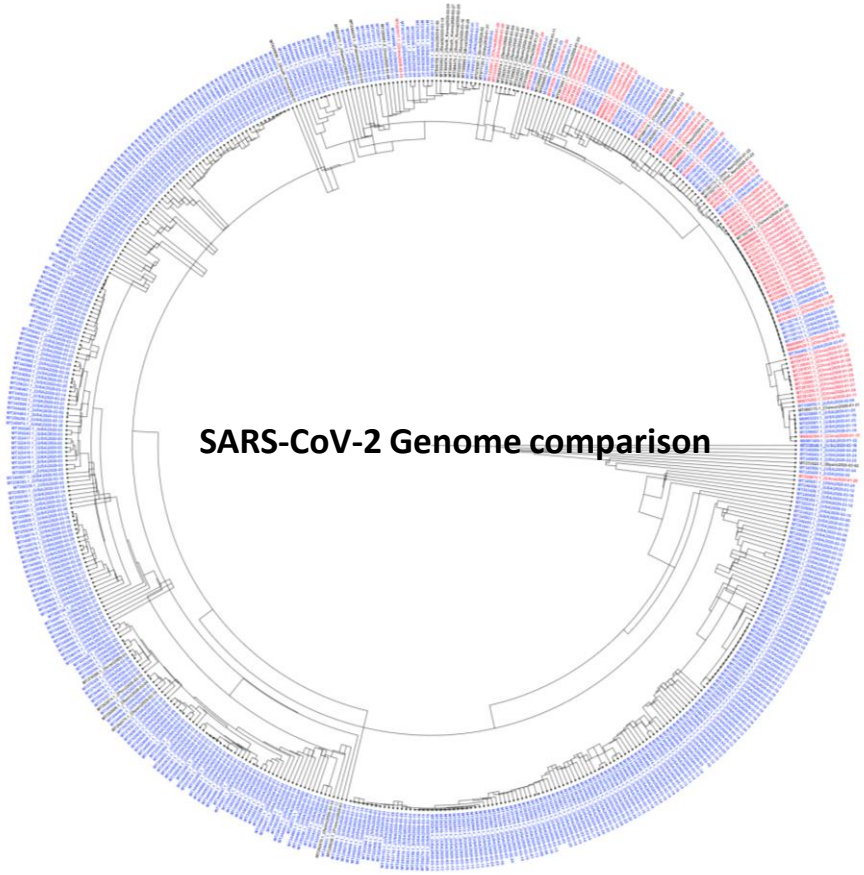
Innovation

- Current work is an attempt to develop efficient peptides for combating the COVID-19 virus spread and similar outbreak. The method is rapid, targeted, and have low toxicity

- This approach can be further modified to target virulent and MDR microorganisms during space travel that may cause infectious diseases in immunocompromised astronauts

Results

- SARS-COV-2 genome ranging from WUHAN to Washington State were downloaded and were manually curated. Out of 4551 genomes under study, 165 genomes made it to the final dataset for target prediction
- **Nine targets were identified in the curated genome, with spike protein being the most promising one.**
- Targets were shared with UPenn to make a further AI prediction of peptides and synthetic production using their proprietary technology
- **The plate testing strategy established by UVM and synthetic peptide is currently under production**



Blue: USA isolates
Red: China isolates

Results

Peptide candidates and genome targets identified for further testing

Sl No.	Gene	Genome target and peptide candidates	Amino Acid sequence	Nucleotide Mutations
1	N	LQLPQGTTLPKG FYA	Sequence is conserved	1 synonymous mutation (gb|MN994467.1)
2	N	VILLNKHIDAYKTF PPTEPKKDKKKK	Sequence is conserved	No nucleotide mutations
3	N	GKGQQQQGQTV	Sequence is conserved	No nucleotide mutations
4	M	SELVIGAVILR	Sequence is conserved	1 synonymous mutation (gb|MT246482.1)
5	M	NGTITVEELKKLLEQWNLVIGFLFL	Sequence is conserved	No nucleotide mutations
6	M	ASFRLFARTRSMWSFNPETNILLNV PLHGT	Sequence is conserved	No nucleotide mutations
7	M	SRYRIGNYKL	Sequence is conserved	No nucleotide mutations
8	S	SETKCTLKSFTVEKGIYQTSNF	Sequence is conserved	No nucleotide mutations
9	ORF3 a	DGTTSPISE	Sequence is conserved	No nucleotide mutations

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Future Work

This technology can be adapted to suit more than a single class of pathogens, rendering it an environmental microbe containment strategy.

Synthetic peptides have no expiration, and in the future, it can be made available for human use as medical countermeasures against pathogenic microbes in long spaceflight travel and extraterrestrial habitats.

References

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- Han Y, Král P: **Computational Design of ACE2-Based Peptide Inhibitors of SARS-CoV-2**. *ACS nano* 2020, 14(4):5143-5147.

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