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T CELL EPITOPE-BASED VACCINE DESIGN, A POTENTIAL CANDIDATE AGAINST FOR SARS-CoV2

IMMUNO-INFORMATICS APPROACH

Cover Story by
- Sumathi Ravi Raj
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In the current scenario where the **COVID-19** cases are continuously increasing there is a dire need of strong vaccine against the virus. In a country like which has often been accused of its slow research progress, this unprecedented attempt serves to be a refreshing breath of air. Vaccine design generally takes a few months to years but through the **immunoinformatics** approach, this potential candidate has been designed within a couple of weeks.

Generally, the epitope regions of an antigen that can be highly immunogenic are expected to be located on the surface, like the membrane or the spikes. A recent research by **Dr Seema Mishra, University of Hyderabad**, advocates that the **T-cell epitopes** in the case of **SARSCoV2** are **non-structural proteins- ORF10, ORF8, ORF6** and also envelope proteins being top-ranked and positively scored for a higher immune response. Both cytotoxic t-cell and helper-cell epitopes were identified using **NetCTLpan version 1.1** [1], **Pickpocket version 1.1** [2] and **NetMHCIIpan version 3.2**[3] prediction tools respectively. **Immune Epitope Database (IEDB)** immunogenicity tool[4] was also used for the prediction of immunogenic regions in these epitopes since an effective T-cell epitope should display high binding to the HLA and as well elicit a significant immune response. The epitopes have also been produced taking into consideration HLA supertypes covering all the predominant HLA in the entire population. This is also vital for a vaccine to be globally effective.



Bioinformatic tools used for predictions of T_H & T_C cell epitopes:

- NetCTLpan version 1.1
- Pickpocket version 1.1
- NetMHCIIpan version 3.2



Protein sequences of drug targets:

>YP_009725255.1 ORF10 protein [Severe acute respiratory syndrome coronavirus 2]

MGYINVFAFPFTIYSLLLCRMNSRNYIAQVDVNFNLT

>QID21074.1 orf8 protein [Severe acute respiratory syndrome coronavirus 2]

MKFLVFLGIIITVAAFHQECSLQSQCTQHQPWWDDPCPIHFYSK
WYIRVGARKSAPLIELCVDEAGSKSPIQYIDIGNYTVSCSPFTIN
CQEPKLGSLVWRCSFYEDFLEYHDVRVLDIFI

>YP_009724394.1 ORF6 protein [Severe acute respiratory syndrome coronavirus 2]

MFHLVDFQVTIAEILLIIMRTFKVSIWNLDYIINLIKNLSKSLTEN
KYSQLDEEQPMEID

A clustering approach by the use of the IEDB epitope cluster analysis tool gave a pattern to have a clear representative sequence of these dispersed epitopes. Additionally, it is imperative for the epitope to not have any sequential or structural similarity to the proteins contained in humans, else it will cross-react, leading to damage to the normal human cells. So, a cross-reactivity analysis by the **Multiple Peptide Match tool**[5] of the consensus epitope sequence against the **human proteome** from the **UniProt database**, which did not exhibit any similarity eliminates this cross-reactivity problem. Among all the ranked epitopes, there are two sequences: **MGYINVFAFPFTIYSLLLC** and **KVSIWNLDYIINLI** which are considered immunodominant and should first to in vitro testing.

This immunoinformatics approach uses different **prediction algorithms**, **clustering analysis**, and various computational tools which have helped in minimizing the cost and time in vaccine generation to a boundless extent. With immunotherapy as one of the treatment methods being used, the immunoinformatics approach of vaccine design seems to be a huge ray of hope. However, only immediate in vitro testing and t-cell assays will help generate a powerful vaccine to eradicate the COVID-19 pandemic.

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HERBAL MEDICINE OF COVID-19: *Nigella sativa* a House hold remedy?

-Yasir Arafath
University of Hyderabad

Novel coronavirus SARS CoV-2 is a spreading holocaust. An effective frontline treatment is needed. A foreseeable vaccine can take 12 to 24 months before it is approved for public use. A researcher from the University of Saida, Algeria had explored possible herbal medicine of SARS CoV - 2 with ***Nigella sativa***.

