Computational Resource to fight against Viruses

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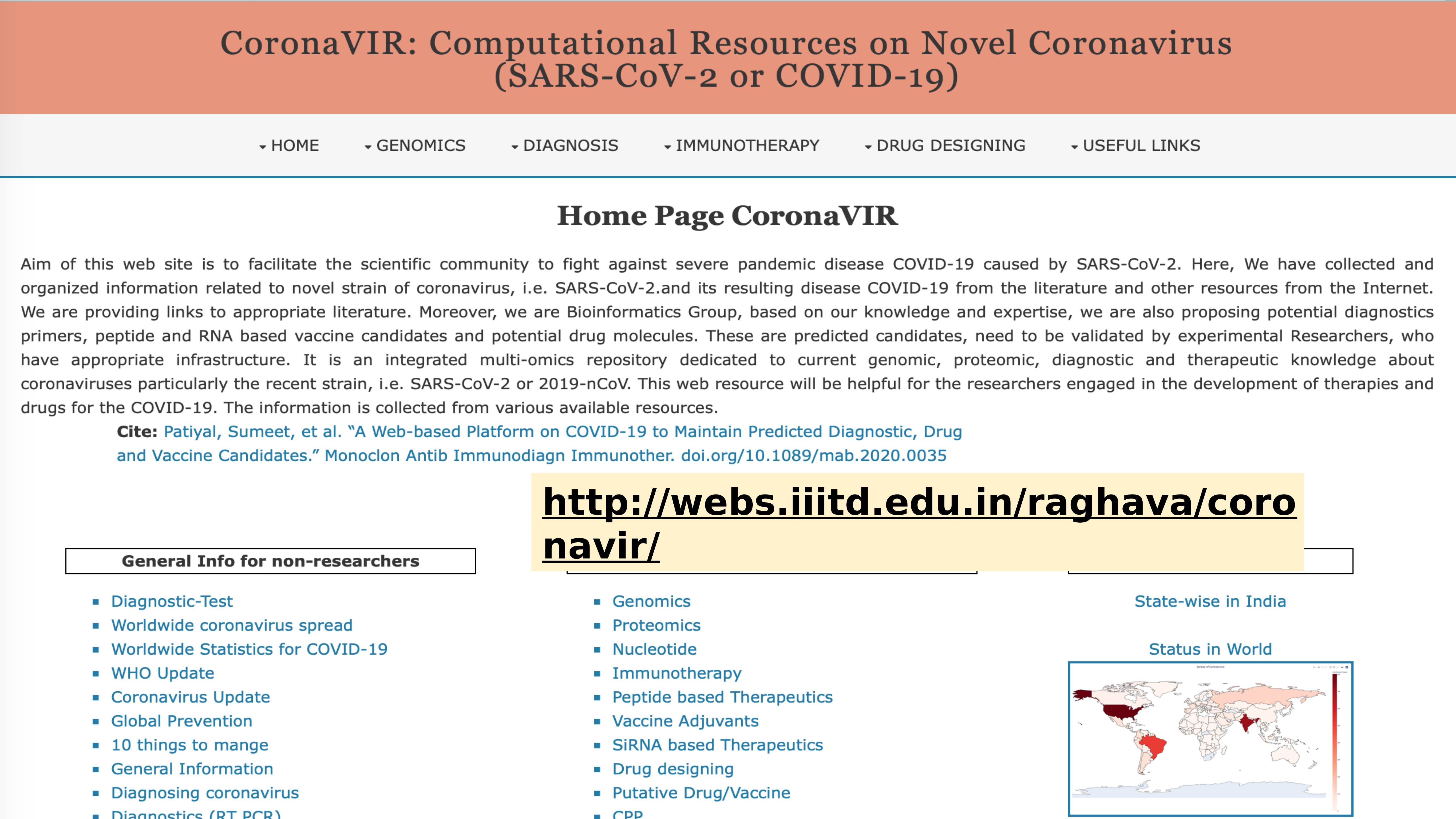
Web Site:
http://webs.iiitd.edu.in/raghava/



CoronaVIR: Computational Resources on Novel Coronavirus (SARS-CoV-2 or COVID-19)

Home Page CoronaVIR

Aim of this web site is to facilitate the scientific community to fight against severe pandemic disease COVID-19 caused by SARS-CoV-2. Here, We have collected and organized information related to novel strain of coronavirus, i.e. SARS-CoV-2.and its resulting disease COVID-19 from the literature and other resources from the Internet. We are providing links to appropriate literature. Moreover, we are Bioinformatics Group, based on our knowledge and expertise, we are also proposing potential diagnostics primers, peptide and RNA based vaccine candidates and potential drug molecules. These are predicted candidates, need to be validated by experimental Researchers, who have appropriate infrastructure. It is an integrated multi-omics repository dedicated to current genomic, proteomic, diagnostic and therapeutic knowledge about coronaviruses particularly the recent strain, i.e. SARS-CoV-2 or 2019-nCoV. This web resource will be helpful for the researchers engaged in the development of therapies and drugs for the COVID-19. The information is collected from various available resources.

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http://webs.iiitd.edu.in/raghava/coronavir/

General Info for non-researchers

- Diagnostic-Test
- Worldwide coronavirus spread
- Worldwide Statistics for COVID-19
- WHO Update
- Coronavirus Update
- Global Prevention
- 10 things to mange
- General Information
- Diagnosing coronavirus
- Diagnostics (RT PCR)

- Genomics
- Proteomics
- Nucleotide
- Immunotherapy
- Peptide based Therapeutics
- Vaccine Adjuvants
- SiRNA based Therapeutics
- Drug designing
- Putative Drug/Vaccine
- CPP

State-wise in India

Status in World

MONOCLONAL ANTIBODIES IN IMMUNODIAGNOSIS AND IMMUNOTHERAPY
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A Web-Based Platform on Coronavirus Disease-19 to Maintain Predicted Diagnostic, Drug, and Vaccine Candidates

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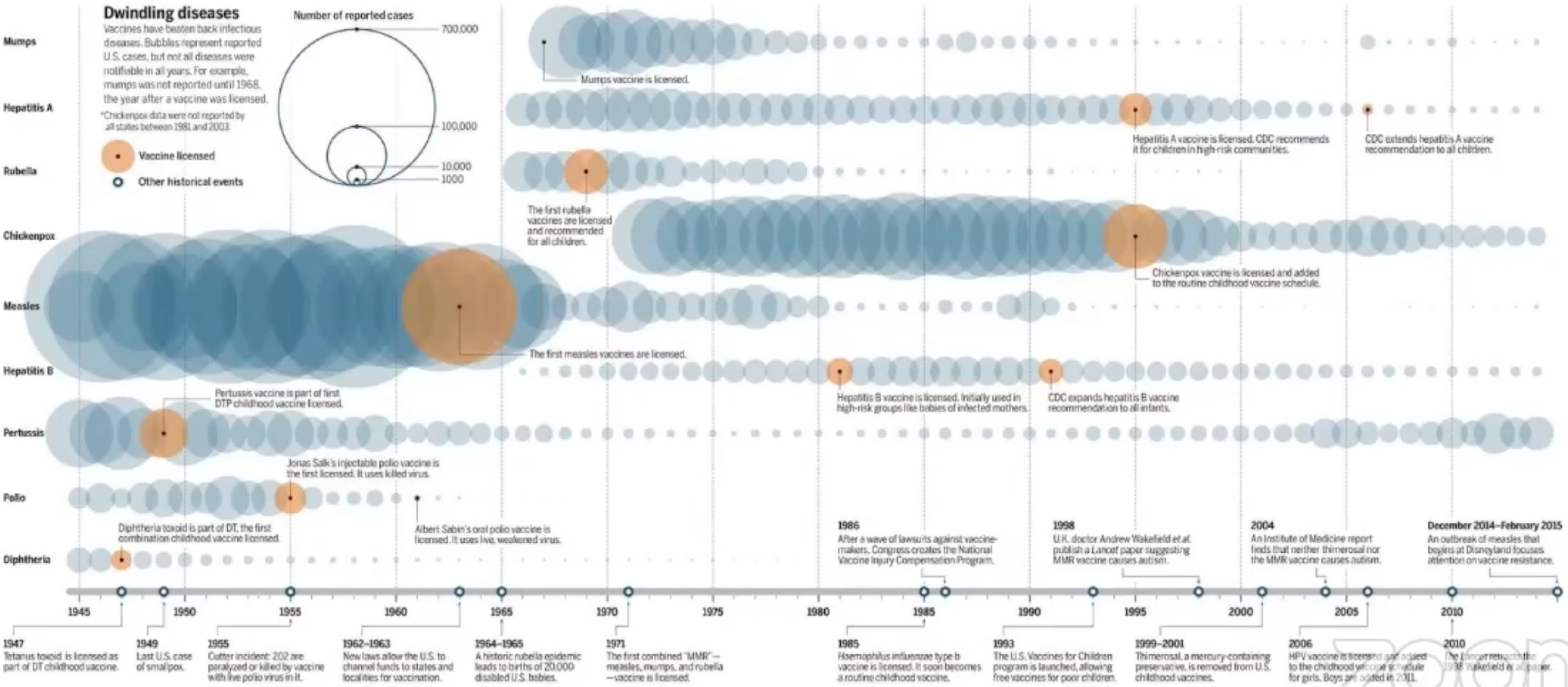
Sukriti Sahai,[3] Piyush Agrawal,[1] Lubna Maryam,[1] Chakit Arora,[1] and Gajendra P.S. Raghava[1]

A web-based resource CoronaVIR (https://webs.iiitd.edu.in/raghava/coronavir/) has been developed to maintain the predicted and existing information on coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We have integrated multiple modules, including ‘‘Genomics,’’ ‘‘Diagnosis,’’ ‘‘Immunotherapy,’’ and ‘‘Drug Designing’’ to understand the holistic view of this pandemic medical disaster. The genomics module provides genomic information of different strains of this virus to understand genomic level alterations. The diagnosis module includes detailed information on currently-in-use diagnostics tests as well as five novel

History of Viral Vaccines



Dwindling diseases

Vaccines have beaten back infectious diseases. Bubbles represent reported U.S. cases, but not all diseases were notifiable in all years. For example, mumps was not reported until 1968, the year after a vaccine was licensed.

*Chickenpox data were not reported by all states between 1981 and 2003.

Mumps vaccine is licensed.

Hepatitis A vaccine is licensed. CDC recommends it for children in high-risk communities.

CDC extends hepatitis A vaccine recommendation to all children.

The first rubella vaccines are licensed and recommended for all children.

Chickenpox vaccine is licensed and added to the routine childhood vaccine schedule.

The first measles vaccines are licensed.

Hepatitis B vaccine is licensed. Initially used in high-risk groups like babies of infected mothers.

CDC expands hepatitis B vaccine recommendation to all infants.

Pertussis vaccine is part of first DTP childhood vaccine licensed.

Jonas Salk's injectable polio vaccine is the first licensed. It uses killed virus.

Albert Sabin's oral polio vaccine is licensed. It uses live, weakened virus.

Diphtheria toxoid is part of DT, the first combination childhood vaccine licensed.

1986
After a wave of lawsuits against vaccine-makers, Congress creates the National Vaccine Injury Compensation Program.

1998
U.K. doctor Andrew Wakefield *et al.* publish a *Lancet* paper suggesting MMR vaccine causes autism.

2004
An Institute of Medicine report finds that neither thimerosal nor the MMR vaccine causes autism.

December 2014–February 2015
An outbreak of measles that begins at Disneyland focuses attention on vaccine resistance.

1947
Tetanus toxoid is licensed as part of DT childhood vaccine.

1949
Last U.S. case of smallpox.

1955
Cutter incident: 202 are paralyzed or killed by vaccine with live polio virus in it.

1962–1963
New laws allow the U.S. to channel funds to states and localities for vaccination.

1964–1965
A historic rubella epidemic leads to births of 20,000 disabled U.S. babies.

1971
The first combined "MMR"—measles, mumps, and rubella—vaccine is licensed.

1985
Haemophilus influenzae type b vaccine is licensed. It soon becomes a routine childhood vaccine.

1993
The U.S. Vaccines for Children program is launched, allowing free vaccines for poor children.

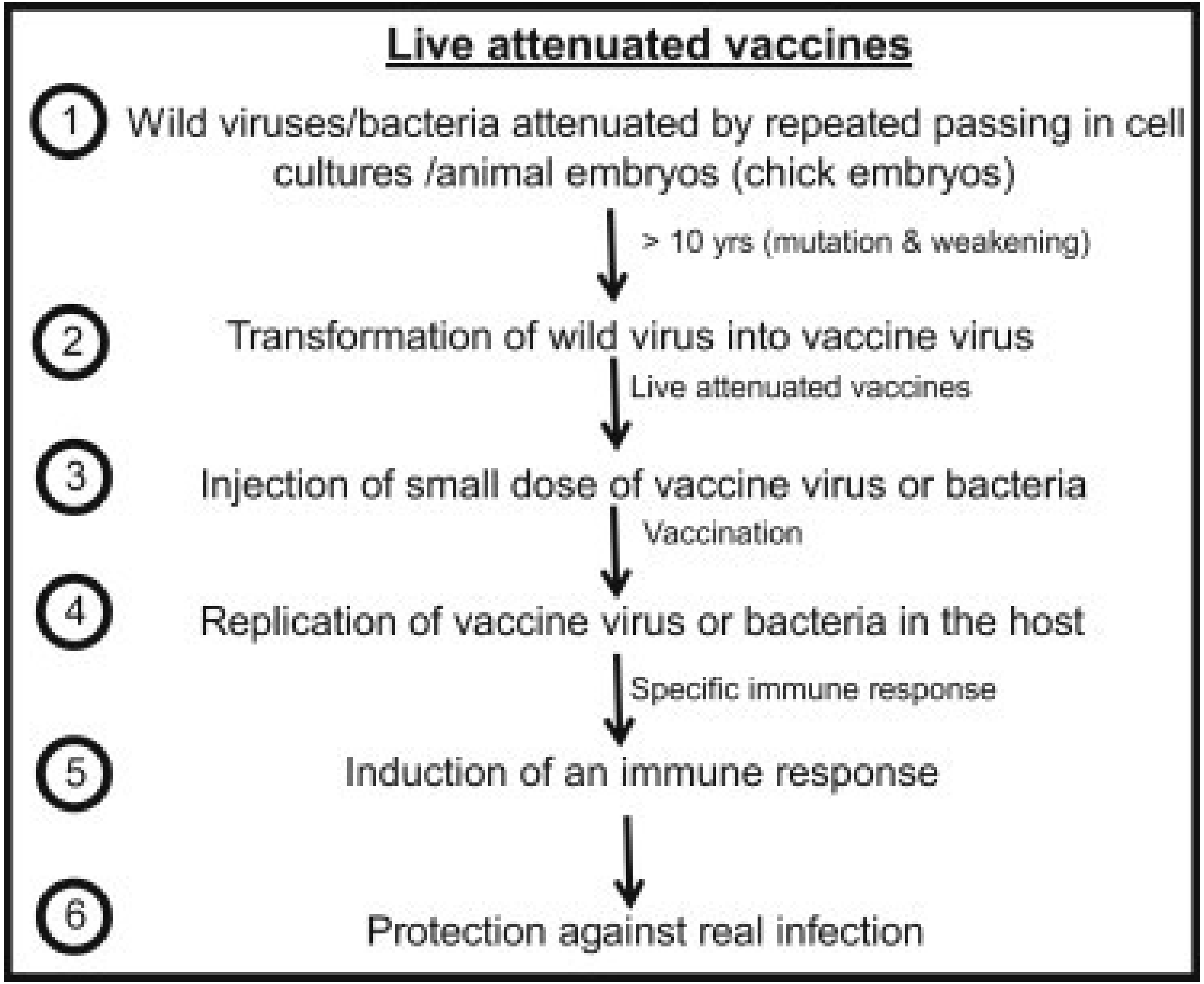
1999–2001
Thimerosal, a mercury-containing preservative, is removed from U.S. childhood vaccines.

2006
HPV vaccine is licensed and added to the childhood vaccine schedule for girls. Boys are added in 2011.

2010
The Lancet retracts the 1998 Wakefield et al. paper.

Traditional Approach: Live Attenuated Vaccines (LAVs)

Bharat Biotech has also used this approach to produce vaccine against coronavirus named “COVAXIN”



Live attenuated vaccines

① Wild viruses/bacteria attenuated by repeated passing in cell cultures /animal embryos (chick embryos)

↓ > 10 yrs (mutation & weakening)

