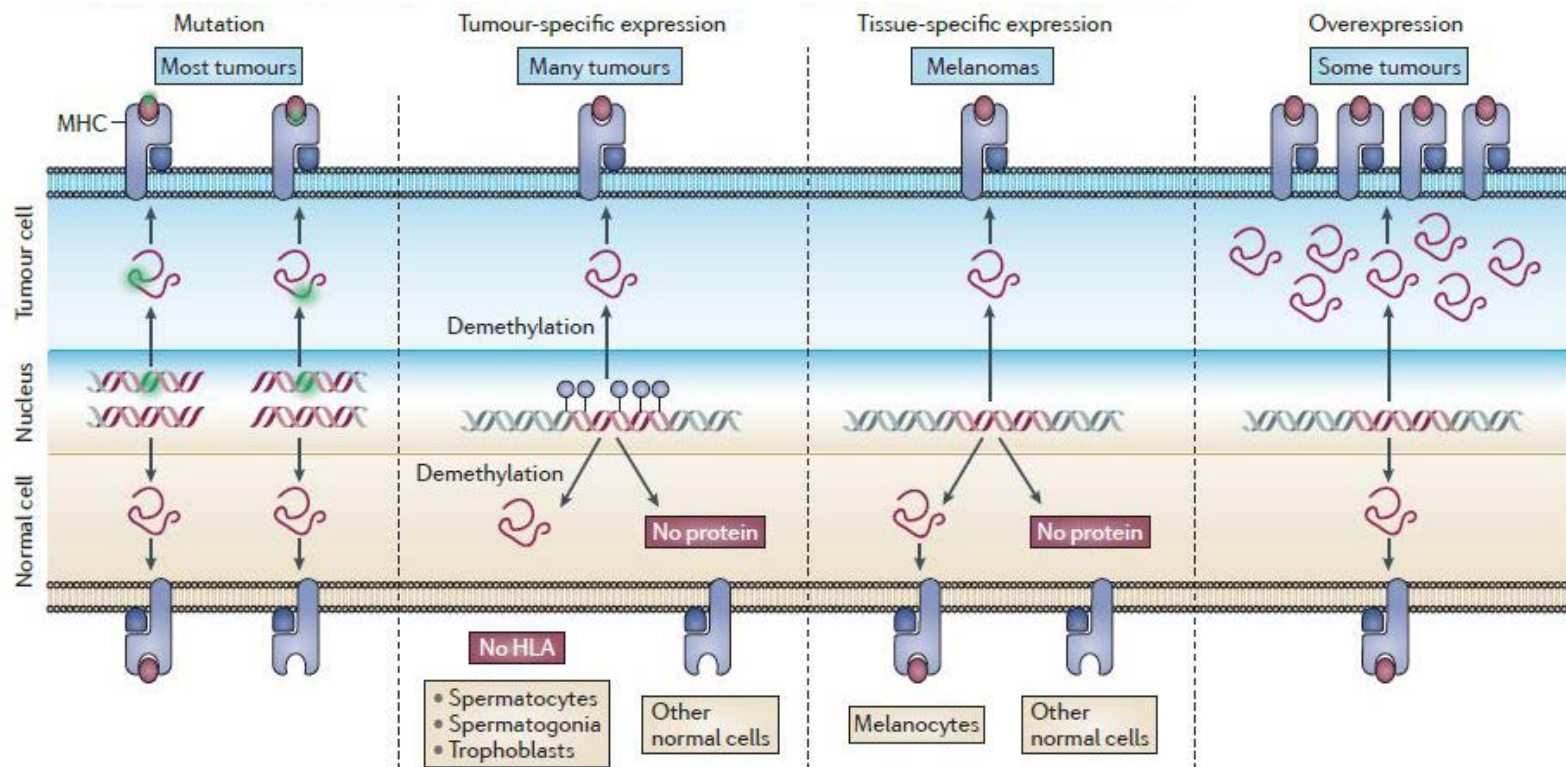




# Cancer Epitope Database and Analysis Resource (CEDAR)

Presented by: Alessandro Sette, IEDB Principal Investigator

# Cancer Epitopes are derived from Cancer Antigens



Coulie et al, Nat Rev Cancer. 2014 Feb

# Motivation for the CEDAR Project



- IEDB hosts epitope data for
  - Allergy
  - Infectious diseases
  - Autoimmune diseases
  - Transplantation / Alloantigens
  - But **NOT** Cancer

We received funding from the National Cancer Institute to develop a resource for cancer epitopes