Nigella sativa (NS) popularly known as black cumin(Kalonji) is used as a medicinal plant in various traditional forms of medicine like Unani, Tibb, Ayurveda, and Sidha (1). It has properties like antihypertensive, analgesics, anti-diabetics, anti-cancer, anti-microbial, anti-inflammatory, etc (1) (2). Thus, it is considered as "There is healing in Black Cumin for all diseases except death".

A potential drug target (**Mpro**)/**chymotrypsin-like protease (3CLpro)** has been successfully crystallized from **COVID-19(6LU7)** by Liu et al (2020)(3). Docking of compounds from *Nigella sativa* and drugs against **CoVs (3CLpro/Mpro)** (PDB ID **6LU7** and **2GTB**) were performed using **Molecular Operating Environment software (MOE)**(4). **Nigelledine** from NS docked into **6LU7 active site** gives energy complex which is close to chloroquine and better than hydroxychloroquine and favipiravir. Docking into 2GTB active site showed that **α -Hederin** gives energy score which is better than chloroquine, hydroxychloroquine, and favipiravir. Nigellidine and α -Hederin appeared to have the best potential to act as COVID-19 treatment. Those results encourage further in vitro and in vivo investigations and also encourage traditional use of ***Nigella sativa*** preventively.



A study in *frontiers of immunology* had suggested three methods to prevent infection - **Immune modulation; vaccine** and **improvement in human behavior**, personal hygiene being the others. Immune modulation is the regulatory adjustment of the immune system. A recent study of clinical features of patients infected with COVID-19 in Wuhan, china reported that severe cases admitted to the intensive care unit (ICU) showed high levels of pro-inflammatory cytokines including **TNF α (Tumor necrosis factor Alpha)** that are reasoned to promote disease severity (5) (6). **Thymoquinone (TQ)** is an abundant component of ***Nigella sativa*** seed oil extract. TQ is known to inhibit TNF- α -induced inflammation (7). TQ is not only a pulmonary protective but also a nephroprotective in diseases caused by inflammation and oxidative stress. TQ is also known for its testicular protective function.

A study published in the Journal of Molecular Biology Reports in 2014 concluded that treatment of cells with *Nigella sativa* (NS) extracts prior to infection with CoV - 2012 decreased replication of the virus (8). This could possibly help in the cure of COVID-19.

Nigella sativa with its immunomodulation property and other health benefits can be considered to be a drug to prevent or to treat the viral infection caused by SARS CoV-2. Further clinical trials are yet to be conducted using *Nigella sativa* that might unravel how exactly we can use it in the current COVID-19 pandemic state.

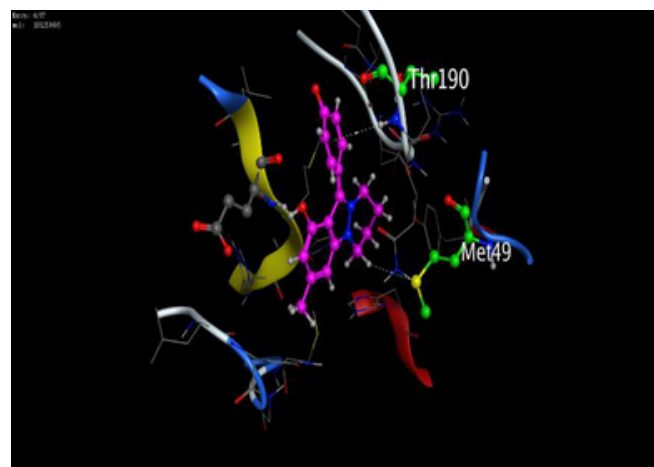


Figure: 3D diagram interaction between Nigellidine and 6LU7.