② Transformation of wild virus into vaccine virus

↓ Live attenuated vaccines

③ Injection of small dose of vaccine virus or bacteria

↓ Vaccination

④ Replication of vaccine virus or bacteria in the host

↓ Specific immune response

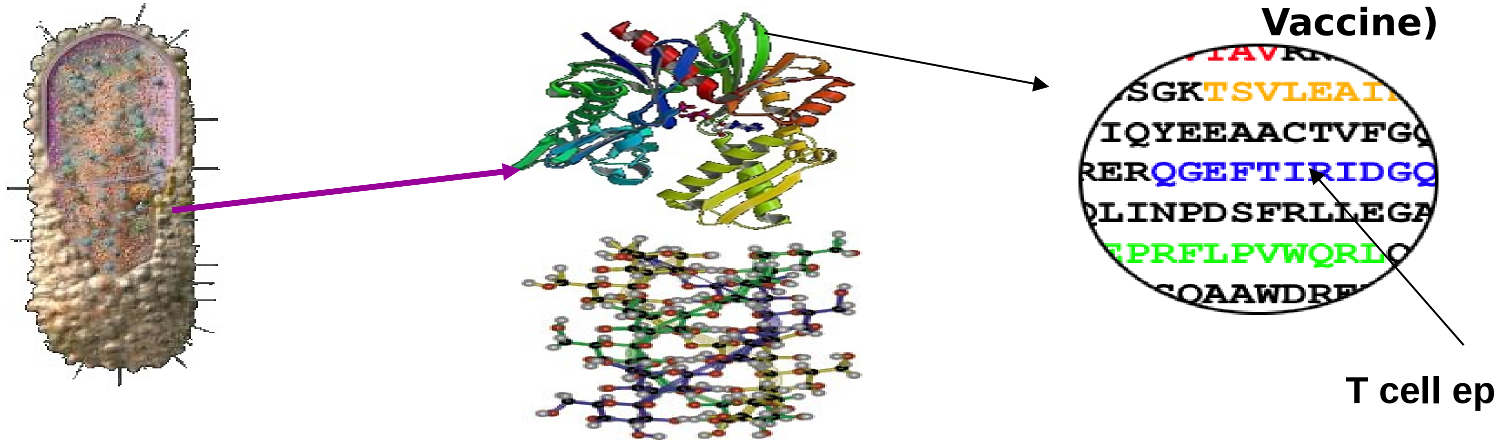
⑤ Induction of an immune response

↓

⑥ Protection against real infection

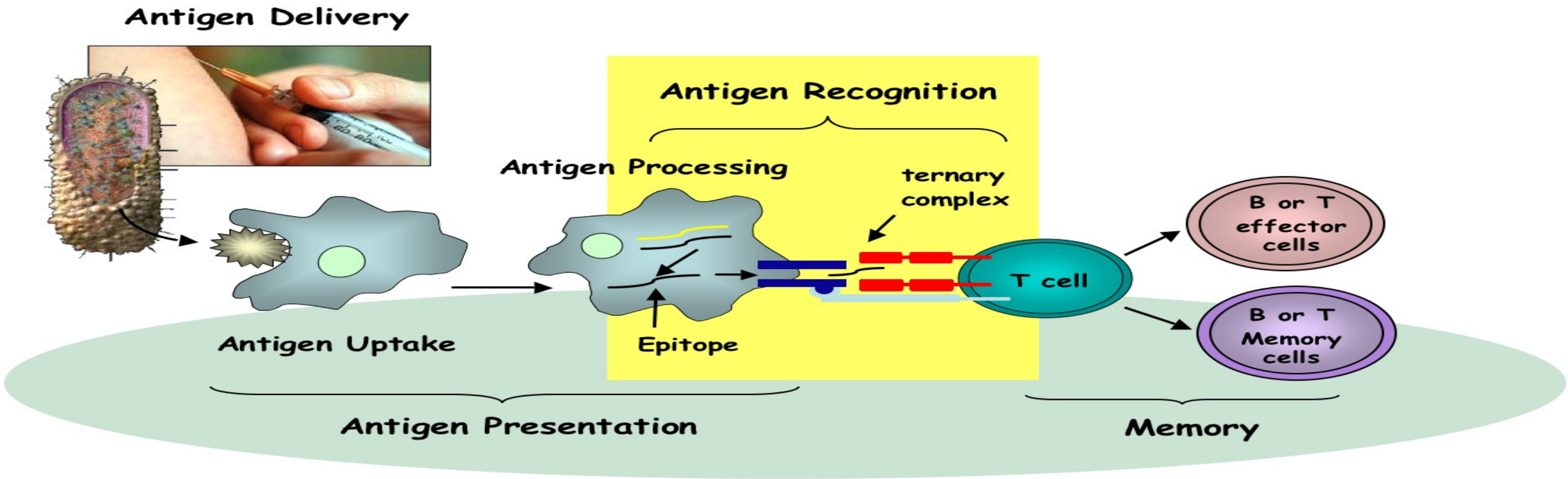
Biomolecules Based Vaccines

WHOLE ORGANISM → **Purified Antigen** → **Epitopes (Subunit Vaccine)**

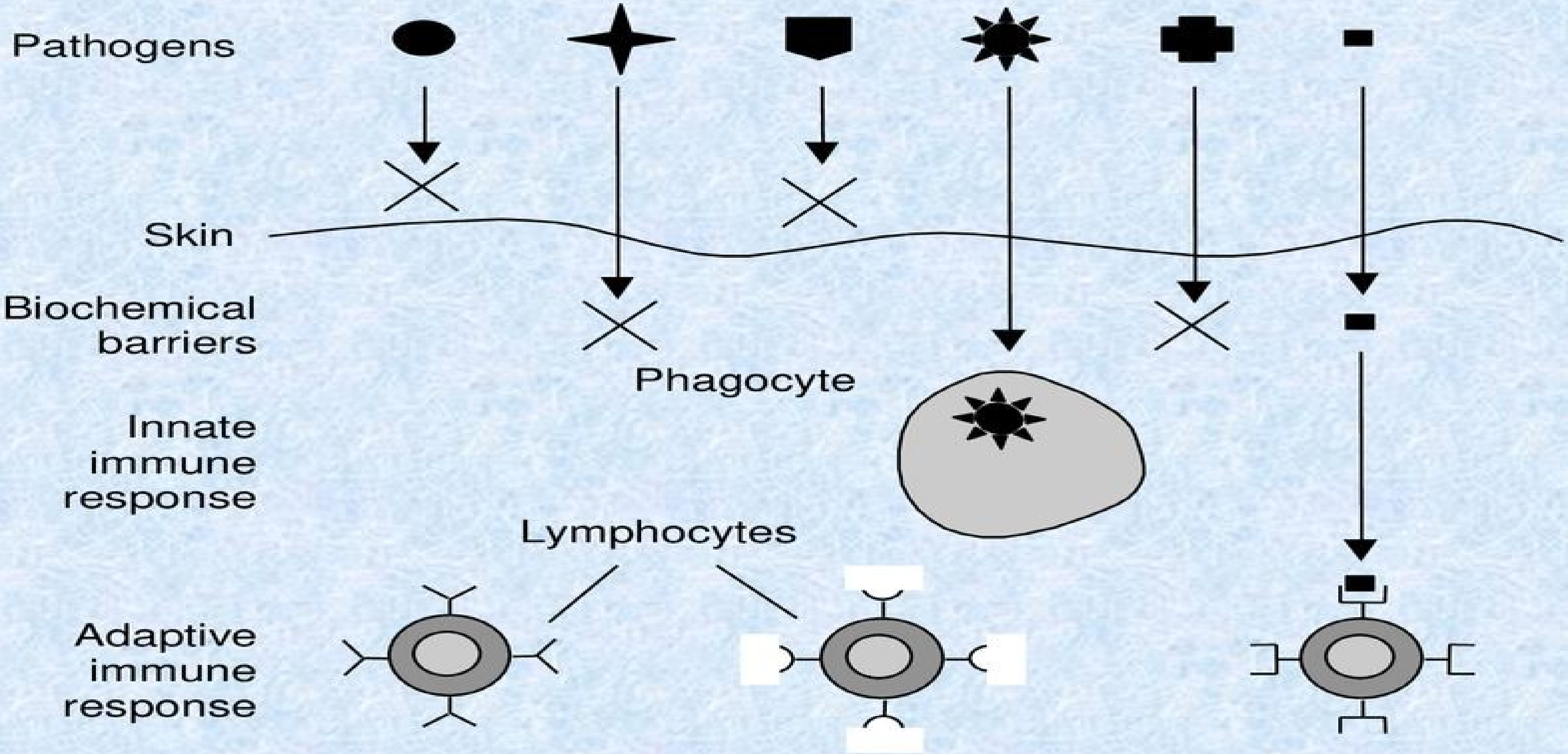


T cell epitope

Attenuated

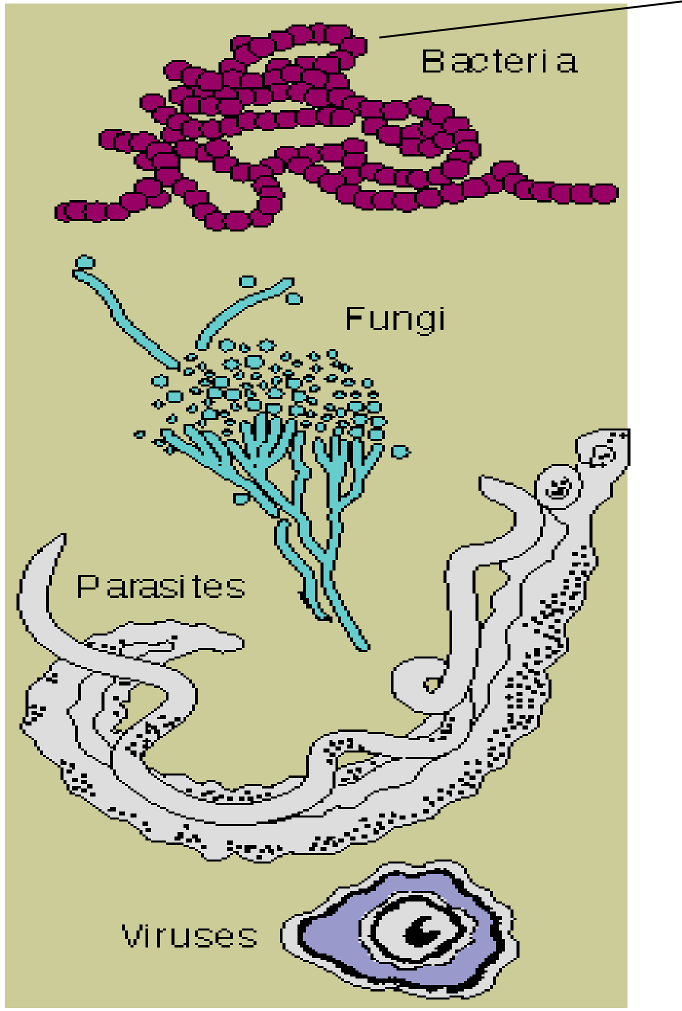


Multiple layers of the immune system

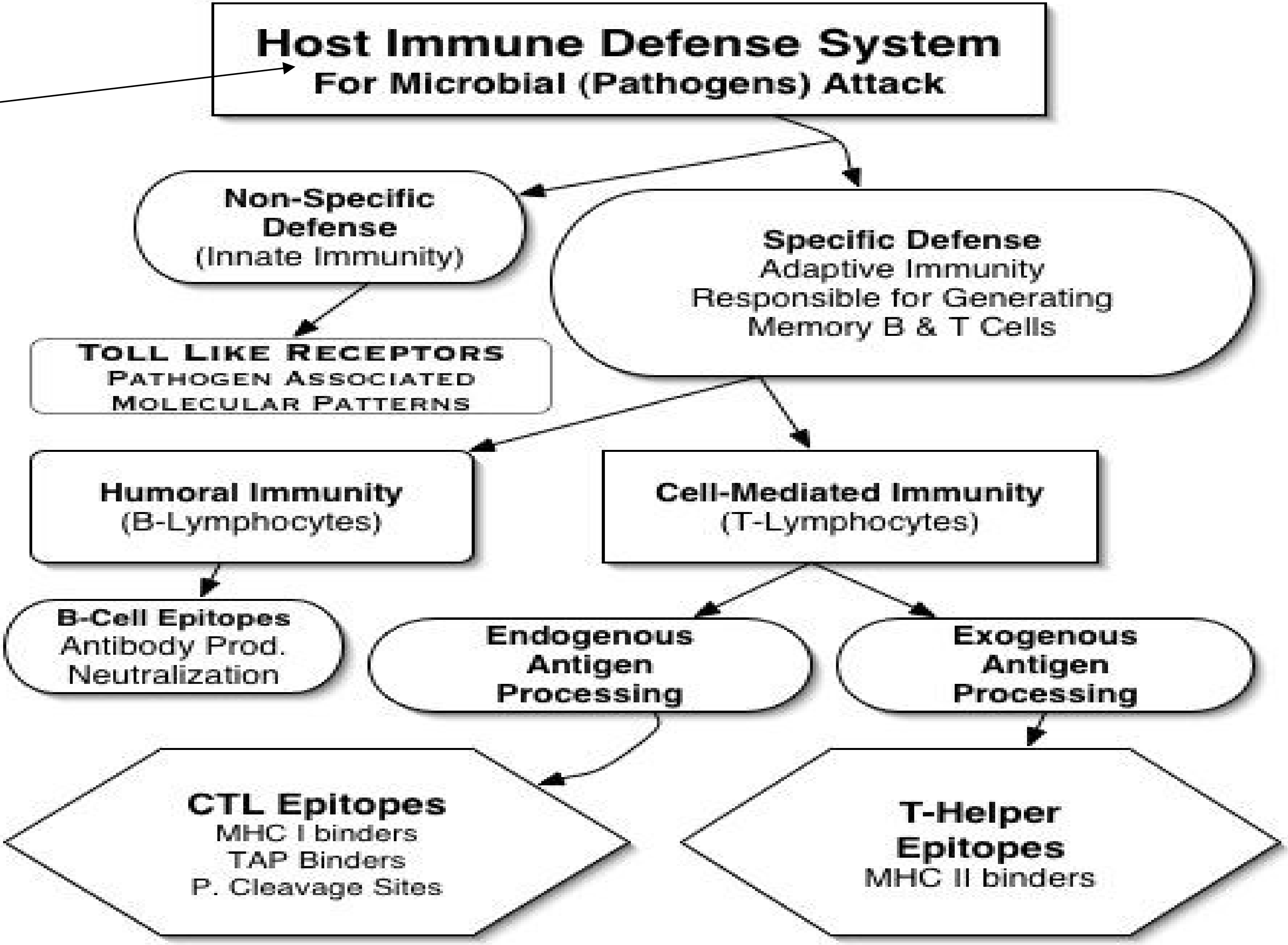


Different arms of Immune System

Disease Causing Agents



Pathogens/Invaders



Host Immune Defense System
For Microbial (Pathogens) Attack

Non-Specific Defense
(Innate Immunity)

Toll Like Receptors
Pathogen Associated Molecular Patterns

Specific Defense
Adaptive Immunity
Responsible for Generating
Memory B & T Cells

Humoral Immunity
(B-Lymphocytes)

Cell-Mediated Immunity
(T-Lymphocytes)

B-Cell Epitopes
Antibody Prod.
Neutralization

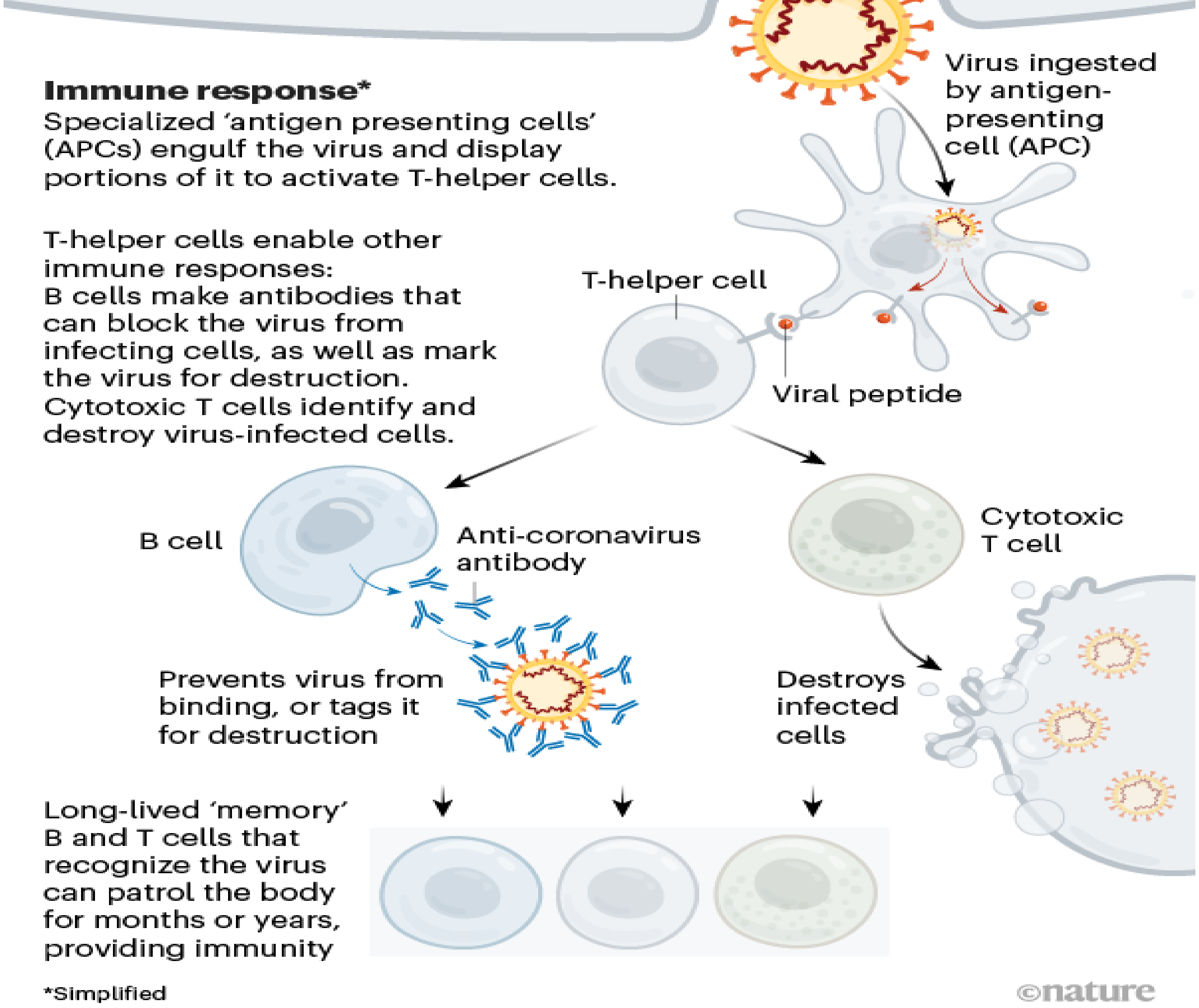
Endogenous Antigen Processing

Exogenous Antigen Processing

CTL Epitopes
MHC I binders
TAP Binders
P. Cleavage Sites

T-Helper Epitopes
MHC II binders

Mechanism of vaccine



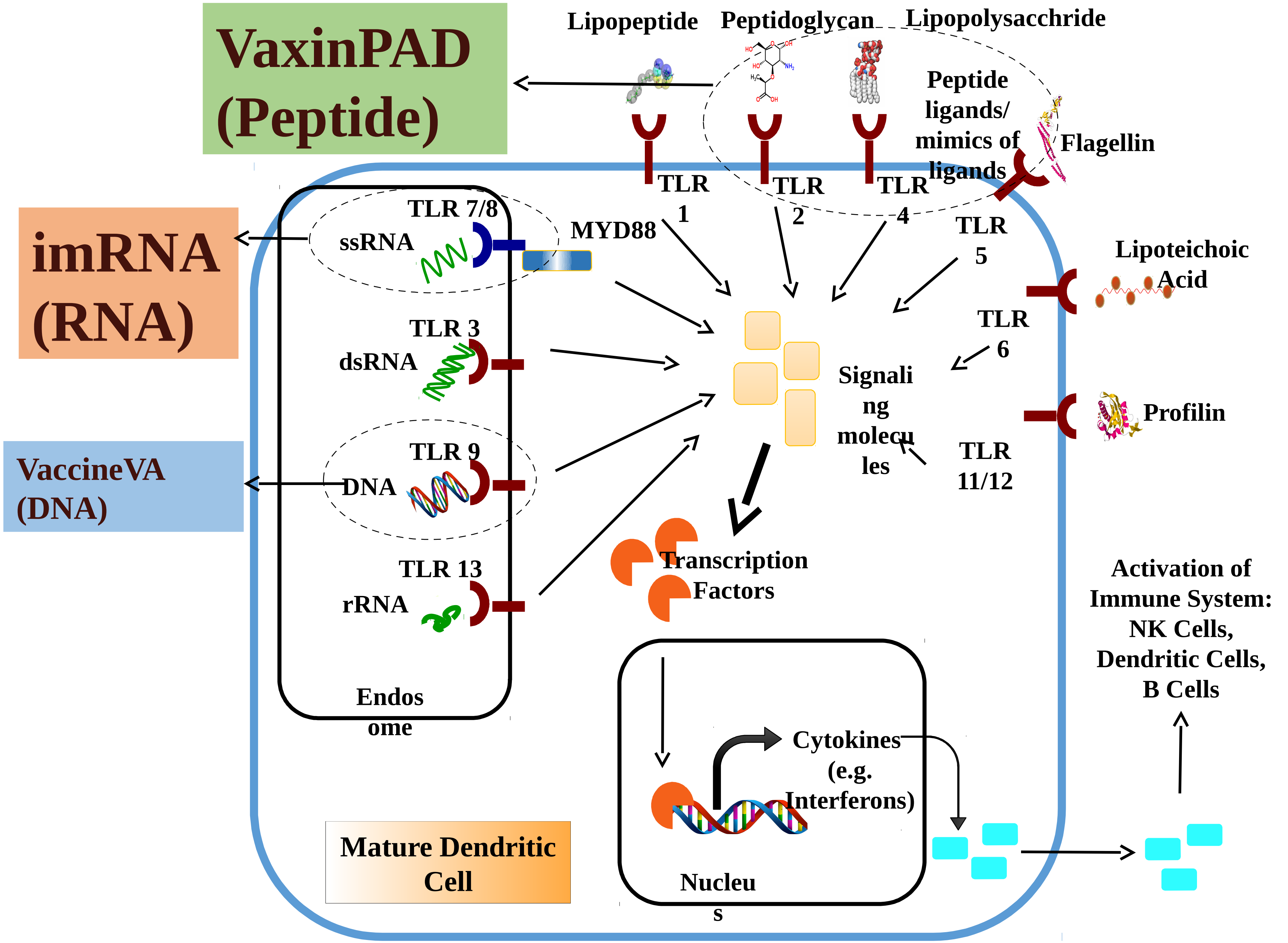
Immune response*

Specialized 'antigen presenting cells' (APCs) engulf the virus and display portions of it to activate T-helper cells.

T-helper cells enable other immune responses:
B cells make antibodies that can block the virus from infecting cells, as well as mark the virus for destruction.
Cytotoxic T cells identify and destroy virus-infected cells.

Long-lived 'memory' B and T cells that recognize the virus can patrol the body for months or years, providing immunity

*Simplified



VaxinPAD (Peptide)

imRNA (RNA)

VaccineVA (DNA)

Lipopeptide

Peptidoglycan

Lipopolysacchride

Peptide ligands/ mimics of ligands

Flagellin

TLR 1

TLR 2

TLR 4

TLR 5

Lipoteichoic Acid

TLR 6

Profilin

TLR 11/12

TLR 7/8

ssRNA

MYD88

TLR 3

dsRNA

TLR 9

DNA

TLR 13

rRNA

Endosome

Signaling molecules

Transcription Factors

Cytokines (e.g. Interferons)

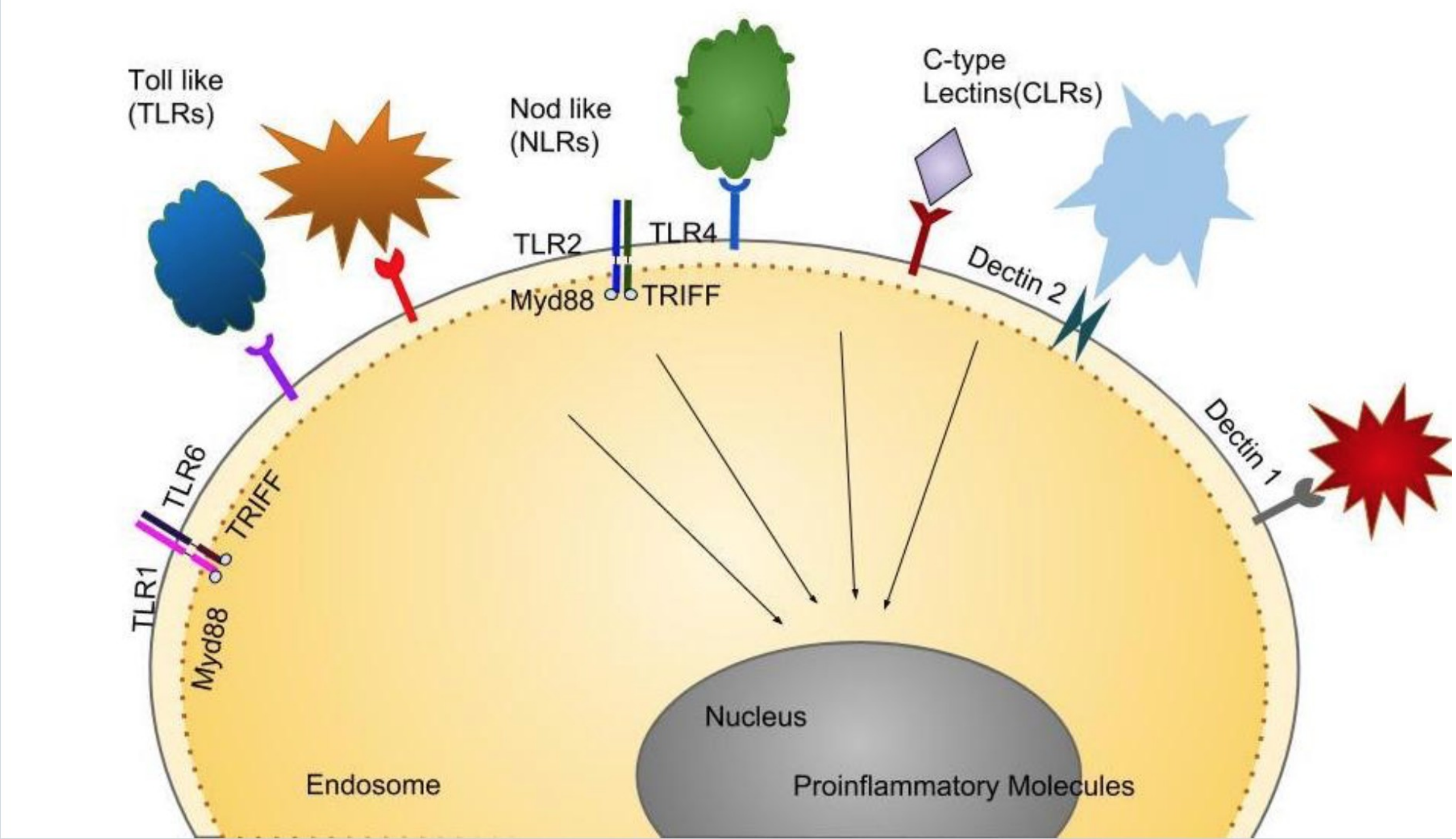
Nucleus

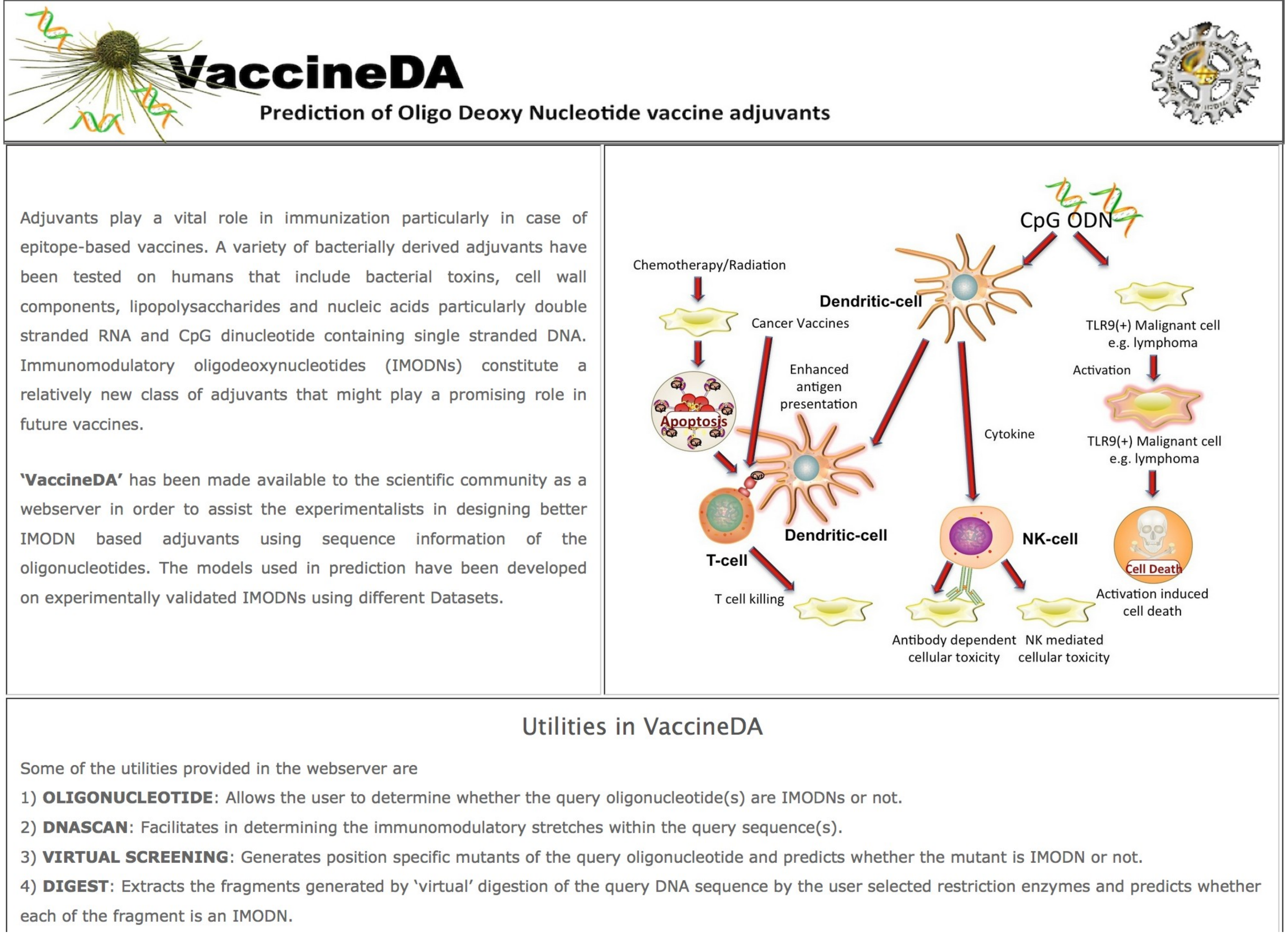
Activation of Immune System: NK Cells, Dendritic Cells, B Cells

Mature Dendritic Cell

PRRDB 2.0 : Pattern Recognition Receptor Database

HOME ▾ SEARCH ▾ BROWSE ▾ TOOLS ▾ INFORMATION ▾ DEVELOPERS





Adjuvants play a vital role in immunization particularly in case of epitope-based vaccines. A variety of bacterially derived adjuvants have been tested on humans that include bacterial toxins, cell wall components, lipopolysaccharides and nucleic acids particularly double stranded RNA and CpG dinucleotide containing single stranded DNA. Immunomodulatory oligodeoxynucleotides (IMODNs) constitute a relatively new class of adjuvants that might play a promising role in future vaccines.