# Motivation for the CEDAR Project (II)



1

## IMPORTANCE

- Cancer epitopes play a key role in cancer immunology and immunotherapy
- They are important in understanding the biological mechanisms associated with treatment efficacy and developing more effective therapeutic approaches

2

## COMMUNITY NEED

- Several resources attempted to catalog cancer epitopes (e.g. TANTIGEN, CAPEd, NEPdb, dbPepNEO, etc.)
  - Existing resources do not capture all epitope data in a granular fashion linked to the biological, immunological, and clinical contexts
  - All resources only provide limited computational prediction and analysis tools

*We developed The Cancer Epitope Database and Analysis Resource to fill these gaps*

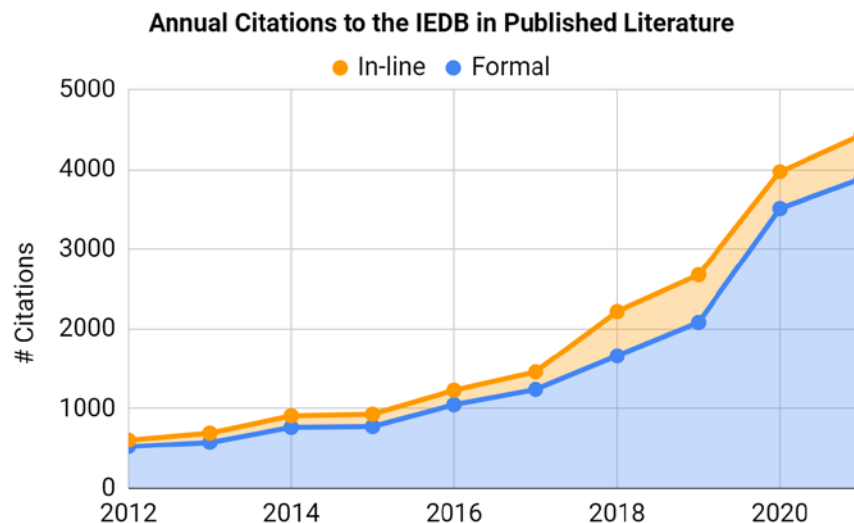
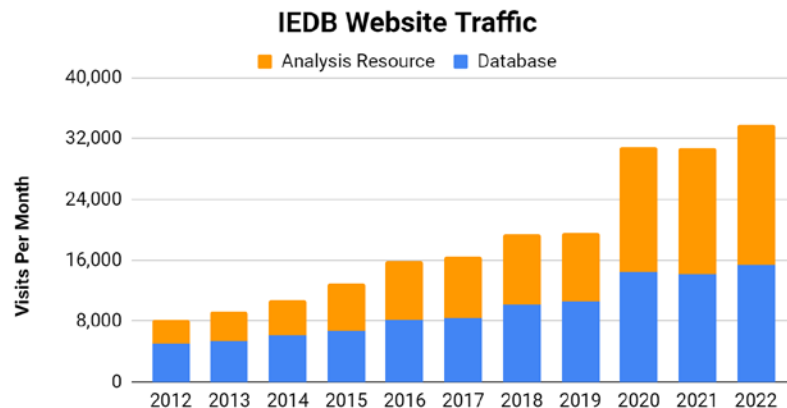
# Building on IEDB's Success

(Immune Epitope Database, [www.iedb.org](http://www.iedb.org))

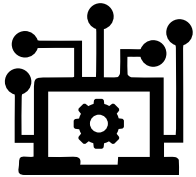
**1** 19 years of experience and learnings

**2** Tried and tested IT and curation processes

**3** Engaged user base with continuous growth over the years



# Cancer Epitope Database and Analysis Resource (CEDAR)



## Database

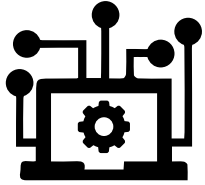
Comprehensively cataloging all cancer epitope-related data linked to the biological, immunological, and clinical contexts



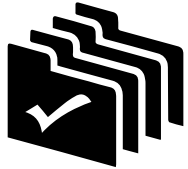
## Analysis Resource

Computational epitope prediction and analysis tools providing researchers access to predictive strategies and objective evaluations of their performance

# Specific Aims of the CEDAR Project



1) Establish the CEDAR database, ontology, and query and reporting functionality



2) Curate literature epitope data, relevant to cancer immunology

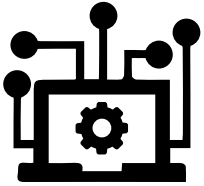


3) Provide a validated set of cancer epitope prediction and analysis tools



4) Implement a multifaceted outreach program to engage the cancer research community

1



**Establish the CEDAR database, ontology,  
and query and reporting functionality**



# 1 CEDAR Database Design Process

- **Reached Out to Experts:** Interviewed cancer experts to identify important search fields for cancer research
- **Prototyped User Interfaces:** Designed database query interface wireframes
- **Introduced Cancer Curation Rules,** for example:
  - i. Captured cancer types in more detail
  - ii. Distinguished vaccination types (prophylactic / therapeutic)
  - iii. Distinguished between allo- and xeno-adoptive transfer.