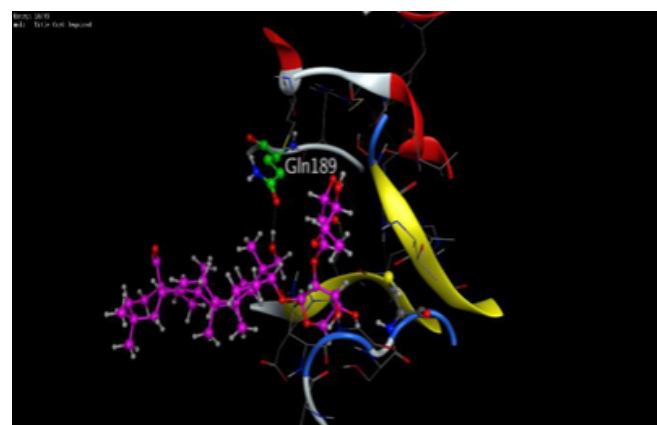


Figure: 3D diagram interaction between Alpha hederin and 2GTB.

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HELPING A SCIENTIST FROM HOME?

-Sarthak Satpathy
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Collaboration in science along with the distribution of tasks are ways in which we can speed our research. Here are two examples where the strength of the crowd is helping our scientists to deliver their results quickly which are being used in our battle against the global pandemic.

Folding@home

How about Folding@home? Most experimental methods for determining protein structures give only a single snapshot of these. Hence, computer simulations can help us understand the dynamics and particularly binding sites of drugs that can be missed in a static picture. Folding@home (**FAH or F@h**) project has helped multiple researchers working in various diseases like cancers, infectious diseases, and neurological disorders to understand the biology of the diseases and design appropriate therapeutics. Currently, there are many tasks for understanding **COVID-19 better**. The core team requests the volunteers to download the software and run the simulations on their personal computers. This way massive parallelization gives them the computing power similar to those of supercomputers. The Folding@home software runs alongside your regular computer usage like writing emails, using WordProcessors and doing an internet search.

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“ FOLDING REFERS TO THE WAY HUMAN PROTEIN FOLDS IN THE CELLS THAT MAKE UP YOUR BODY. WE RELY ON THE PROTEINS TO KEEP US HEALTHY AND THEY ASSEMBLE THEMSELVES BY FOLDING. BUT WHEN THEY MISFOLD, THERE CAN BE SERIOUS CONSEQUENCES TO A PERSON’S HEALTH.”

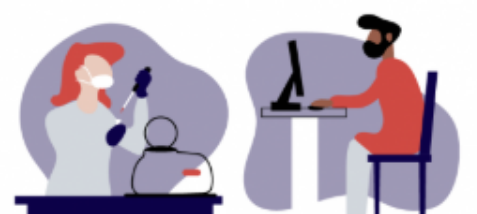
Illustration by Atreya sai (@atreyasai)



Folding@home is a project focused on disease research. The problems we're solving require so many computer calculations – and we need your help to find the cures!

- www.foldingathome.org





COVID-19 researcher



coordinator



volunteers



Aim:

Put the wider scientific community at the service of COVID-19 research.

Motivation:

Most current plans to fight COVID-19 rely on the assumption that treatments and/or vaccines will be available in a few months. Delays in these treatments will have enormous consequences, both in terms of economic impact and human lives.

Hence, this does not require much investment on the side of the volunteers. The published results from the simulations are available on their website.

Crowdfightcovid19

A group of scientists started an initiative through a website, **crowdfightcovid19.org** to put all available resources at the service of the fight against COVID-19. The architecture of this initiative has three groups: scientists working on **COVID-19 research**, **volunteers**, and a **coordinator** who bridges the demand of the scientists to the skills of the volunteers. **Scientists** can be people from **academia or industry** who are working on **understanding the coronavirus, finding inhibitors, looking for vaccines** and other related problems. The volunteers can be anyone from a virologist to an Artificial Intelligence expert or a bioinformatician. People from a non-science background can also volunteer. The qualification can vary from an undergraduate student to a retired scientific expert. Once a volunteer signs up they can choose from a set of tasks that suits their skills and expertise. In their latest task distribution, some of the researchers sought literature surveys, Some were looking for data sources and some experts in programming.

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