'VaccineDA' has been made available to the scientific community as a webserver in order to assist the experimentalists in designing better IMODN based adjuvants using sequence information of the oligonucleotides. The models used in prediction have been developed on experimentally validated IMODNs using different Datasets.

Utilities in VaccineDA

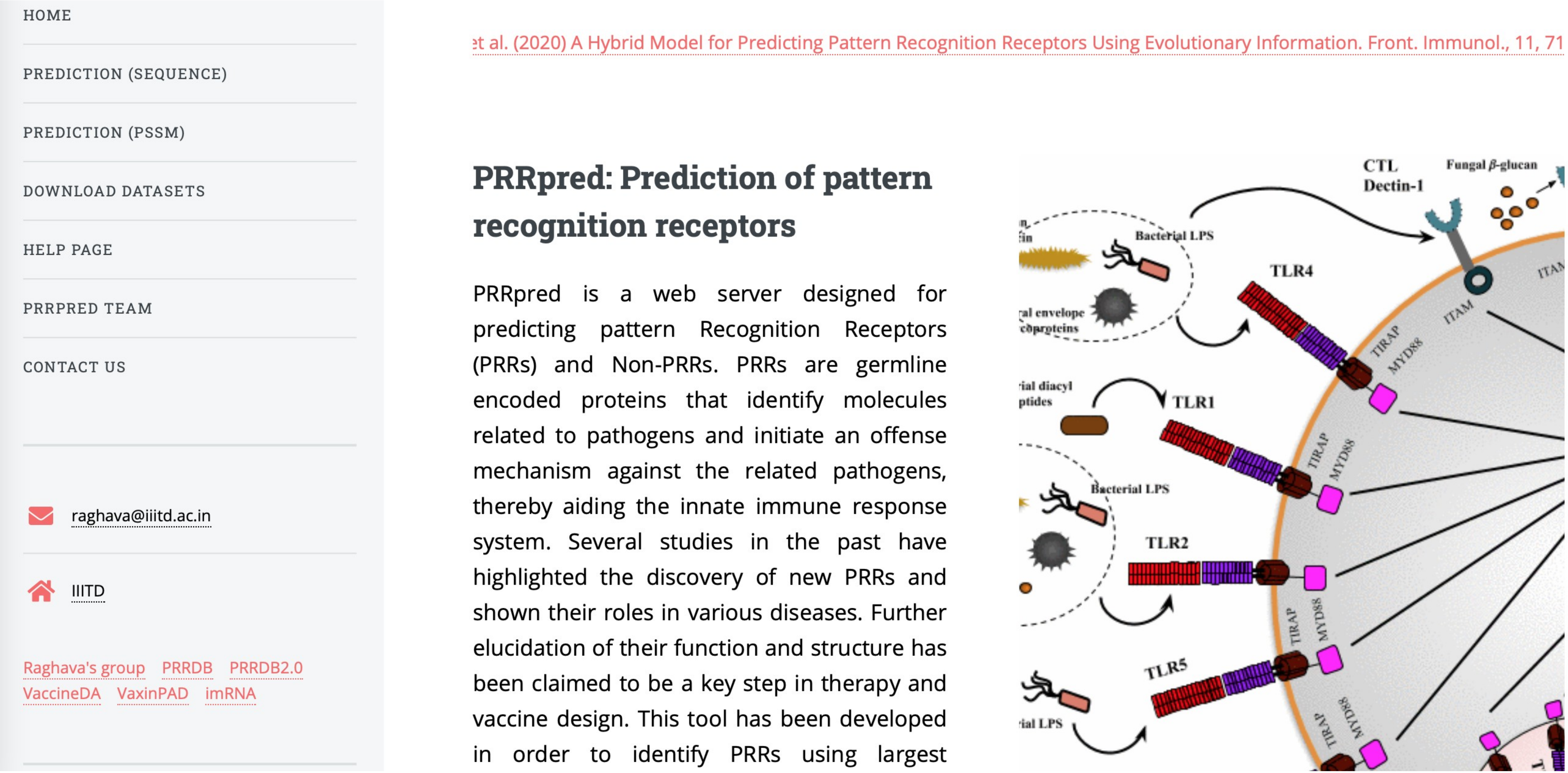
Some of the utilities provided in the webserver are

1) **OLIGONUCLEOTIDE**: Allows the user to determine whether the query oligonucleotide(s) are IMODNs or not.

2) **DNASCAN**: Facilitates in determining the immunomodulatory stretches within the query sequence(s).

3) **VIRTUAL SCREENING**: Generates position specific mutants of the query oligonucleotide and predicts whether the mutant is IMODN or not.

4) **DIGEST**: Extracts the fragments generated by 'virtual' digestion of the query DNA sequence by the user selected restriction enzymes and predicts whether each of the fragment is an IMODN.



HOME

PREDICTION (SEQUENCE)

PREDICTION (PSSM)

DOWNLOAD DATASETS

HELP PAGE

PRRPRED TEAM

CONTACT US

✉ raghava@iiitd.ac.in

IIITD

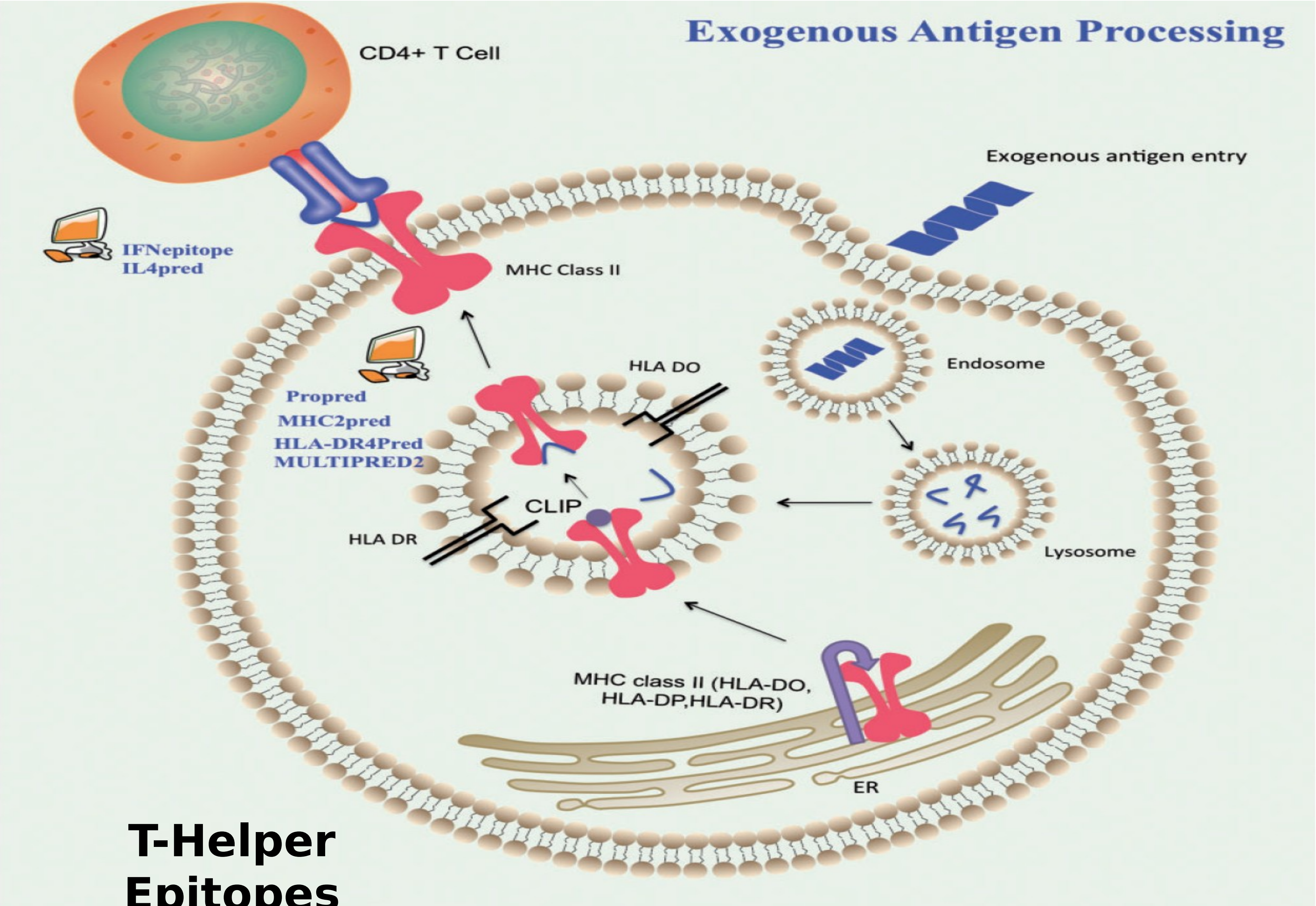
Raghava's group PRRDB PRRDB2.0
VaccineDA VaxinPAD imRNA

et al. (2020) A Hybrid Model for Predicting Pattern Recognition Receptors Using Evolutionary Information. Front. Immunol., 11, 71

PRRpred: Prediction of pattern recognition receptors

PRRpred is a web server designed for predicting pattern Recognition Receptors (PRRs) and Non-PRRs. PRRs are germline encoded proteins that identify molecules related to pathogens and initiate an offense mechanism against the related pathogens, thereby aiding the innate immune response system. Several studies in the past have highlighted the discovery of new PRRs and shown their roles in various diseases. Further elucidation of their function and structure has been claimed to be a key step in therapy and vaccine design. This tool has been developed in order to identify PRRs using largest

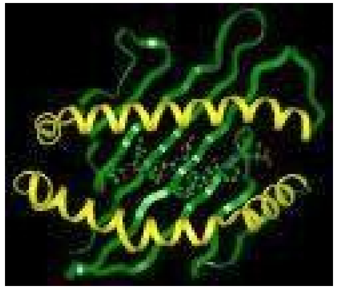
Cell Mediated Immunity (T-cell Epitopes)

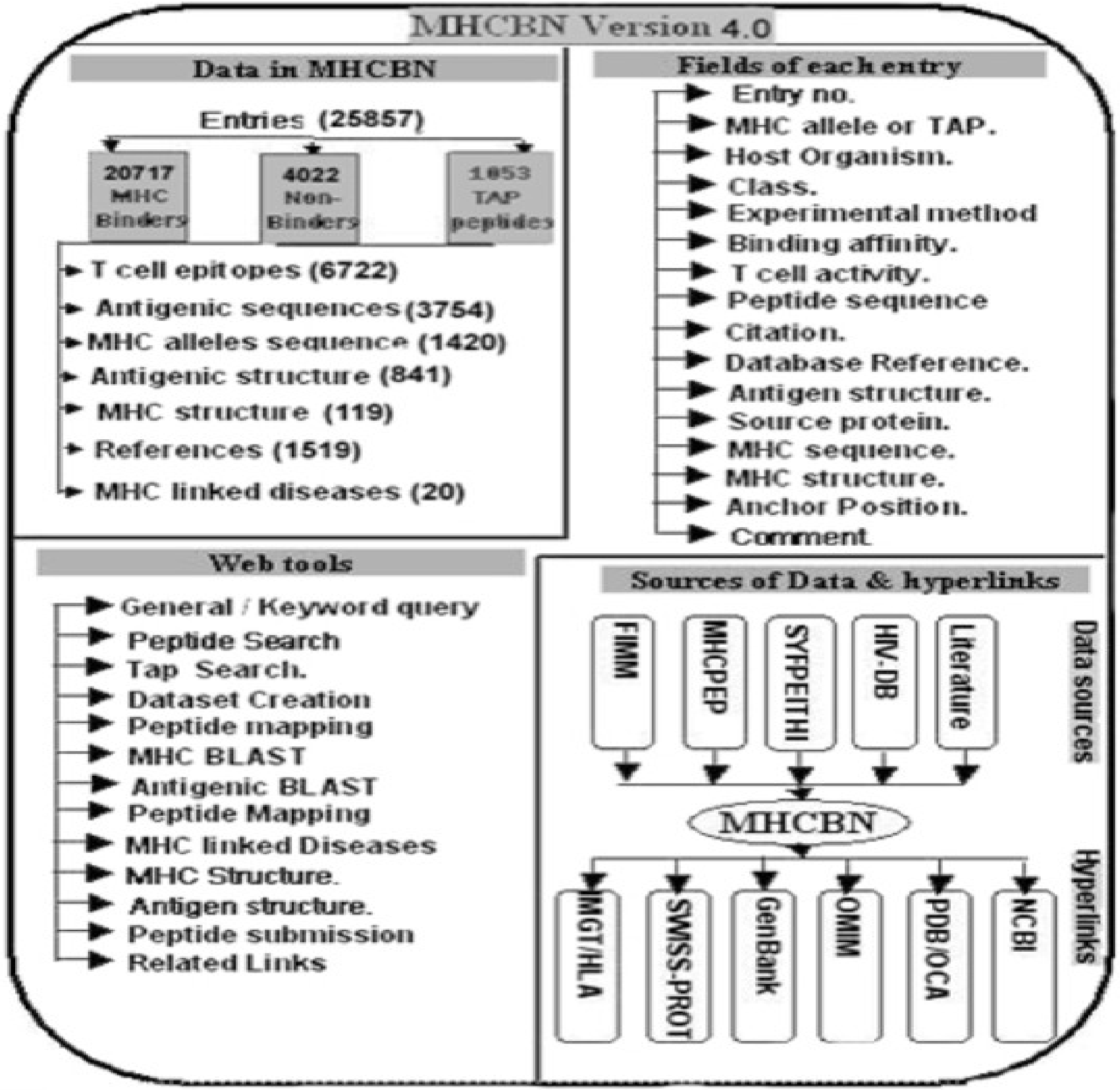


T-Helper Epitopes

MHCBN: A database of MHC/TAP binders and T-cell epitopes

Distributed by EBI, UK

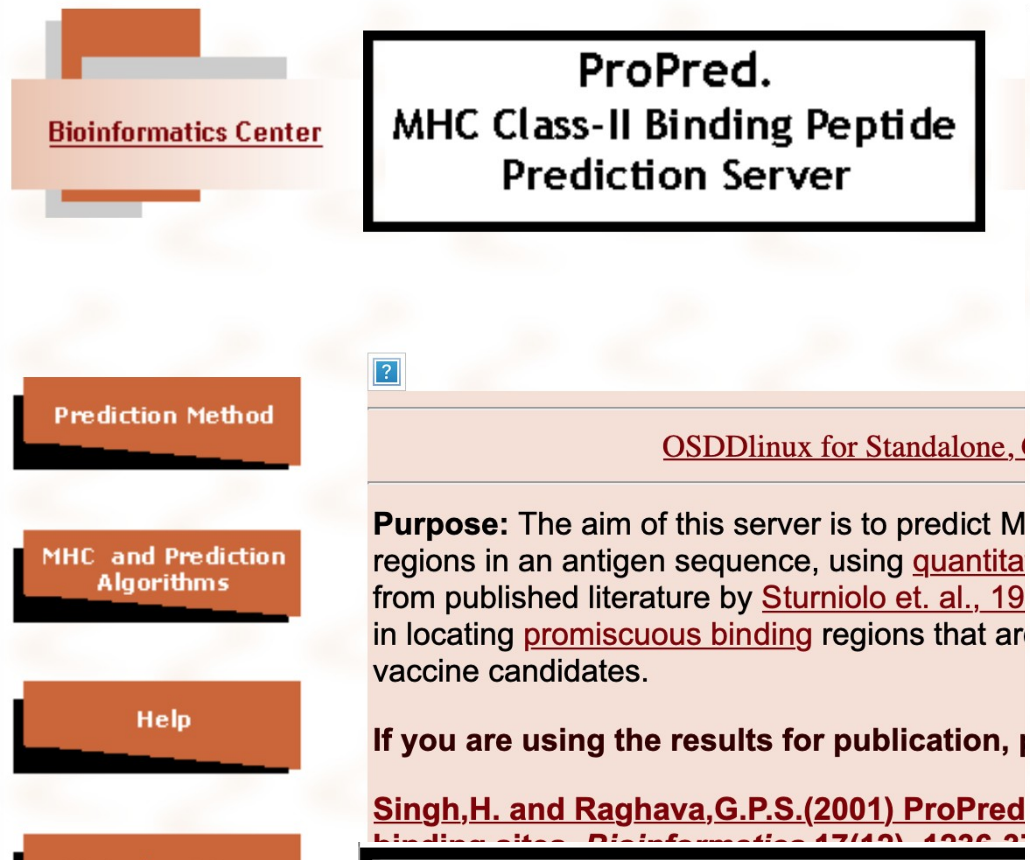




Reference database in T-cell epit
Highly Cited (~230 citations)

Bhasin et al. (2003)
Bioinformatics 19: 665

Bhasin et al. (2004) NAR



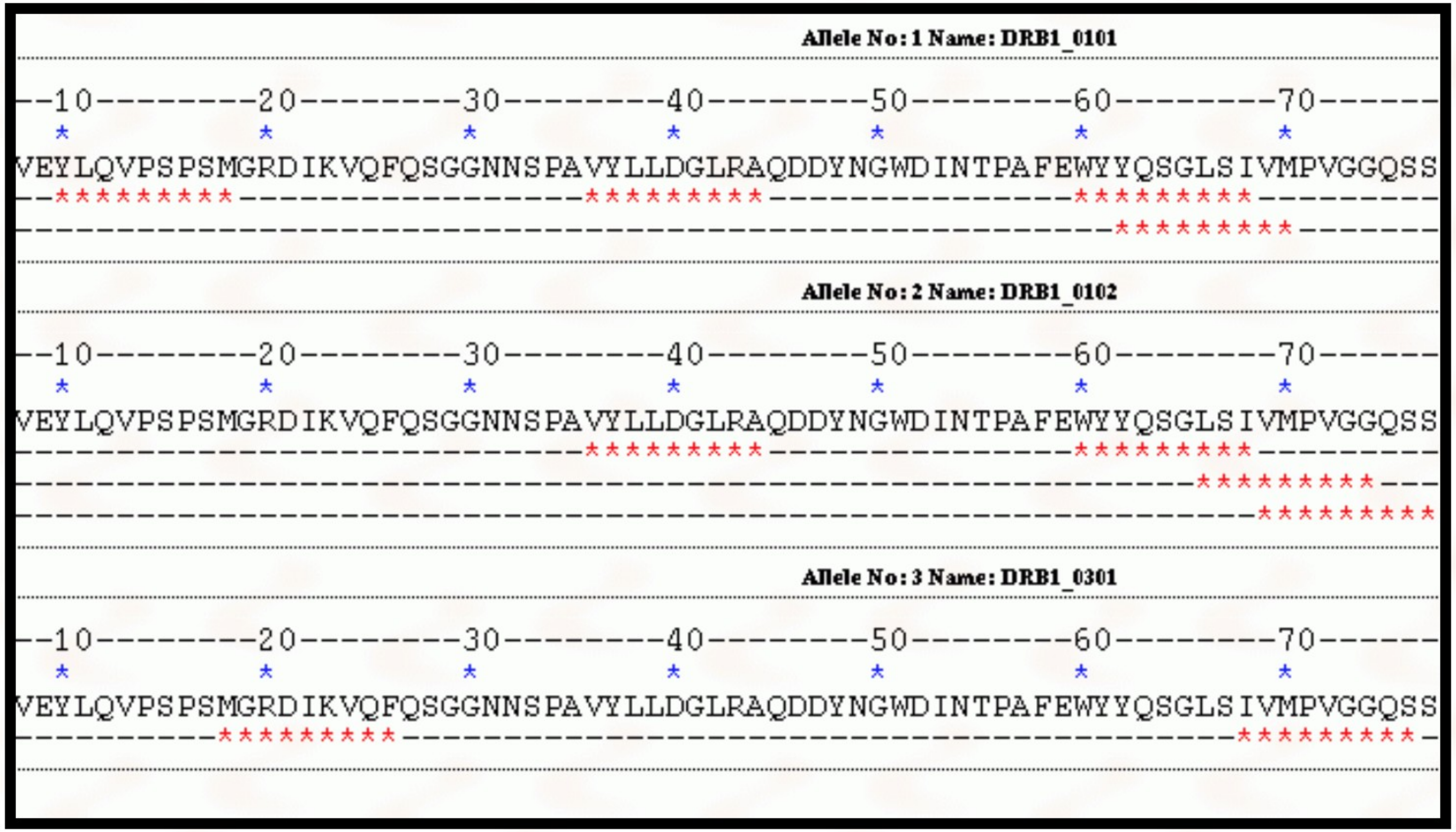
ProPred.
MHC Class-II Binding Peptide
Prediction Server

OSDDlinux for Standalone,

Purpose: The aim of this server is to predict M
regions in an antigen sequence, using quantita
from published literature by Sturniolo et. al., 19
in locating promiscuous binding regions that ar
vaccine candidates.

If you are using the results for publication,

Singh,H. and Raghava,G.P.S.(2001) ProPred



Allele No: 1 Name: DRB1_0101

```
--10--------20--------30--------40--------50--------60--------70------
  *         *         *         *         *         *         *
VEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQSGLSIVMPVGGQSS
--*********-----------------*********---------------*********---------
------------------------------------------------------*********-------
```

Allele No: 2 Name: DRB1_0102

```
--10--------20--------30--------40--------50--------60--------70------
  *         *         *         *         *         *         *
VEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQSGLSIVMPVGGQSS
----------------------------*********---------------*********---------
----------------------------------------------------------*********---
-------------------------------------------------------------*********
```

Allele No: 3 Name: DRB1_0301

```
--10--------20--------30--------40--------50--------60--------70------
  *         *         *         *         *         *         *
VEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQSGLSIVMPVGGQSS
----------*********-----------------------------------------*********-
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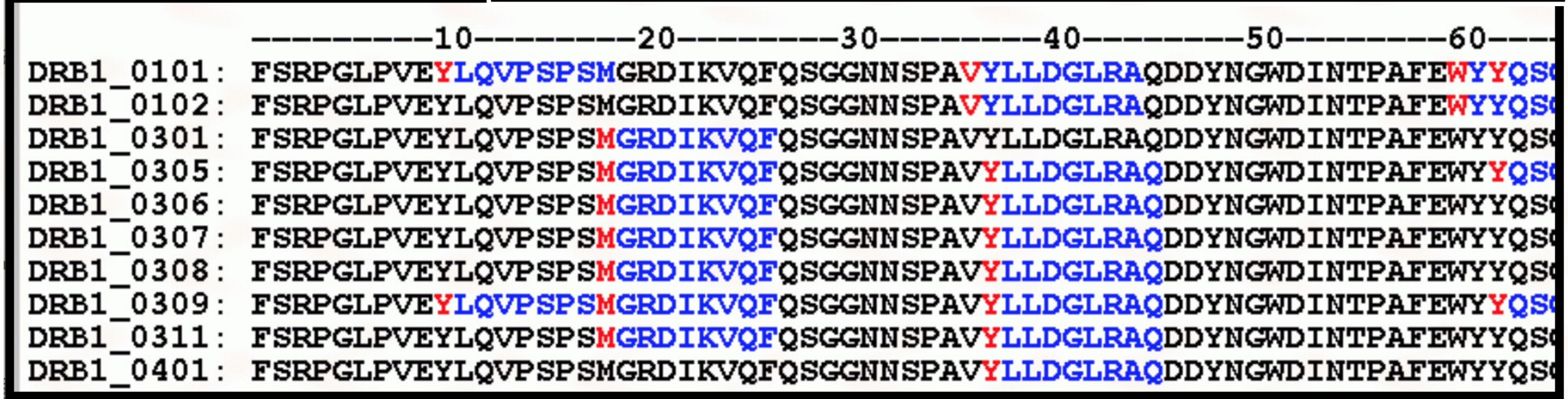

```
             --------10--------20--------30--------40--------50--------60----
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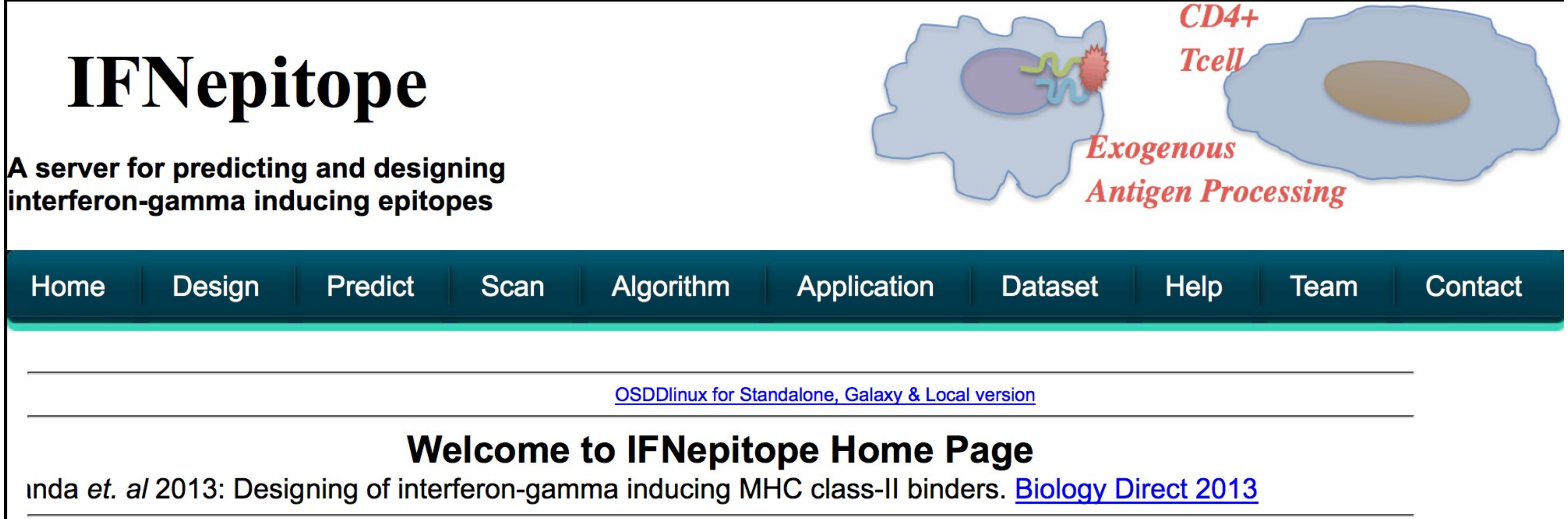
DRB1_0102 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
DRB1_0301 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
DRB1_0305 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
DRB1_0306 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
DRB1_0307 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
DRB1_0308 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
DRB1_0309 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
DRB1_0311 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
DRB1_0401 :  FSRPGLPVEYLQVPSPSMGRDIKVQFQSGGNNSPAVYLLDGLRAQDDYNGWDINTPAFEWYYQS
```



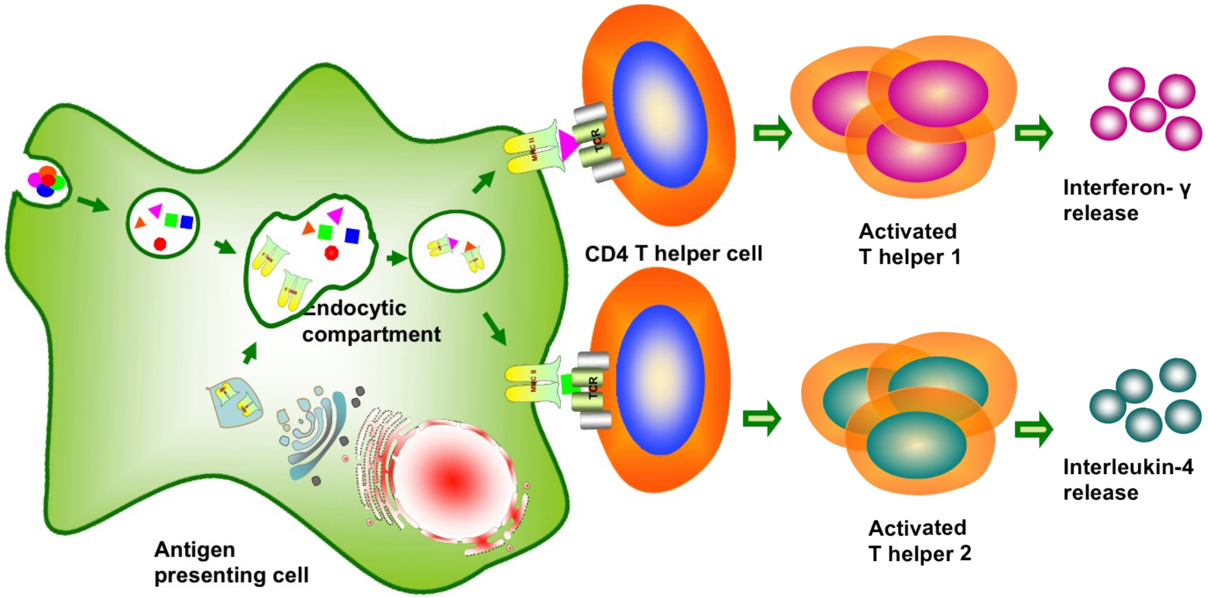
IFNepitope

A server for predicting and designing interferon-gamma inducing epitopes

OSDDlinux for Standalone, Galaxy & Local version

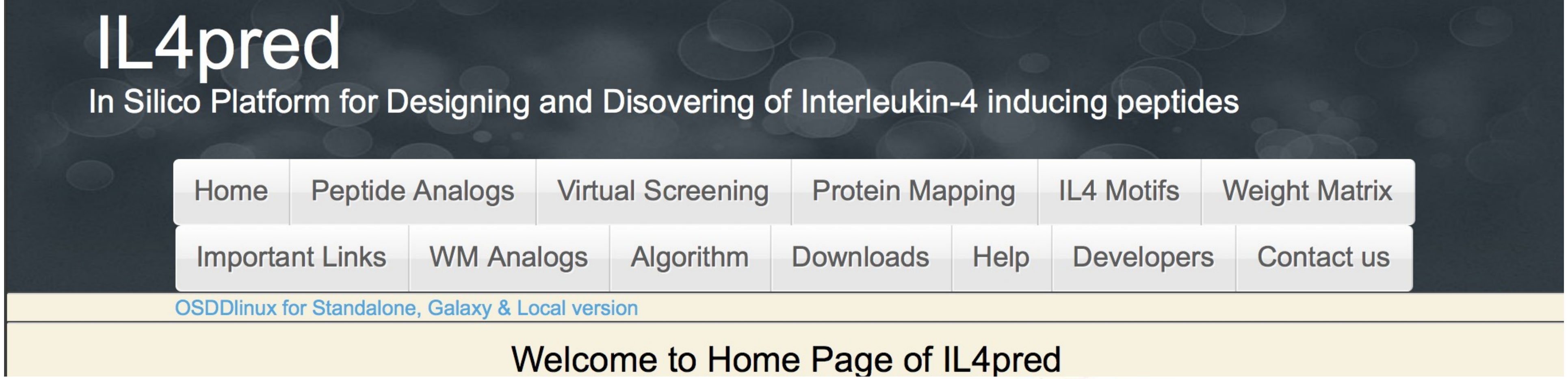
Welcome to IFNepitope Home Page

nda *et. al* 2013: Designing of interferon-gamma inducing MHC class-II binders. Biology Direct 2013



► IFN-γ inducing peptides

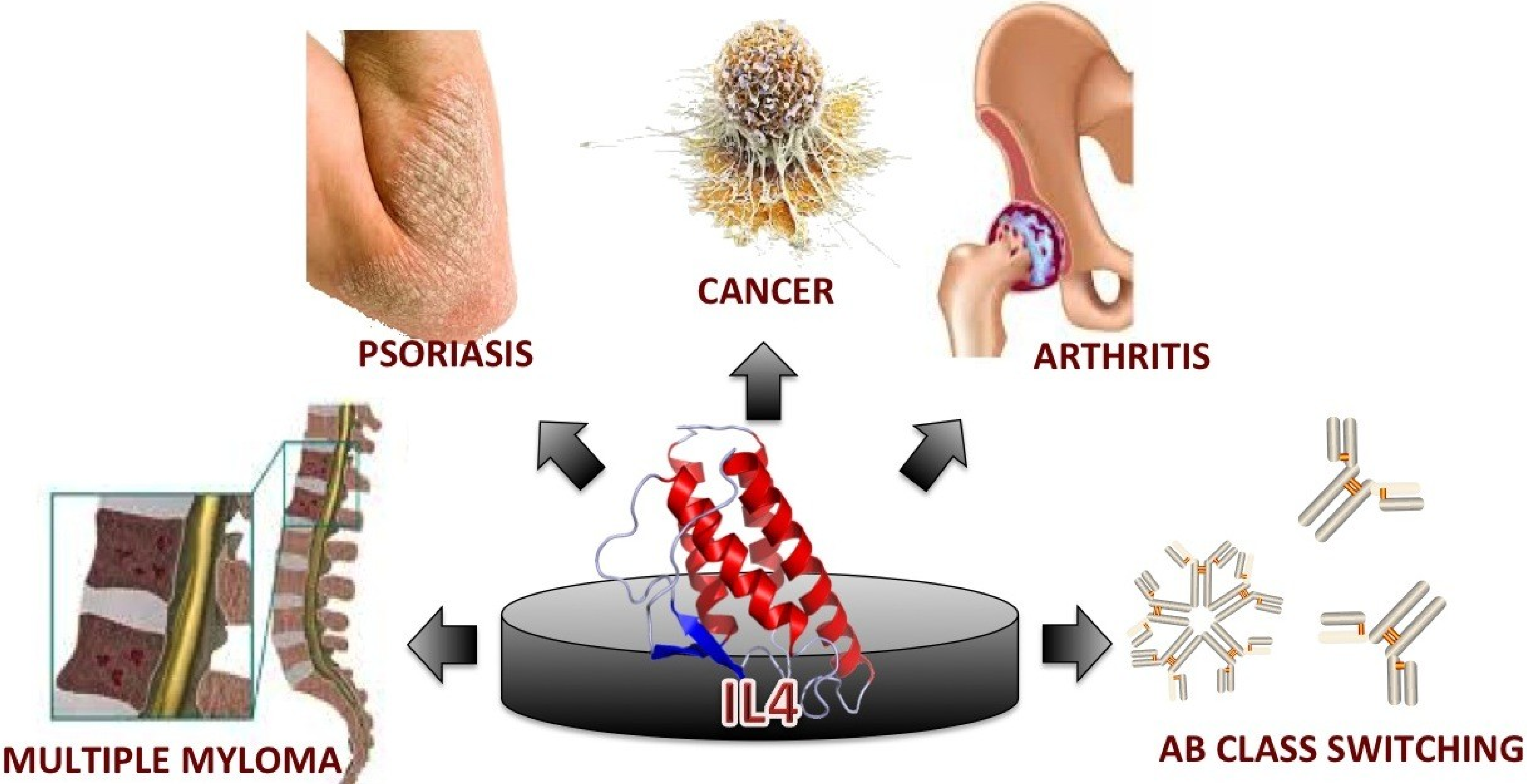
🟩 IFN-γ non-inducing peptides



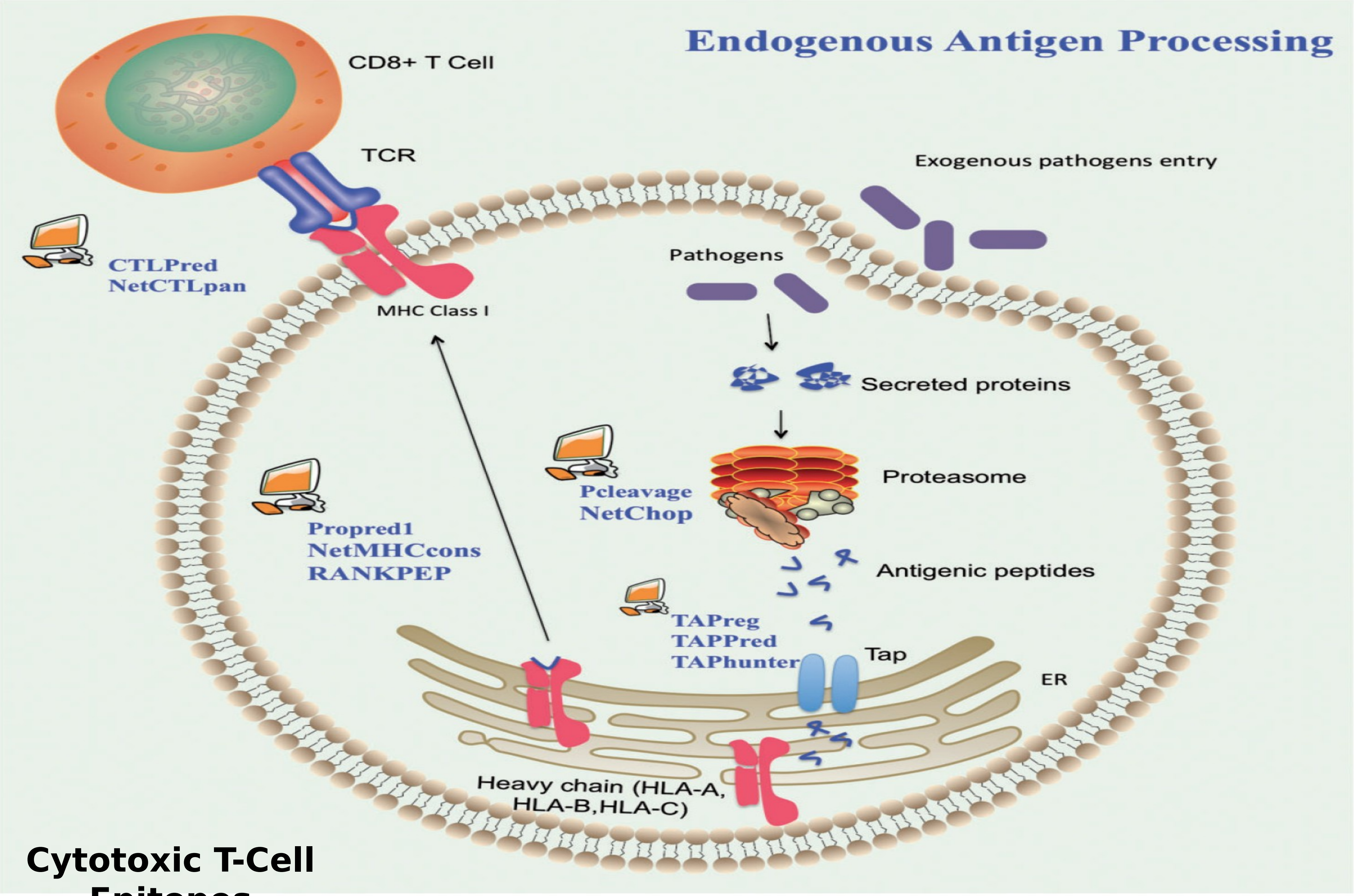
IL4pred

In Silico Platform for Designing and Disovering of Interleukin-4 inducing peptides

Welcome to Home Page of IL4pred



Cell Mediated Immunity (T-cell Epitopes)



Cytotoxic T-Cell Epitopes

```
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DRB1_0102: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0301: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0305: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0306: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0307: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0308: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0309: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0311: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0401: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0402: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0404: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0405: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0408: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
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DRB1_0423: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
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DRB1_0804: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0806: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0813: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_0817: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_1101: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
DRB1_1102: MKVKYALLSAGALQLLVVGCGSSHHETHYGYATLSYADYWAGELGQSRDVLLAGNAEADRAG
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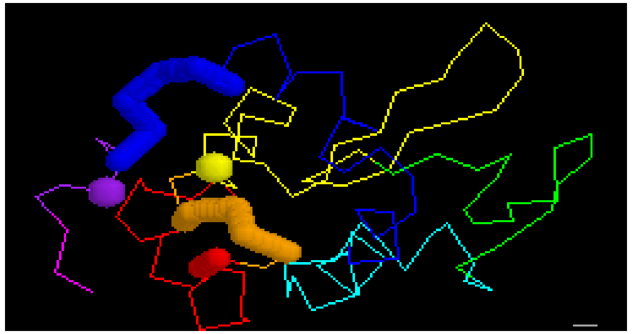
Types of epitopes

Conformational

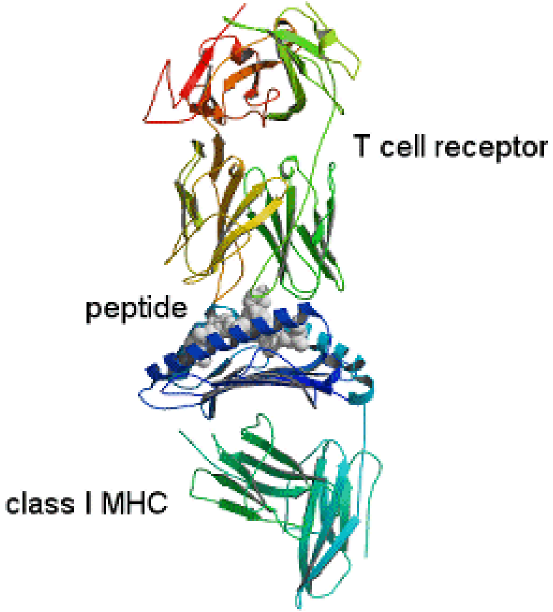
B cell Epitope



Non-Conformational

Linear B cell Epitope

T cell Epitope



CTL epitope

Class I MHCs

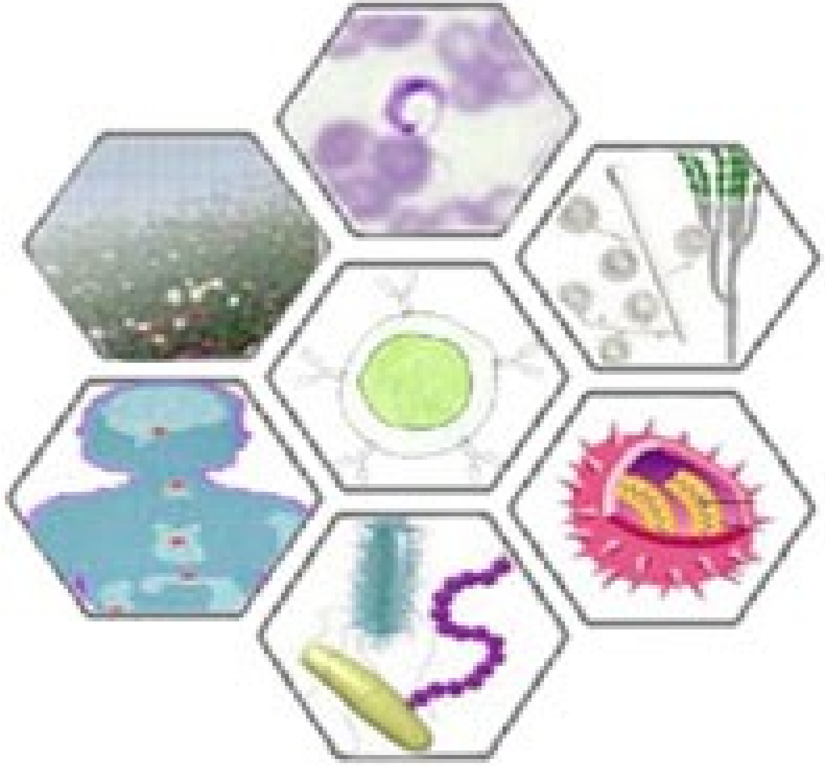
Endogenous Antigen Processing

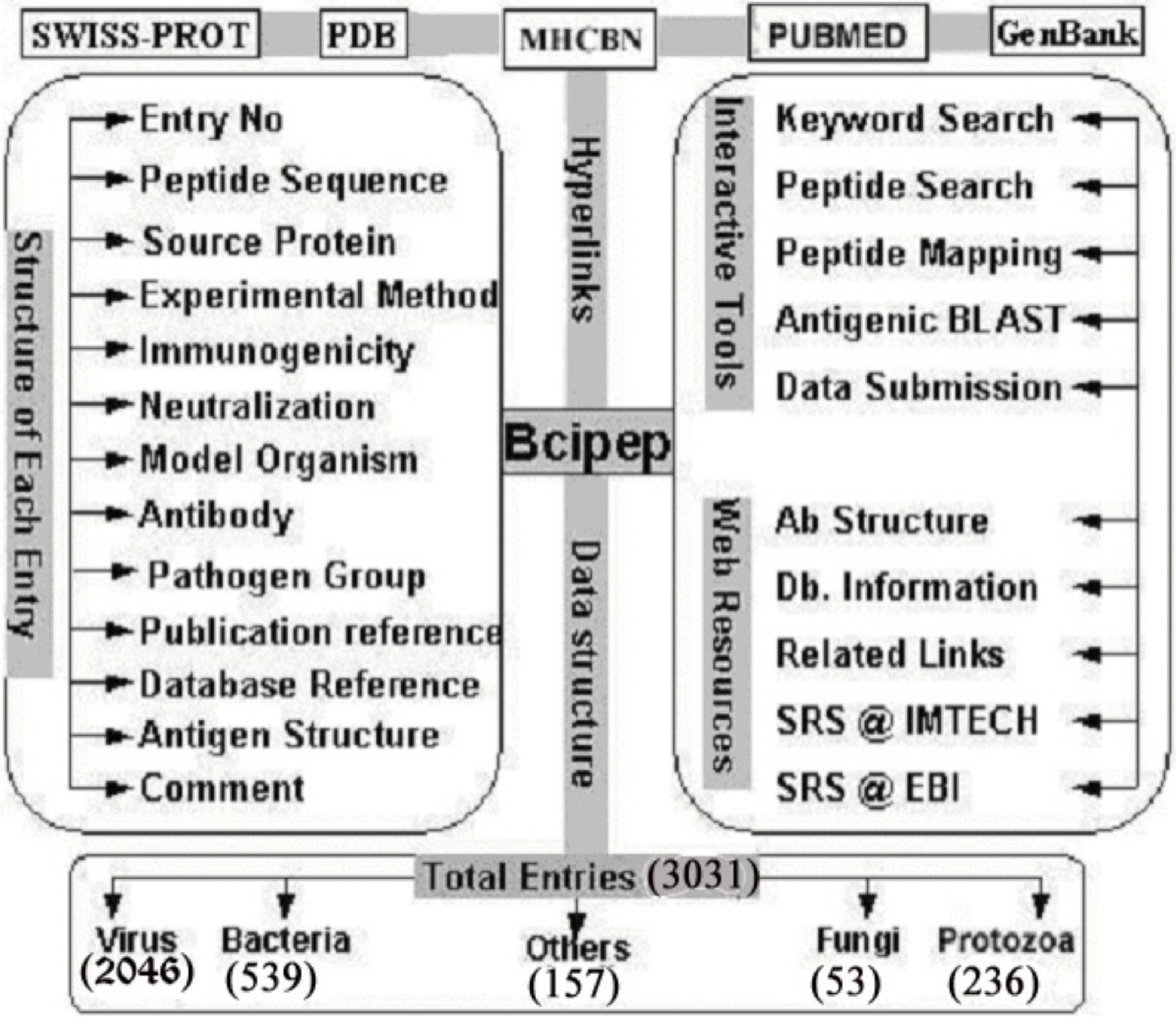
Helper T cell epitope

Class II MHCs

Exogenous Antigen Processing

BCIPEP: A database of B-cell epitopes.



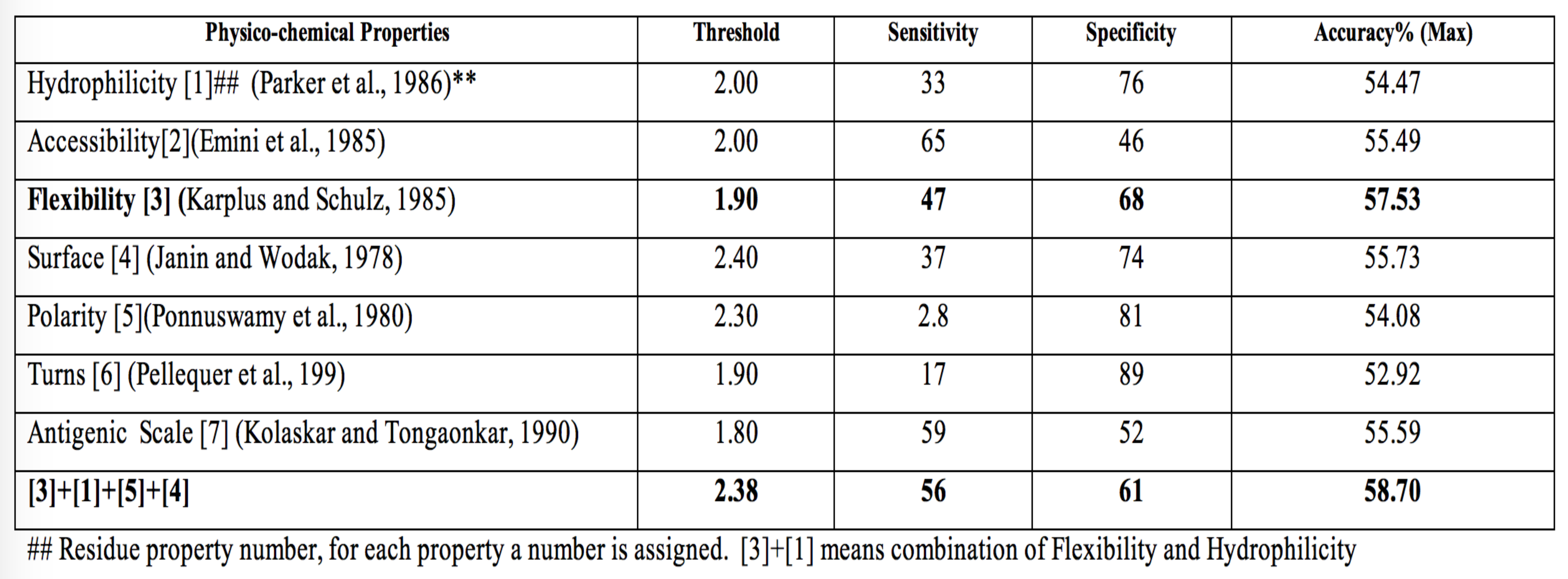


Saha et al.(2005) BMC Genomics 6:79.

Saha et al. (2006) NAR (Online)

BCEpred: Benchmarking of physicocemical properties used in existing B-cell epitope prediction methods

In 2003, we evaluate parmeters on 1029 non-redudant B-cell epitopes obtained from BCIpep and 1029 random peptide. Saha and Raghava (2004) ICARIS 197-204



Physico-chemical Properties	Threshold	Sensitivity	Specificity	Accuracy% (Max)
Hydrophilicity [1]## (Parker et al., 1986)**	2.00	33	76	54.47
Accessibility[2](Emini et al., 1985)	2.00	65	46	55.49
Flexibility [3] (Karplus and Schulz, 1985)	**1.90**	**47**	**68**	**57.53**
Surface [4] (Janin and Wodak, 1978)	2.40	37	74	55.73
Polarity [5](Ponnuswamy et al., 1980)	2.30	2.8	81	54.08
Turns [6] (Pellequer et al., 199)	1.90	17	89	52.92
Antigenic Scale [7] (Kolaskar and Tongaonkar, 1990)	1.80	59	52	55.59
[3]+[1]+[5]+[4]	**2.38**	**56**	**61**	**58.70**

Residue property number, for each property a number is assigned. [3]+[1] means combination of Flexibility and Hydrophilicity

OSDDlinux for Standalone, Galaxy & Local version

Artificial neural network based B-cell epitope prediction server

Datasets

B-cell and epitope of antigen

Recurrent neural network

The aim of ABCpred server is to predict *B cell epitope(s)* in an antigen sequence, using artificial neural network. This is the first server developed based on recurrent neural network (machine based technique) using fixed length patterns.

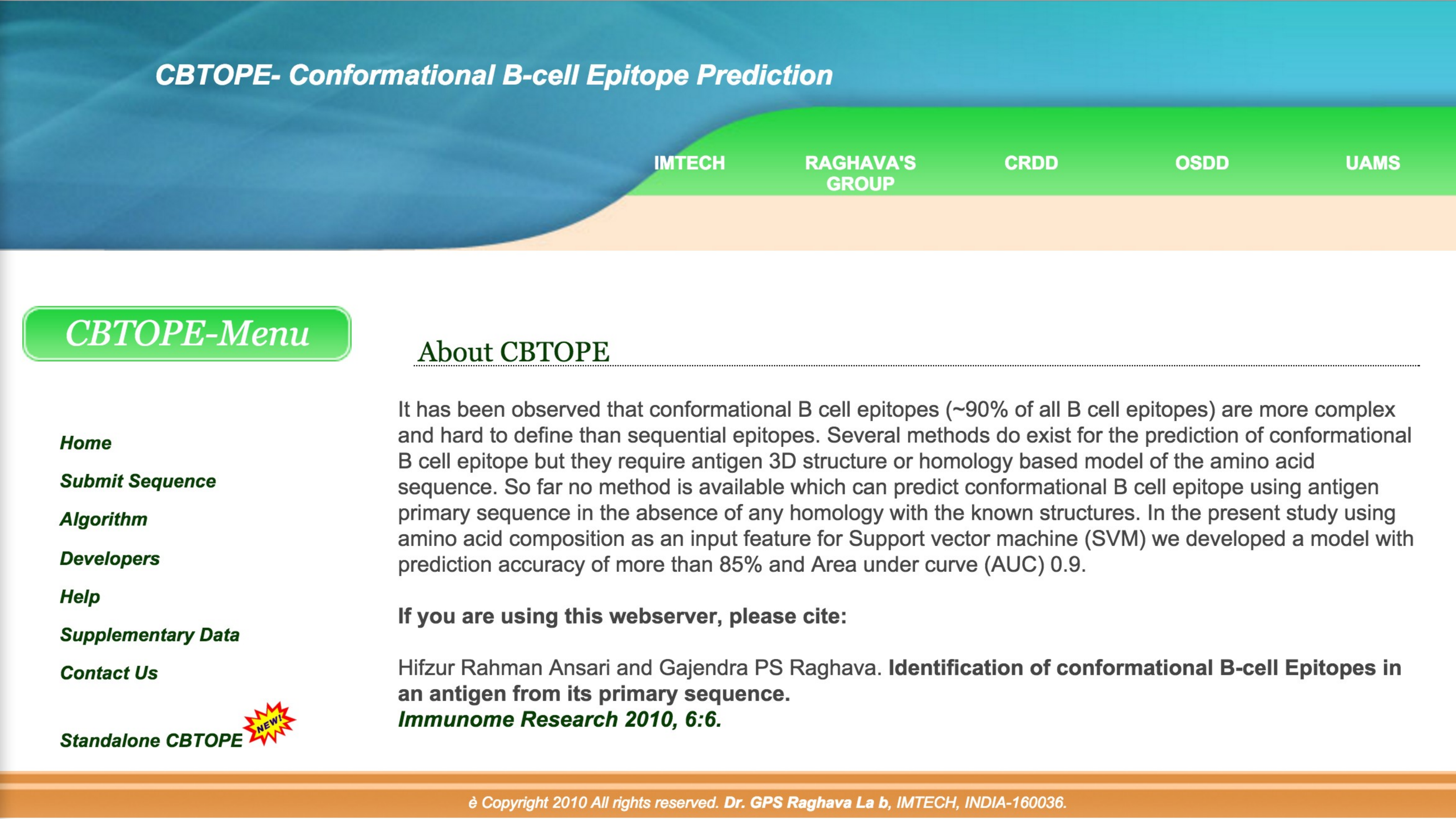
Algorithm: The machine-learning technique need fixed length patterns for training or testing whereas B-cell epitopes vary 5 to 30 residues as reported in literature(Bcipep database **Bcipep**). In order to overcome this problem we made an attempt to create datasets of fixed length patterns from B-cell epitopes by eliminating or adding residues at terminals. The dataset used for training and testing consists of 700 B-cell epitopes and 700 non B-cell epitopes (random peptides) of maximum length of 20 residues. We tried different neural networks and achived an accuracy of 65.93% using recurrent neural network.

Users can select window length of 10, 12, 14, 16 and 20 as predicted epitope length. It presents the results in graphical and tabular frame. In case of graphical frame, this server plot the epitopes in blue color along protein backbone (black color), which assist the users in rapid visulaziation of B-cell epitope on protein. The tabular output is in the form of a table, which will provide the aminoacids length from N-terminal to C-terminal in a protein predicted by the server.

The server is able to predict epitopes with **65.93% accuracy** using recurrent neural network.

Please cite following paper if you are using ABCpred server
Saha, S and Raghava G.P.S. (2006) Prediction of Continuous B-cell Epitopes in an Antigen Using Recurrent Neural Network. Proteins,**65(1)**,40-48 PMID: 16894596

Contact : G.P.S. Raghava   Bioinformatics Centre   Institute of Microbial Technology,India



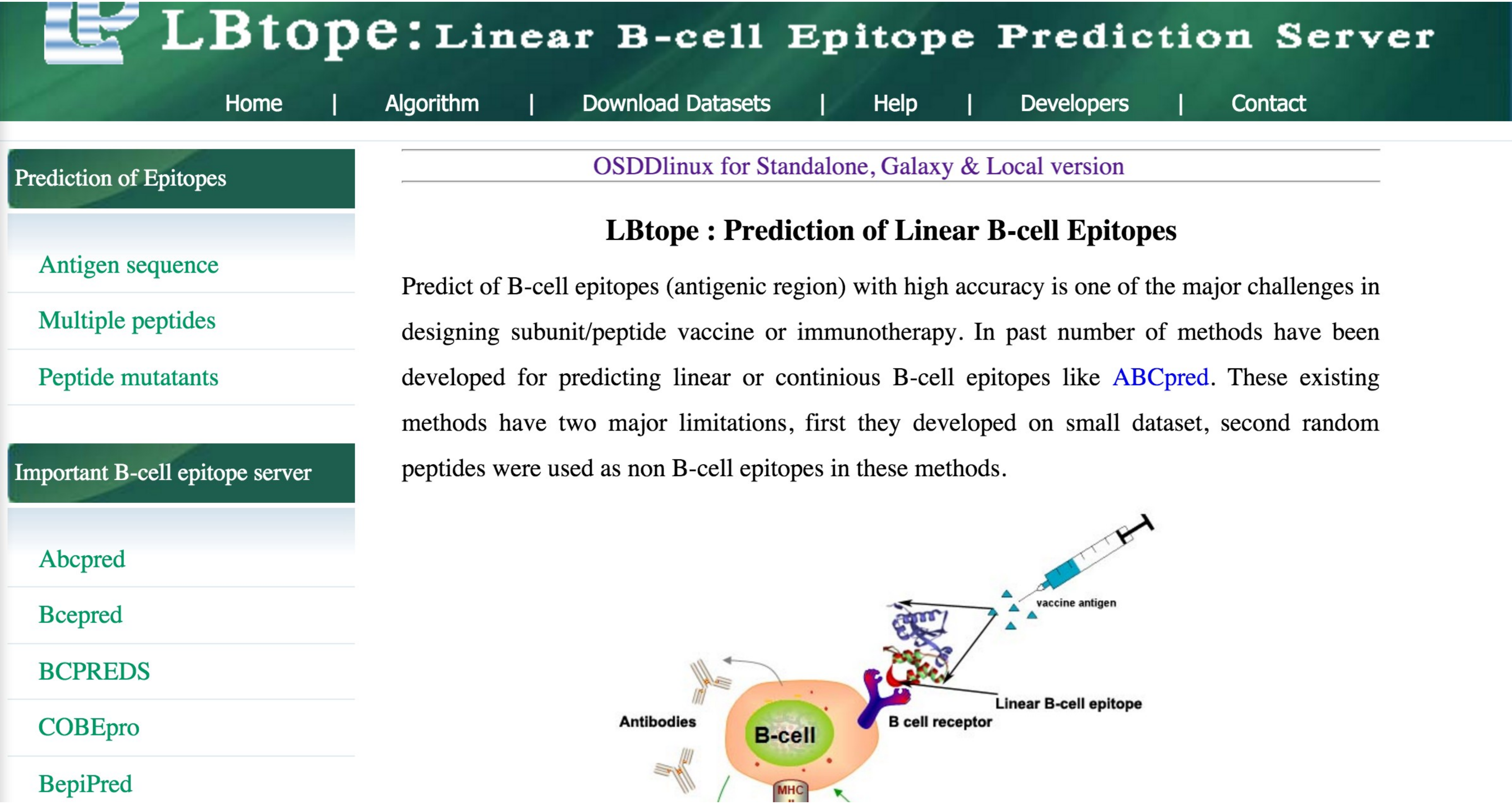
CBTOPE- Conformational B-cell Epitope Prediction

About CBTOPE

It has been observed that conformational B cell epitopes (~90% of all B cell epitopes) are more complex and hard to define than sequential epitopes. Several methods do exist for the prediction of conformational B cell epitope but they require antigen 3D structure or homology based model of the amino acid sequence. So far no method is available which can predict conformational B cell epitope using antigen primary sequence in the absence of any homology with the known structures. In the present study using amino acid composition as an input feature for Support vector machine (SVM) we developed a model with prediction accuracy of more than 85% and Area under curve (AUC) 0.9.

If you are using this webserver, please cite:

Hifzur Rahman Ansari and Gajendra PS Raghava. **Identification of conformational B-cell Epitopes in an antigen from its primary sequence.**
Immunome Research 2010, 6:6.



LBtope: Linear B-cell Epitope Prediction Server

Home | Algorithm | Download Datasets | Help | Developers | Contact

Prediction of Epitopes

- Antigen sequence
- Multiple peptides
- Peptide mutatants

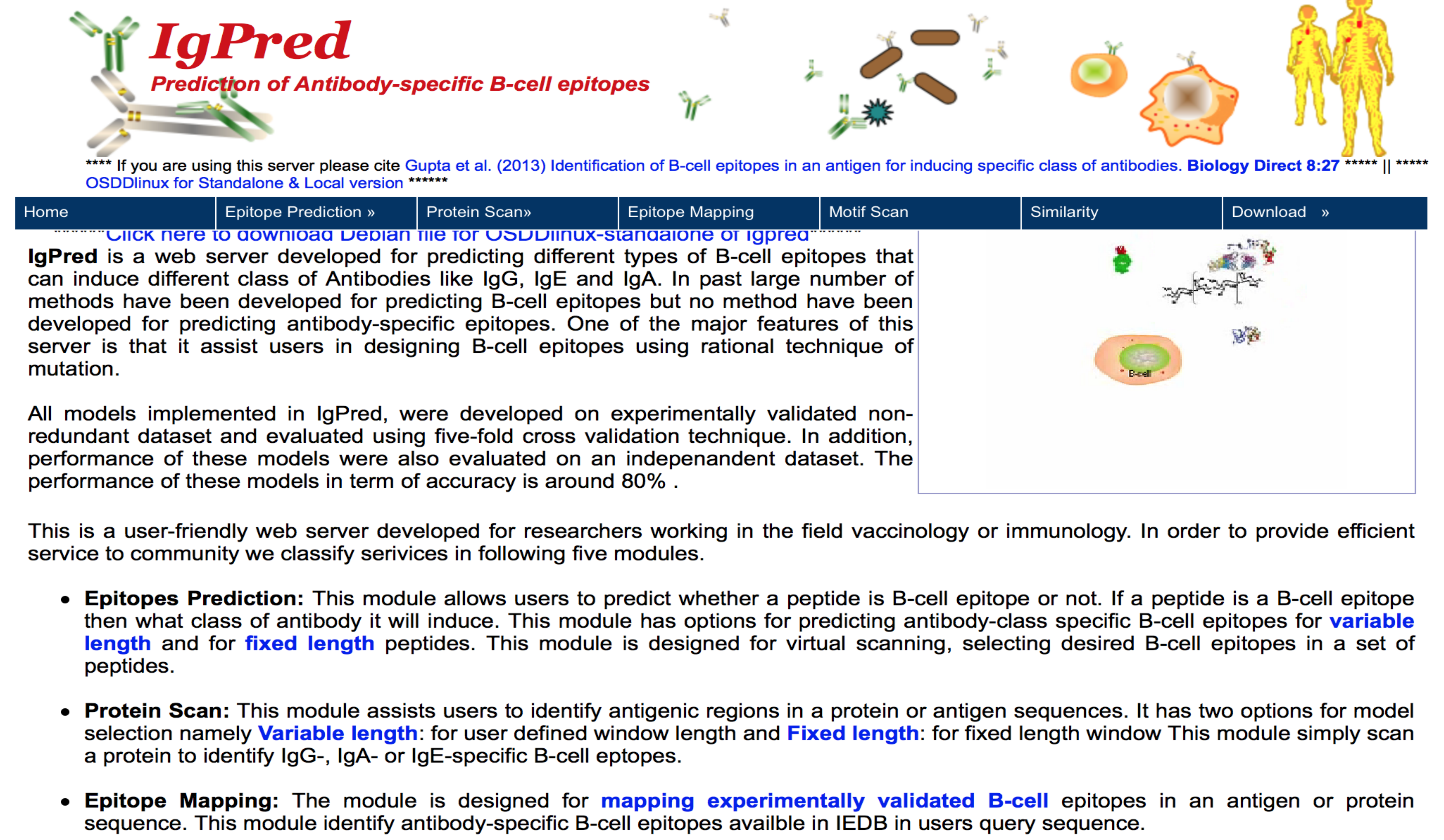
Important B-cell epitope server

- Abcpred
- Bcepred
- BCPREDS
- COBEpro
- BepiPred

OSDDlinux for Standalone, Galaxy & Local version

LBtope : Prediction of Linear B-cell Epitopes

Predict of B-cell epitopes (antigenic region) with high accuracy is one of the major challenges in designing subunit/peptide vaccine or immunotherapy. In past number of methods have been developed for predicting linear or continious B-cell epitopes like ABCpred. These existing methods have two major limitations, first they developed on small dataset, second random peptides were used as non B-cell epitopes in these methods.



**** If you are using this server please cite Gupta et al. (2013) Identification of B-cell epitopes in an antigen for inducing specific class of antibodies. **Biology Direct 8:27** ***** || ***** OSDDlinux for Standalone & Local version ******

******Click here to download Debian file for OSDDlinux-standalone of Igpred******

IgPred is a web server developed for predicting different types of B-cell epitopes that can induce different class of Antibodies like IgG, IgE and IgA. In past large number of methods have been developed for predicting B-cell epitopes but no method have been developed for predicting antibody-specific epitopes. One of the major features of this server is that it assist users in designing B-cell epitopes using rational technique of mutation.

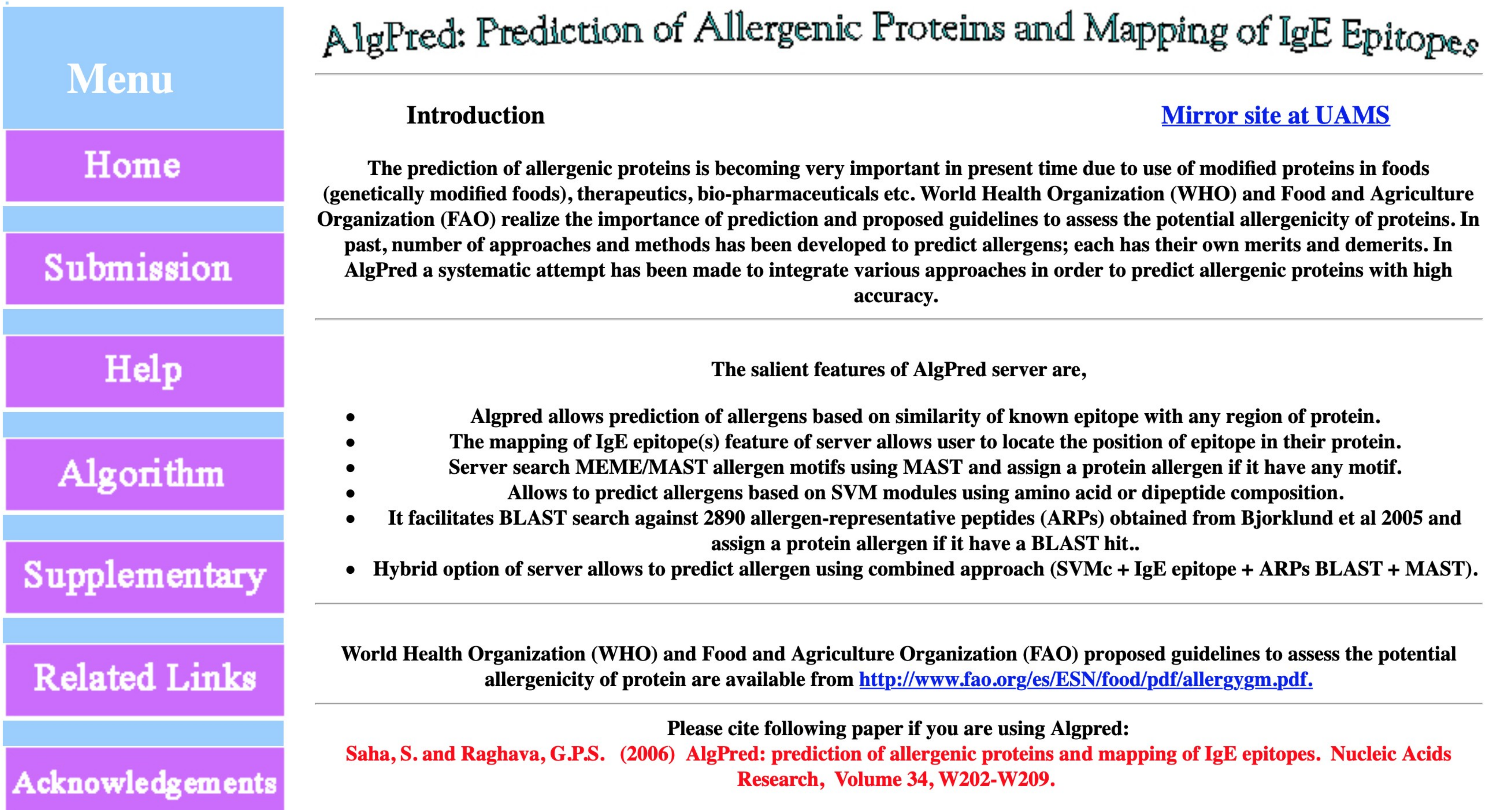
All models implemented in IgPred, were developed on experimentally validated non-redundant dataset and evaluated using five-fold cross validation technique. In addition, performance of these models were also evaluated on an indepenandent dataset. The performance of these models in term of accuracy is around 80% .

This is a user-friendly web server developed for researchers working in the field vaccinology or immunology. In order to provide efficient service to community we classify serivices in following five modules.

- **Epitopes Prediction:** This module allows users to predict whether a peptide is B-cell epitope or not. If a peptide is a B-cell epitope then what class of antibody it will induce. This module has options for predicting antibody-class specific B-cell epitopes for **variable length** and for **fixed length** peptides. This module is designed for virtual scanning, selecting desired B-cell epitopes in a set of peptides.

- **Protein Scan:** This module assists users to identify antigenic regions in a protein or antigen sequences. It has two options for model selection namely **Variable length**: for user defined window length and **Fixed length**: for fixed length window This module simply scan a protein to identify IgG-, IgA- or IgE-specific B-cell eptopes.

- **Epitope Mapping:** The module is designed for **mapping experimentally validated B-cell** epitopes in an antigen or protein sequence. This module identify antibody-specific B-cell epitopes availble in IEDB in users query sequence.



AlgPred: Prediction of Allergenic Proteins and Mapping of IgE Epitopes

Introduction **Mirror site at UAMS**

The prediction of allergenic proteins is becoming very important in present time due to use of modified proteins in foods (genetically modified foods), therapeutics, bio-pharmaceuticals etc. World Health Organization (WHO) and Food and Agriculture Organization (FAO) realize the importance of prediction and proposed guidelines to assess the potential allergenicity of proteins. In past, number of approaches and methods has been developed to predict allergens; each has their own merits and demerits. In AlgPred a systematic attempt has been made to integrate various approaches in order to predict allergenic proteins with high accuracy.

The salient features of AlgPred server are,

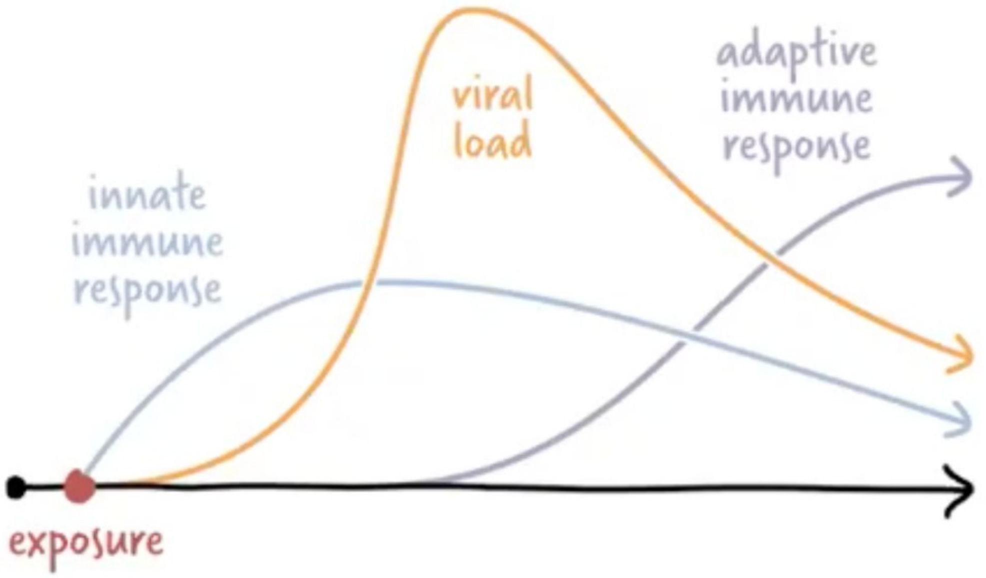
- **Algpred allows prediction of allergens based on similarity of known epitope with any region of protein.**
- **The mapping of IgE epitope(s) feature of server allows user to locate the position of epitope in their protein.**
- **Server search MEME/MAST allergen motifs using MAST and assign a protein allergen if it have any motif.**
- **Allows to predict allergens based on SVM modules using amino acid or dipeptide composition.**
- **It facilitates BLAST search against 2890 allergen-representative peptides (ARPs) obtained from Bjorklund et al 2005 and assign a protein allergen if it have a BLAST hit..**
- **Hybrid option of server allows to predict allergen using combined approach (SVMc + IgE epitope + ARPs BLAST + MAST).**

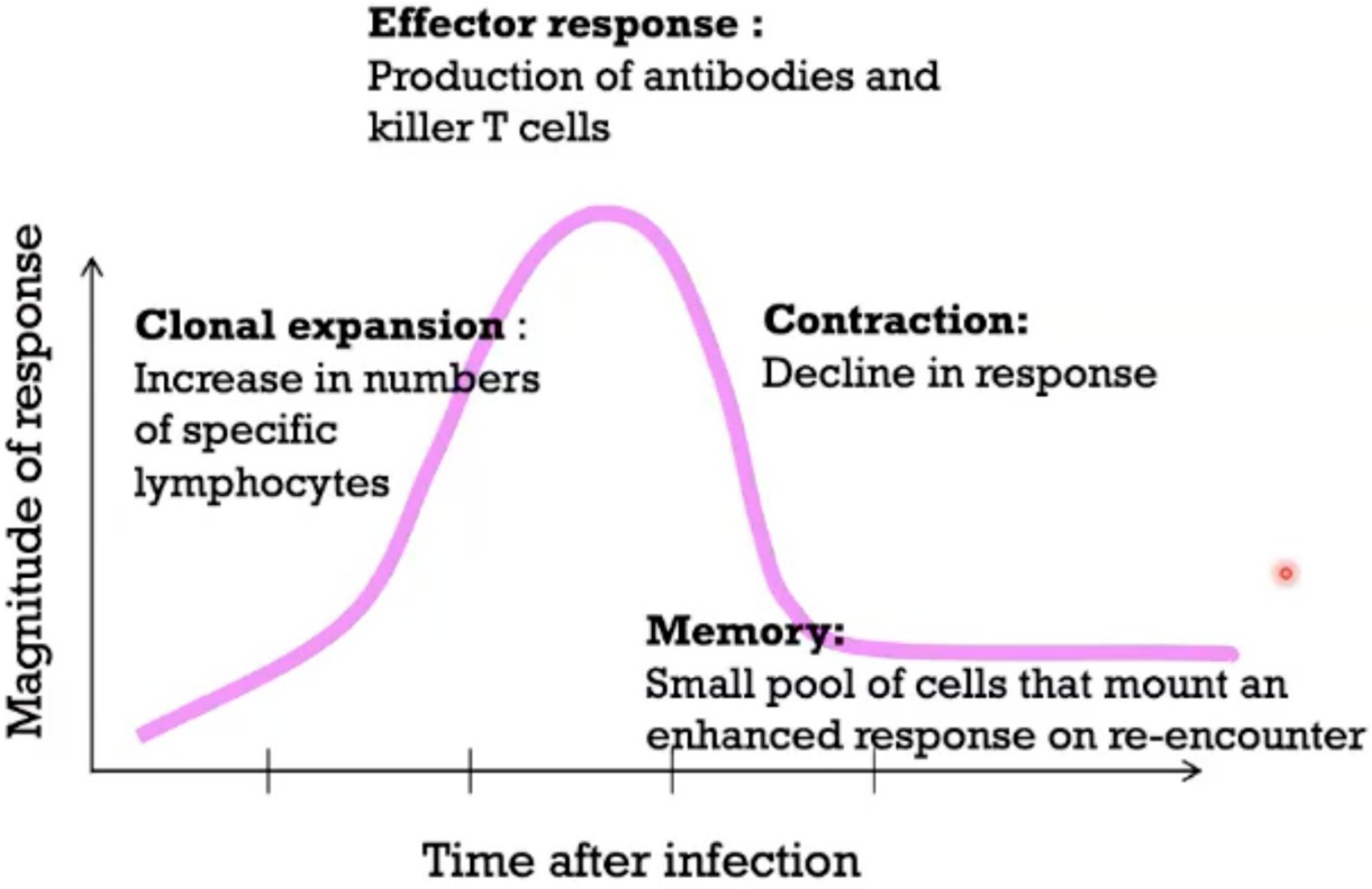
World Health Organization (WHO) and Food and Agriculture Organization (FAO) proposed guidelines to assess the potential allergenicity of protein are available from http://www.fao.org/es/ESN/food/pdf/allergygm.pdf.

Please cite following paper if you are using Algpred:

Saha, S. and Raghava, G.P.S. (2006) AlgPred: prediction of allergenic proteins and mapping of IgE epitopes. Nucleic Acids Research, Volume 34, W202-W209.

Immune Response





Effector response :
Production of antibodies and killer T cells

Clonal expansion :
Increase in numbers of specific lymphocytes

Contraction:
Decline in response

Memory:
Small pool of cells that mount an enhanced response on re-encounter

Web servers for designing epitope-based vaccine

T-Cell Epitopes

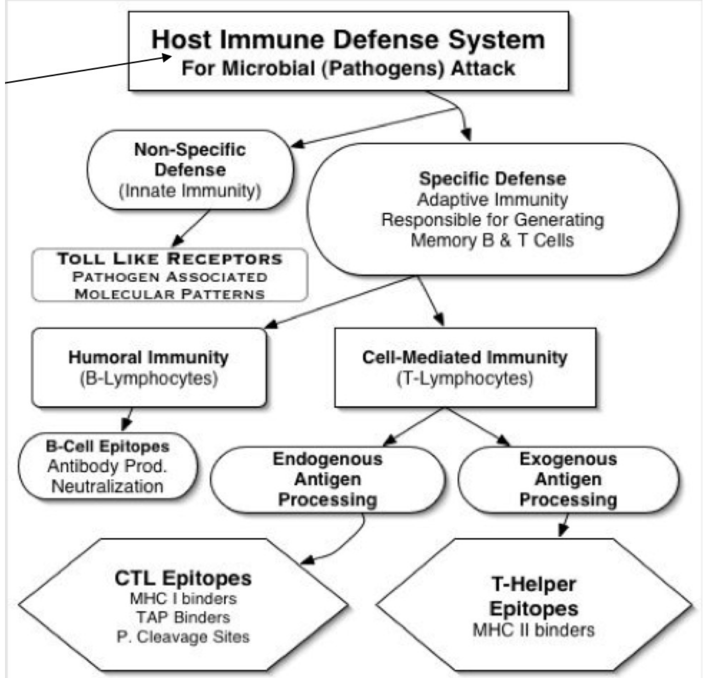
Propred: Promiscuous MHC-II binders
MHCBN: Database of MHC
IL4Pred: Prediction of interleukin-4
--
Propred1: for promiscuous MHC I binders
Pcleavage: Proteome cleavage sites
TAPpred: for predicting TAP binders
CTLpred: Prediction of CTL epitopes

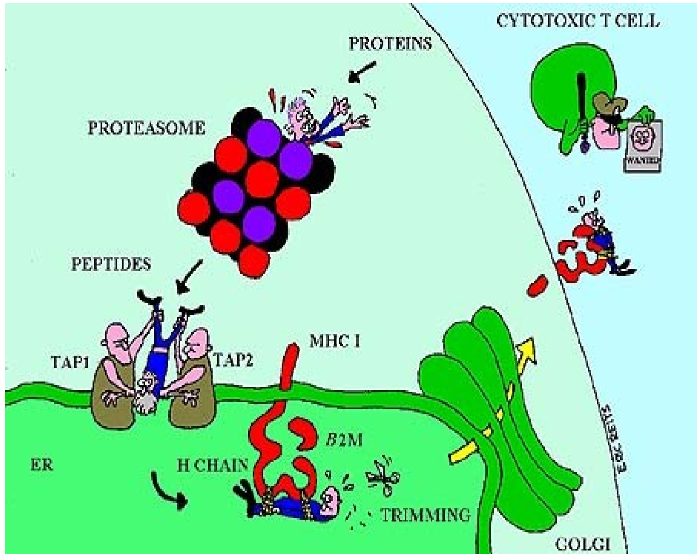
B-Cell Epitopes

BCIpep: Database of B-cell eptioes;
Lbtope: Prediction of B-cell epitopes
ALGpred: Allergens and IgE eptopes
IgPred: Antibody-specific epitopes

Vaccine Adjuvants

PRRDB: A database of PRRs & ligands
VaccineDA: DNA-based adjuvants
imRNA: Immunomulatory RNAs
VaccinePAD: Peptide-based adjuvants
PolysacDB: Polysaccharide antigens





Briefings in Bioinformatics, 18(3), 2017, 467–478

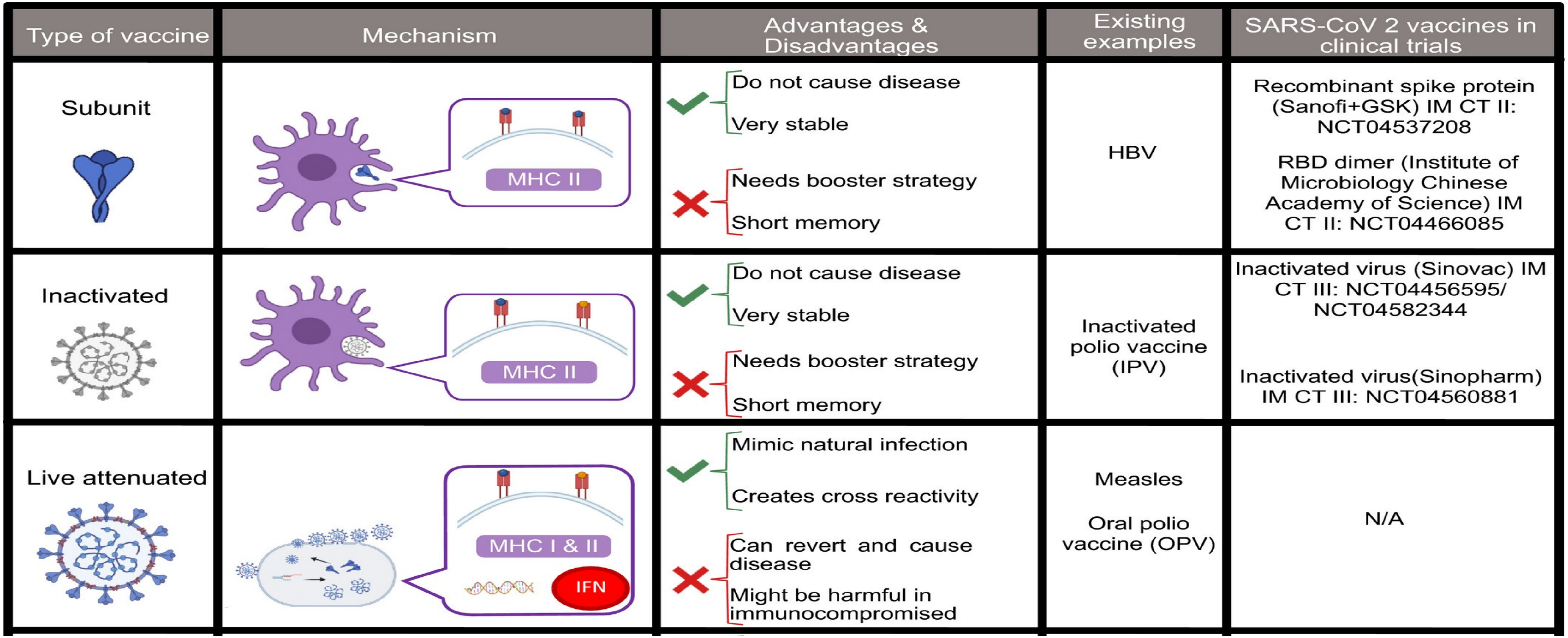
doi: 10.1093/bib/bbw025
Advance Access Publication Date: 25 March 2016
Software Review

Novel *in silico* tools for designing peptide-based subunit vaccines and immunotherapeutics

Sandeep Kumar Dhanda, Salman Sadullah Usmani, Piyush Agrawal, Gandharva Nagpal, Ankur Gautam and Gajendra P.S. Raghava

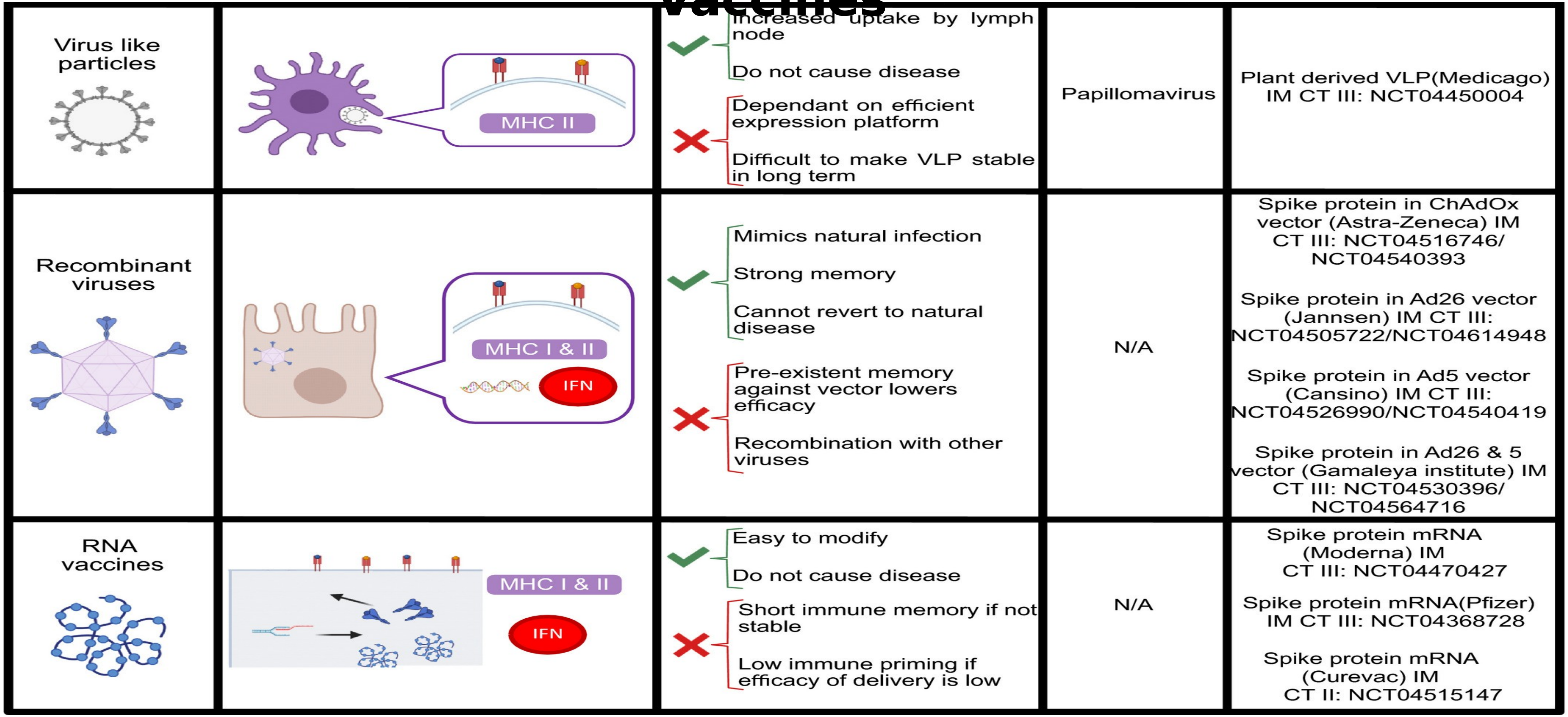
Corresponding author. Gajendra P.S. Raghava, Bioinformatics Centre, Institute of Microbial Technology, Sector 39A, Chandigarh 160036, India.
Tel.: +91-172-2690557; Fax: +91-172-2690632; E-mail: raghava@imtech.res.in

Types of Vaccines



Type of vaccine	Mechanism	Advantages & Disadvantages	Existing examples	SARS-CoV 2 vaccines in clinical trials
Subunit	MHC II	✓ Do not cause disease Very stable ✗ Needs booster strategy Short memory	HBV	Recombinant spike protein (Sanofi+GSK) IM CT II: NCT04537208 RBD dimer (Institute of Microbiology Chinese Academy of Science) IM CT II: NCT04466085
Inactivated	MHC II	✓ Do not cause disease Very stable ✗ Needs booster strategy Short memory	Inactivated polio vaccine (IPV)	Inactivated virus (Sinovac) IM CT III: NCT04456595/ NCT04582344 Inactivated virus(Sinopharm) IM CT III: NCT04560881
Live attenuated	MHC I & II IFN	✓ Mimic natural infection Creates cross reactivity ✗ Can revert and cause disease Might be harmful in immunocompromised	Measles Oral polio vaccine (OPV)	N/A

Types of Vaccines



Virus like particles		✓ Increased uptake by lymph node Do not cause disease ✗ Dependant on efficient expression platform Difficult to make VLP stable in long term	Papillomavirus	Plant derived VLP(Medicago) IM CT III: NCT04450004
Recombinant viruses		✓ Mimics natural infection Strong memory Cannot revert to natural disease ✗ Pre-existent memory against vector lowers efficacy Recombination with other viruses	N/A	Spike protein in ChAdOx vector (Astra-Zeneca) IM CT III: NCT04516746/ NCT04540393 Spike protein in Ad26 vector (Jannsen) IM CT III: NCT04505722/NCT04614948 Spike protein in Ad5 vector (Cansino) IM CT III: NCT04526990/NCT04540419 Spike protein in Ad26 & 5 vector (Gamaleya institute) IM CT III: NCT04530396/ NCT04564716
RNA vaccines		✓ Easy to modify Do not cause disease ✗ Short immune memory if not stable Low immune priming if efficacy of delivery is low	N/A	Spike protein mRNA (Moderna) IM CT III: NCT04470427 Spike protein mRNA(Pfizer) IM CT III: NCT04368728 Spike protein mRNA (Curevac) IM CT II: NCT04515147

CoronaVIR: Computational Resources on Novel Coronavirus (SARS-CoV-2 or COVID-19)

▾ HOME ▾ GENOMICS ▾ DIAGNOSIS ▾ IMMUNOTHERAPY ▾ DRUG DESIGNING ▾ USEFUL LINKS

Home Page CoronaVIR

Aim of this web site is to facilitate the scientific community to fight against severe pandemic disease COVID-19 caused by SARS-CoV-2. Here, We have collected and organized information related to novel strain of coronavirus, i.e. SARS-CoV-2.and its resulting disease COVID-19 from the literature and other resources from the Internet. We are providing links to appropriate literature. Moreover, we are Bioinformatics Group, based on our knowledge and expertise, we are also proposing potential diagnostics primers, peptide and RNA based vaccine candidates and potential drug molecules. These are predicted candidates, need to be validated by experimental Researchers, who have appropriate infrastructure. It is an integrated multi-omics repository dedicated to current genomic, proteomic, diagnostic and therapeutic knowledge about coronaviruses particularly the recent strain, i.e. SARS-CoV-2 or 2019-nCoV. This web resource will be helpful for the researchers engaged in the development of therapies and drugs for the COVID-19. The information is collected from various available resources.

Cite: Patiyal, Sumeet, et al. "A Web-based Platform on COVID-19 to Maintain Predicted Diagnostic, Drug and Vaccine Candidates." Monoclon Antib Immunodiagn Immunother. doi.org/10.1089/mab.2020.0035

General Info for non-researchers

- Diagnostic-Test
- Worldwide coronavirus spread
- Worldwide Statistics for COVID-19
- WHO Update
- Coronavirus Update
- Global Prevention
- 10 things to mange
- General Information
- Diagnosing coronavirus
- Diagnostics (RT PCR)

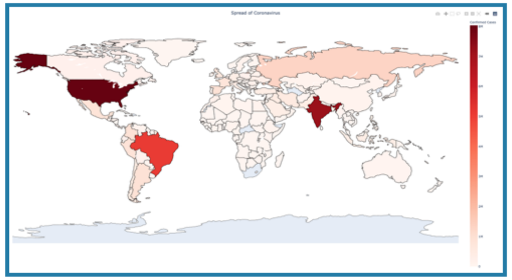
Information for Experts

- Genomics
- Proteomics
- Nucleotide
- Immunotherapy
- Peptide based Therapeutics
- Vaccine Adjuvants
- SiRNA based Therapeutics
- Drug designing
- Putative Drug/Vaccine
- CPP

Status of COVID-19

State-wise in India

Status in World



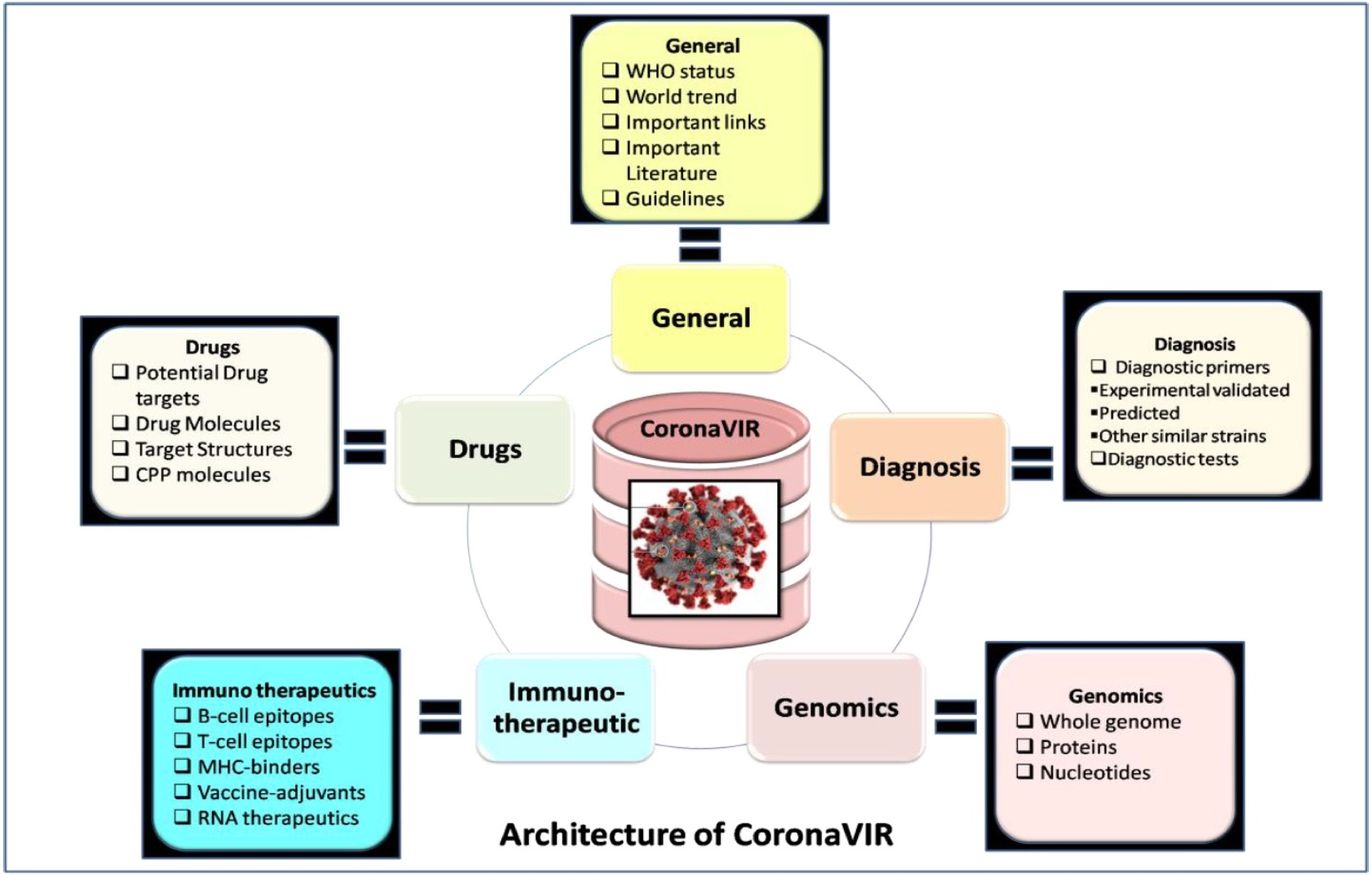

General
☐ WHO status
☐ World trend
☐ Important links
☐ Important Literature
☐ Guidelines
General
Drugs
☐ Potential Drug targets
☐ Drug Molecules
☐ Target Structures
☐ CPP molecules
Drugs
CoronaVIR
Diagnosis
Diagnosis
☐ Diagnostic primers
▪Experimental validated
▪Predicted
▪Other similar strains
☐Diagnostic tests
Immuno therapeutics
☐ B-cell epitopes
☐ T-cell epitopes
☐ MHC-binders
☐ Vaccine-adjuvants
☐ RNA therapeutics
Immuno-therapeutic
Genomics
Genomics
☐ Whole genome
☐ Proteins
☐ Nucleotides
Architecture of CoronaVIR

Table 2. Potential Vaccine Candidates Include IEDB (B Cell and T Cell Assay), B Cell Epitope, T Cell Epitope, Vaccine Adjuvants, MHC Class I and II Binders

Protein	*Potential vaccine candidate*	*IEDB (T cell) (#1)*	*IEDB (B cell) (#1)*	*B cell epitope (#2)*	*T cell epitope (#3)*	*Vaccine adjuvants (#4)*	*MHC class I (#5)*	*MHC class II (#6)*
Nucleocapsid phosphoprotein	LQLPQGTTLPKGFYA	✓	✓	✓	✓	✗	✓	✓
Nucleocapsid phosphoprotein	VILLNKHIDAYKTFPPTEPKKDKKKK	✓	✓	✓	✓	✗	✓	✓
Membrane glycoprotein	EITVATSRTLS	✓	✓	✓	✓	✗	✓	✓
Nucleocapsid phosphoprotein	GKGQQQQGQTV	✓	✓	✓	✓	✗	✓	✗
Membrane glycoprotein	SELVIGAVILR	✗	✓	✓	✓	✓	✓	✓
Envelope protein	ALRLCAYCCN	✓	✗	✓	✓	✓	✓	✓
ORF6	HLVDFQVTIAEILLIIMR	✓	✗	✓	✓	✗	✓	✓
Envelope protein	VFLLVTLAILTALRLCAYCCNI	✓	✗	✓	✓	✓	✓	✓
Membrane glycoprotein	NGTITVEELKKLLEQWNLVIGFLFL	✓	✗	✓	✓	✓	✓	✓
Membrane glycoprotein	ASFRLFARTRSMWSFNPETNILLNVPLHGT	✓	✗	✗	✓	✓	✓	✓
Membrane glycoprotein	SRYRIGNYKL	✓	✗	✗	✓	✓	✓	✓
ORF8	RCSFYEDFLEYHDVR	✗	✗	✓	✓	✓	✓	✓
ORF6	IWNLDYIINLIIKNLSKSLT	✗	✗	✓	✓	✗	✓	✓
Surface glycoprotein	SETKCTLKSFTVEKGIYQTSNF	✗	✗	✓	✓	✗	✓	✓
ORF8	MKFLVFLGIITTVAAFHQECSLQSCTQ	✗	✗	✓	✓	✗	✓	✓
ORF3a	DGTTSPISE	✗	✗	✓	✓	✗	✓	✗
ORF3a	SKIITLKKRWQLALSKGVHFVCNLLL	✗	✗	✓	✓	✓	✓	✗

#1, IEDB; #2, LBtope; #3, CTLPred; #4, VaxinPAD; #5, ProPred 1; #6, ProPred.
IEDB, Immune Epitope Database; MHC, major histocompatibility complex.

Table 4. List of Potential Nucleotide-Based Vaccine Adjuvants, Predicted by the VaccineDA for the 10 Proteins from SARS-CoV-2

Protein name	*Sequence*	*SVM score*	*Length*	*Molecular weight*	*Tm*	*GC content (%)*
Orf8	GCGTTGTTCGTTCTATGAAGACTTTTTAGA	1.885	30	9233.09	57.52	36.67
Orf1ab	ACGTTAATACGTTTTCATCAACTTTTAACG	1.537	30	9130.04	54.79	30
Envelope protein	ACGTTAATAGTTAATAGCGTACTTCTTTTT	1.492	30	9176.08	53.42	26.67
Orf6	ATTATGAGGACTTTTAAAGTTTCCATTTGG	1.33	30	9241.12	54.79	30
Surface glycoprotein	ACTAATGTCTATGCAGATTCATTTGTAATT	1.265	30	9185.09	53.42	26.67
Orf3a	TTCTCTATCTTTATGCTTTAGTCTACTTCT	1.248	30	9044.96	54.79	30
Nucleocapsid glycoprotein	GCGTTGTTCGTTCTATGAAGACTTTTTAGA	1.085	30	9246.08	61.62	46.67
Membrane glycoprotein	TAACTTTAGCTTGTTTTGTGCTTGCTGCTG	1.068	30	9191.04	58.89	40
Orf7a	CTCTAGCTGATAACAAATTTGCACTGACTT	0.797	30	9140.03	57.52	36.67
Orf10	AACGTTTTCGCTTTTCCGTTTACGATATAT	0.796	30	9128.02	56.15	33.33

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SVM, support vector machine.

Table 5. List of the Top 10 OligoNucleotide Candidates That Could Serve as Efficient siRNA Against COVID-19

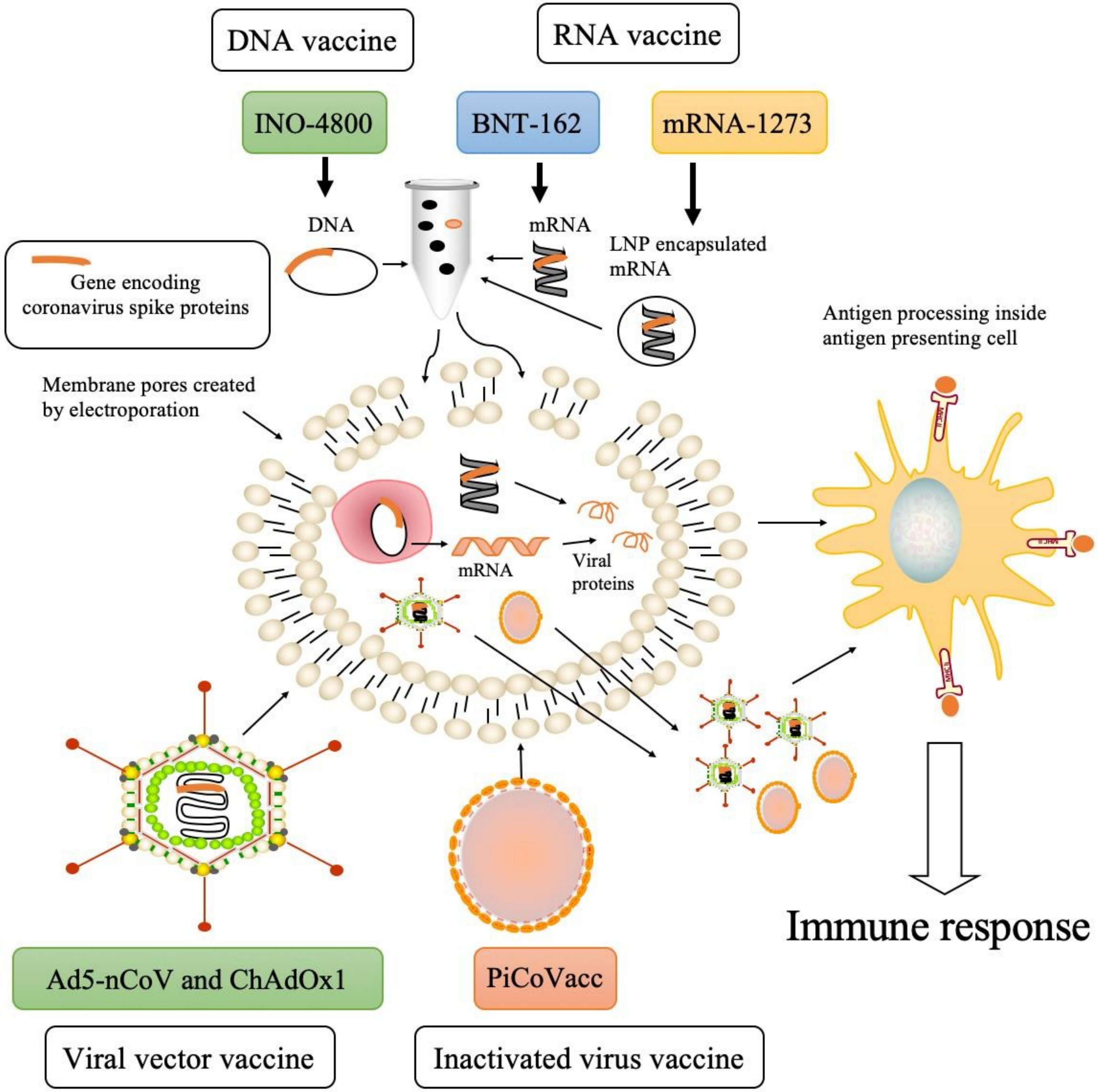
Protein name	*Antisense sequences of siRNA*	*Position on mRNA*	*mRNA target sequence*	*Target accessibility*	*Efficacy*
Orf1ab protein	AAAUUGAUCGUACAACACG	12	CGUGUUGUACGAUCAAUUU	0.637	1.129
Orf3a protein	AACAACAACAGCAAGUUGC	11	GCAACUUGCUGUUGUUGUU	0.979	1.080
Surface protein	UAAGAUUAACACACUGACU	3	AGUCAGUGUGUUAAUCUUA	0.722	1.078
Envelope protein	UUAACUAUUAACGUACCUG	10	CAGGUACGUUAAUAGUUAA	0.768	1.053
Orf6 protein	UUUAUUCUCAGUUAGUGAC	12	GUCACUAACUGAGAAUAAA	0.654	1.034
Nucleocapsid protein	UUUGUAUGCGUCAAUAUGC	8	GCAUAUUGACGCAUACAAA	0.676	1.033
Membrane protein	AAACAAGCUAAAGUUACUG	3	CAGUAACUUUAGCUUGUUU	0.673	1.010
Orf10 protein	UAACUACAUCUACUUGUGC	4	GCACAAGUAGAUGUAGUUA	0.723	0.981
Orf8 protein	UGAUACUCUAAAAAGUCUU	3	AAGACUUUUUAGAGUAUCA	0.947	0.923
Orf7a protein	AAAUUGAGUGCUAAAGCAA	11	UUGCUUUAGCACUCAAUUU	0.791	0.819

TABLE 6. LIST OF POTENTIAL DRUGS THAT COULD BE USED FOR TREATING COVID-19 INFECTION

					Patchdock score	
S. no.	*Drug*	*FDA-status*	*SARS-CoV-2 receptors*	*Targets in DrugBank (PDB ID)*	*SARS-CoV-2*	*Targets in DrugBank*
1	GS-6620	Investigational	RDRP	Hepatitis C virus Ns5b RNA-dependent RNA polymerase (1C2P)	8724	7364
2	Cobicistat	Approved	3C-like proteinase	NA	8096	NA
3	Ritonavir	Approved, investigational	3C-like proteinase	HIV-1 protease (5V4Y)	7802	8016
4	Remdesivir	Investigational	RDRP	RNA-directed RNA polymerase L (NA)	7554	NA
5	Lopinavir	Approved	3C-like proteinase	HIV-1 protease (5V4Y)	7512	7894
6	Camostat myselate	Experimental	TMPRSS2	NA	6396	NA
7	Darunavir	Approved	3C-like proteinase	HIV-1 protease (5V4Y)	5934	7316
8	Fosamprenavir	Approved	3C-like proteinase	HIV-1 protease (5V4Y)	5934	6754

NA, not applicable; RDRP, RNA-dependent RNA polymerase.

Potential Challenges for Coronavirus



Potential Issues

- Induction of cytokine storm (IL-6 or IL-1β)
- Proinflammatory inducing regions
- Hemolytic potency of proteins
- Allergic antigenic regions
- Toxic protein/peptides
- Nucleic acid vaccines may cause mutations
- May induce Hepatitis
- Lung immunopathology

Possible solutions (prediction tools)

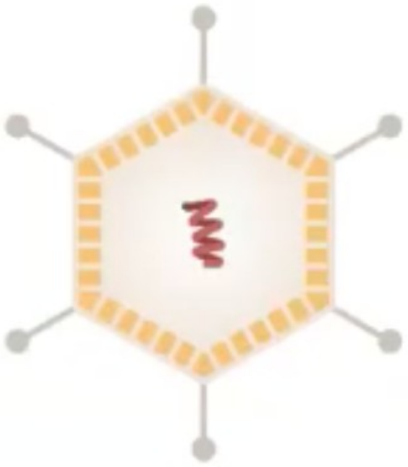
- Identification of hemolytic peptides: HemoPI, HemoPImod, HLPpred-Fuse
- Prediction of toxic peptides: NNTox, ToxinPred
- Prediction allergenic regions: ALGpred, AllerTOP, AllerCATPro
- Pro/Anti inflammatory peptide predictions - PIP-EL, PreAIP, AIPpred
- Method for inducing specific Interleukins: IL-4Pred, IL-10Pred

Genetic vaccines

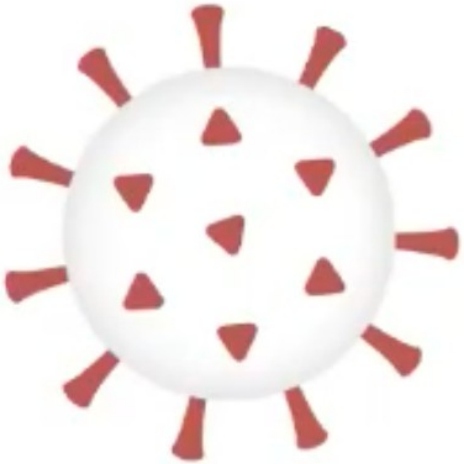
DNA

RNA

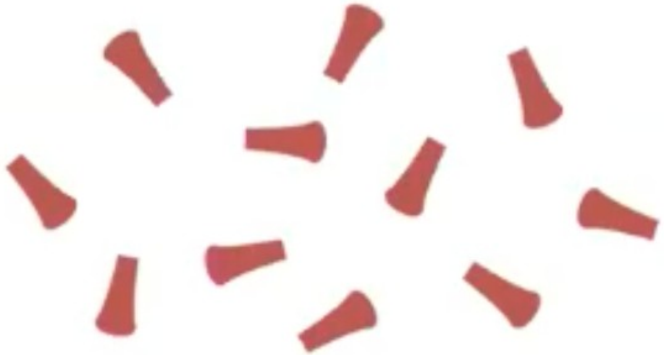
Viral vector vaccines



Adenovirus, AAV, VSV, Measles

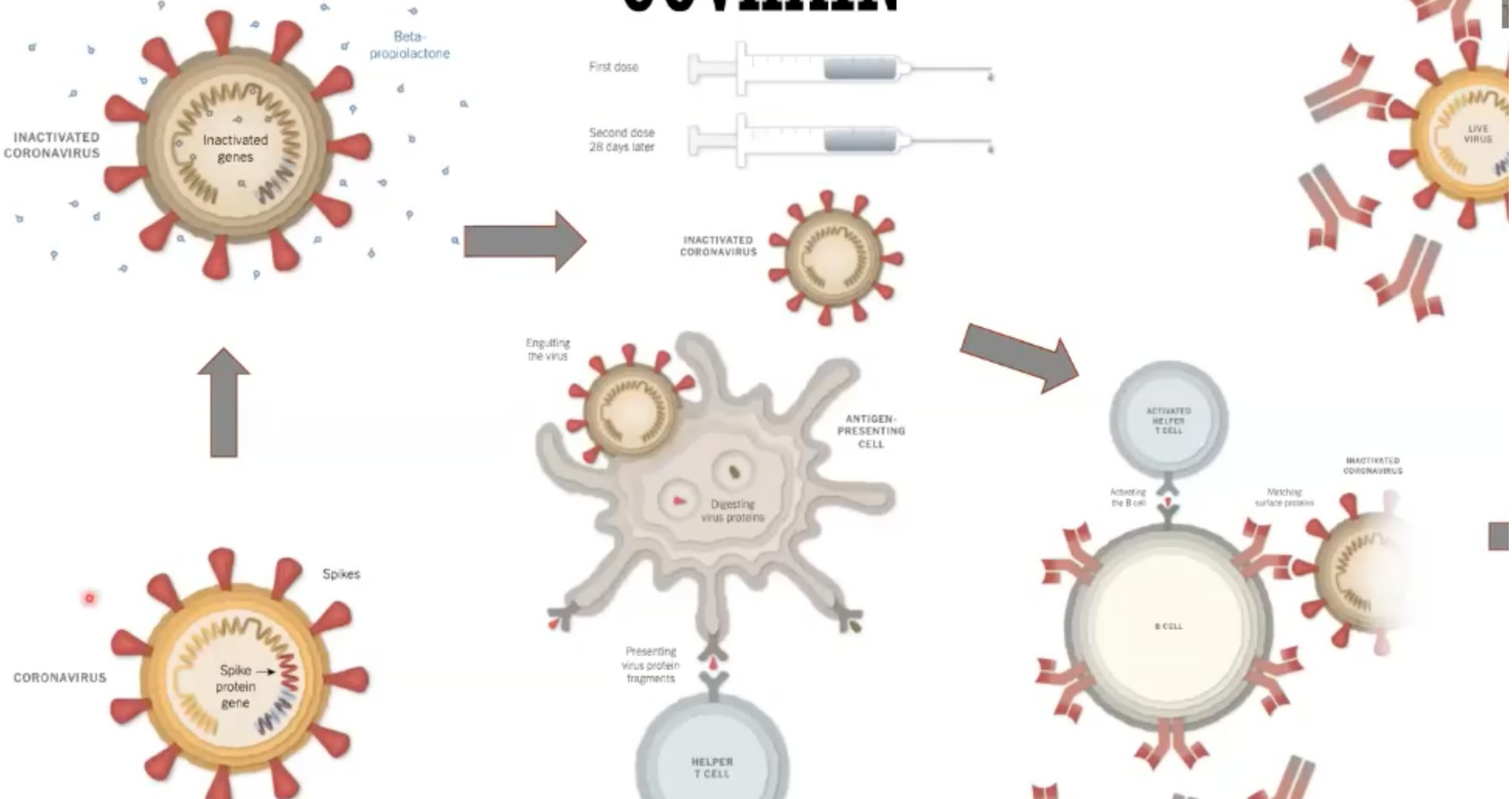


Virus-like particles

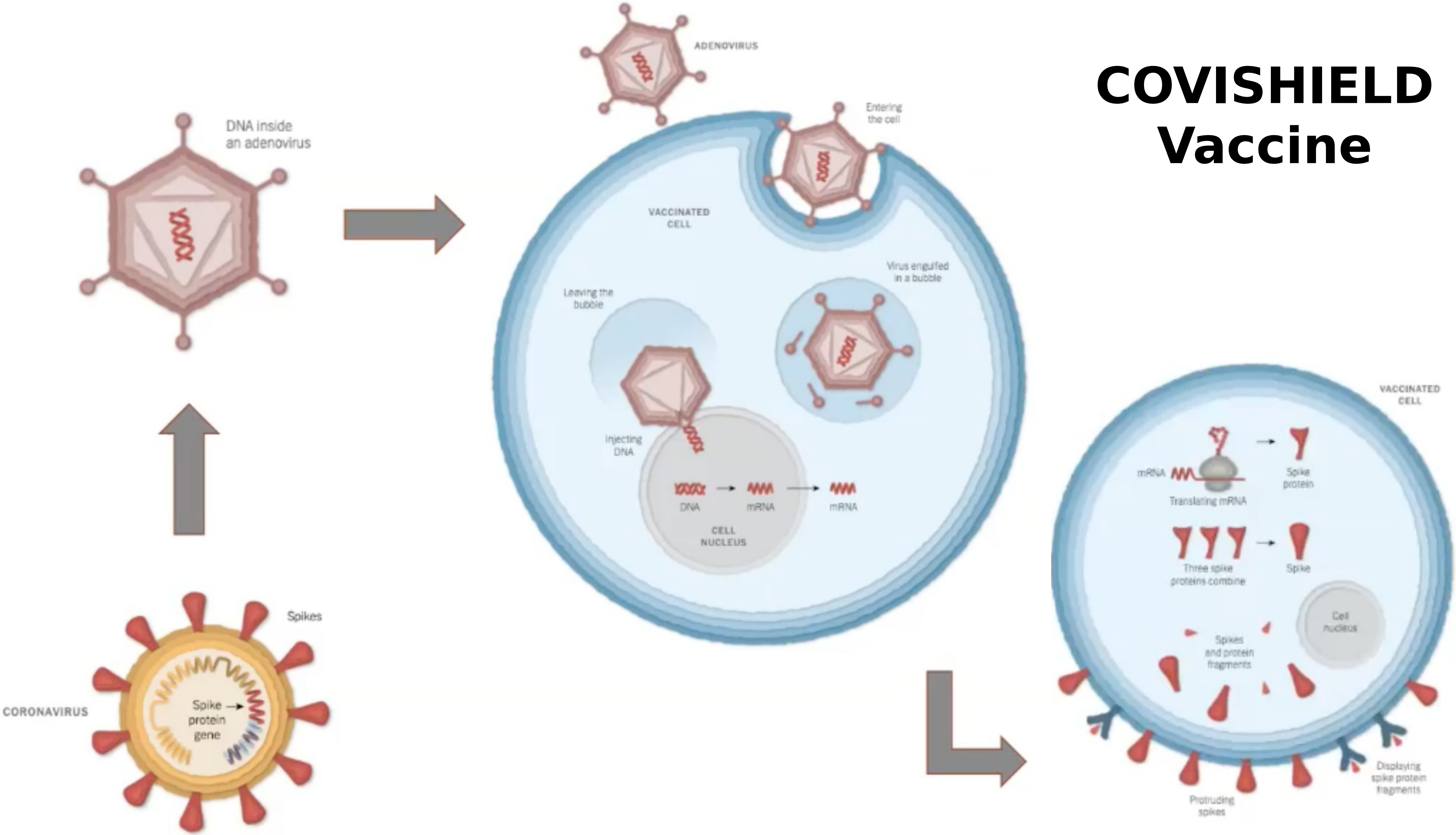


Soluble proteins

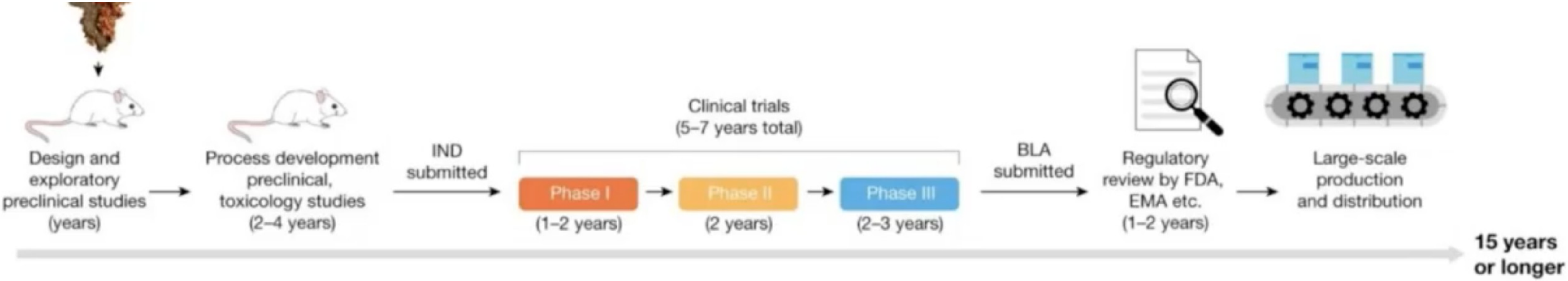
COVAXIN


INACTIVATED CORONAVIRUS
Inactivated genes
Beta-propiolactone
First dose
Second dose 28 days later
INACTIVATED CORONAVIRUS
LIVE VIRUS
CORONAVIRUS
Spike protein gene
Spikes
Engulfing the virus
ANTIGEN-PRESENTING CELL
Digesting virus proteins
Presenting virus protein fragments
HELPER T CELL
ACTIVATED HELPER T CELL
Activating the B cell
Matching surface proteins
INACTIVATED CORONAVIRUS
B CELL

COVISHIELD Vaccine



COVID-19 Vaccine discovery



Design and exploratory preclinical studies (years) → Process development preclinical, toxicology studies (2–4 years) → IND submitted →

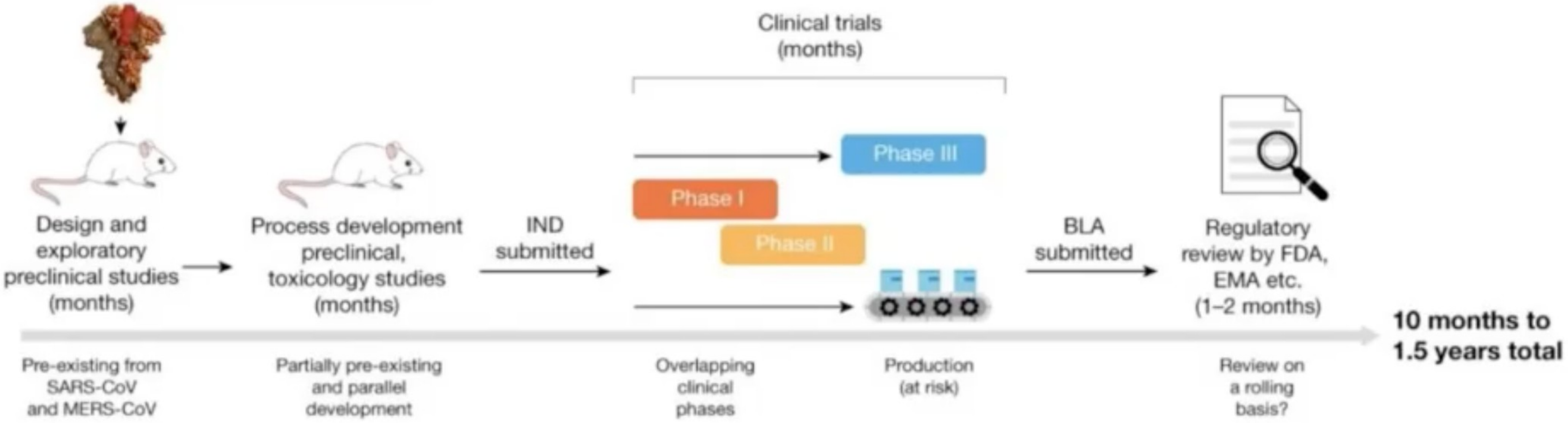
Clinical trials (5–7 years total)

Phase I (1–2 years) → Phase II (2 years) → Phase III (2–3 years)

→ BLA submitted → Regulatory review by FDA, EMA etc. (1–2 years) → Large-scale production and distribution

15 years or longer

SARS-CoV-2 vaccine development



Design and exploratory preclinical studies (months) → Process development preclinical, toxicology studies (months) → IND submitted →

Clinical trials (months)

Phase III

Phase I

Phase II

→ BLA submitted → Regulatory review by FDA, EMA etc. (1–2 months)

10 months to 1.5 years total

Pre-existing from SARS-CoV and MERS-CoV

Partially pre-existing and parallel development

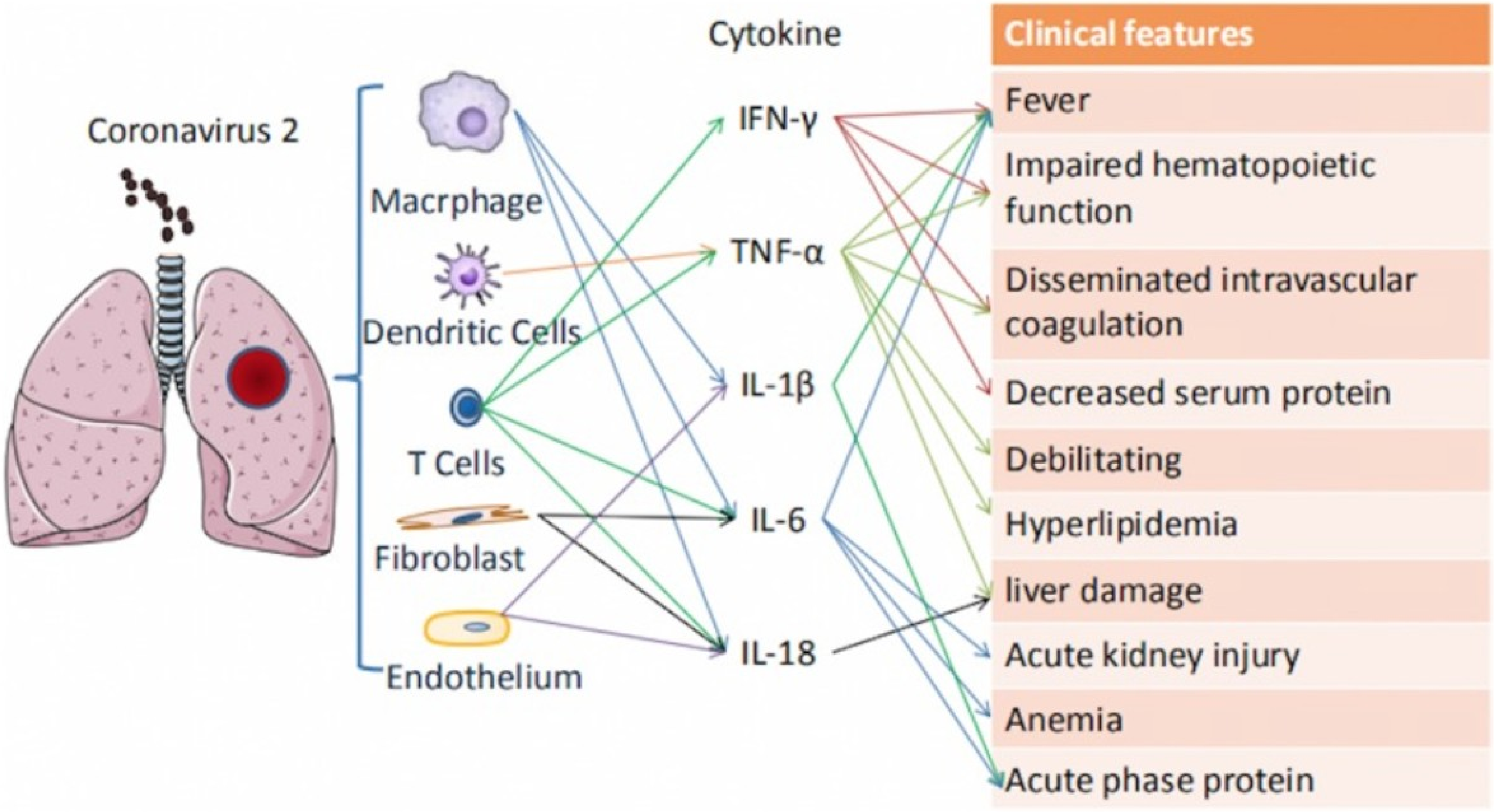
Overlapping clinical phases

Production (at risk)

Review on a rolling basis?

Vaccine in India

S.No.	Product	Indian Manufacturer	Collaborator	Current stage
1	Covishield (Chimpanzee Adenovirus)	Serum Institute of India, Pune	Astra Zeneca	Phase III Emergency approval in India
2	Covaxin (Inactivated Virus)	Bharat Biotech International Ltd, Hyderabad	Indian Council of Medical Research, India	Phase III Emergency approval in India
3	ZyCoV-D (DNA vaccine)	Cadila Healthcare Ltd, Ahmedabad (Zydus Cadila)	Dept of Biotechnology, India	Phase III
4	Sputnik V (Human Adenovirus vaccine)	Dr. Reddy's lab., Hyderabad	Gamaleya National Center, Russia	Phase III



Coronavirus 2

Macrphage

Dendritic Cells

T Cells

Fibroblast

Endothelium

Cytokine

IFN-γ

TNF-α

IL-1β

IL-6

IL-18

Clinical features

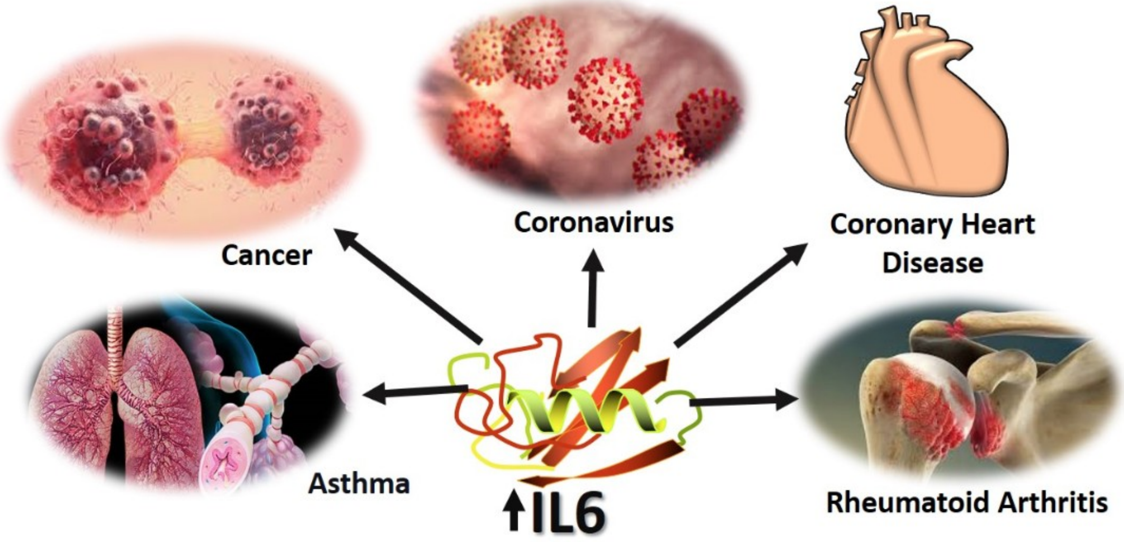
- Fever
- Impaired hematopoietic function
- Disseminated intravascular coagulation
- Decreased serum protein
- Debilitating
- Hyperlipidemia
- liver damage
- Acute kidney injury
- Anemia
- Acute phase protein

IL-6Pred: Prediction of Interleukin-6 inducing peptides

Home Predict Design Protein Scan Motif Scan BLAST Scan General ▾

Welcome to IL-6Pred

SS, Raghava GPS (2020) Computer-aided prediction and design of IL-6 inducing peptides: IL-6 plays a crucial role in COVID-19 Briefings in Bioinformatics, dx.doi.org/10.1093/bib/bbaa



Several methods have been developed for the prediction of the antigenic regions for subunit vaccines designing. Interleukin-6 (IL-6) is a rapidly produced proinflammatory cytokine generated as an immune response in various infections and tissue injuries. Many studies show that high levels of IL-6 are related to a high risk of cancer and other disease conditions such as insulin resistance, asthma, coronary heart disease, advanced-stage cancer. The elevated level of IL-6 causes cytokine release syndrome(CRS) in severe COVID-19 patients. Thus, it is essential to check the subunit vaccine candidate provided to a COVID-19 patient must not be IL-6 inducing peptide. Based on our knowledge, we develop an in silico tool that allows the user to predict, scan, and map the IL-6 inducing/non-inducing peptides.

Thank You