1st In Vivo Process	
In Vivo Process Type	
Disease Name	
Disease Stage	Administration in vivo Administration in vivo to cause disease Administration in vivo to prevent or reduce disease Vaccination Prophylactic vaccination Therapeutic vaccination
Immunogen Reference Name	
Immunogen	Occurrence of infectious disease Occurrence of allergy Occurrence of autoimmune disease Occurrence of cancer Occurrence of disease Exposure with existing immune reactivity without evidence for disease Documented exposure without evidence for disease
Adjuvants	Environmental exposure to endemic/ubiquitous agent without evidence for disease Exposure without evidence for disease Transplant/transfusion No immunization
Route	Unknown

# The CEDAR database base is available at [cedar.iedb.org](http://cedar.iedb.org)



Help | More CEDAR

Home | Specialized Searches | Analysis Resource

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[Learn More](#)

## Upcoming Events & News

AAI Exhibitor Booth May 6-10  
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\* register [here](#)

[IEDB SARS-CoV-2 Epitope Analysis Videos](#)

## Summary Metrics

Peptidic Epitopes	1,239,866
Non-Peptidic Epitopes	57
T Cell Assays	97,299
B Cell Assays	99,380
MHC Ligand Assays	3,833,304
Epitope Source Organisms	1,459
Restricting MHC Alleles	628
References	3,910

## START YOUR SEARCH HERE

### Epitope ?

- Any
- Linear peptide
- Exact M
- Discontinuous
- Non-peptidic



### Assay ?

- T Cell
  - B Cell
  - MHC Ligand
- Ex: Cytotoxicity
- Outcome:  Positive  Negative



### Epitope Source ?

- Antigen
- Cancer-associated antigens:
- Neoantigen
  - Viral antigen
  - Germline/Self/Host antigen
  - Other antigens from same reference



### MHC Restriction ?

- Any
  - Class I
  - Class II
  - Non-classical
- Ex: HLA-A\*02:01



### Host ?

- Any
  - Human
  - Mouse
  - Non-human primate
- Ex: C57BL/6



### Immune Exposure ?

- Any
- Naturally occurring disease
- Animal model of cancer
- Vaccination



## Epitope Analysis Resource

### T Cell Epitope Prediction ?

Scan peptide sequences for amino acid patterns indicative of:

- MHC I Binding
- MHC II Binding

Analyze T cell receptors (TCR) available:

- TCRMatch

### B Cell Epitope Prediction ?

- Antigen Sequence Properties
- Antigen Sequence Properties

### Epitope Analysis Tools ?

Analyze epitope sets of:

- Clusters with Similar Sequences
- Peptide Synthesis Prediction Tool
- Peptide Similarity using PEPMatch

### Benchmarks ?

Assess tools using standardized metrics:

- Benchmark I
- Benchmark II
- Benchmark III

Cancer-specific search parameters

# Example Query: Prostate-specific Antigen



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Exact Match:

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 MHC Ligand

Ex: Cytotoxicity

Outcome:  Positive  Negative

### Epitope Source ?

Antigen:

Cancer-associated:  Nucleic acid  
 Virus  
 Gene  
 Other

### MHC Restriction ?

Any

Host ?

Any  
 Human  
 Mouse  
 Non-human  
 Other

Ex:

- Prostate-specific antigen [P07288] (Homo sapiens (human))
- Acid phosphatase, prostate [A0A0G2K4B4] (Rattus norvegicus...)
- Prostate and testis-expressed 5 [Q9D262] (Mus musculus (mo...))
- Prostate-associated microseminoprotein [B1AWI6] (Mus musc...)
- Prostate and testis expressed protein 1 [Q8WXA2] (Homo sapi...)
- Prostate and testis expressed protein 3 [B3GLJ2] (Homo sapie...)
- Prostate and testis expressed protein 4 [P0C8F1] (Homo sapie...)
- Putative Dresden prostate carcinoma protein 2 [Q86SG4] (Ho...)
- Testis, prostate and placenta-expressed protein [Q6URK8] (Ho...)
- Prostate androgen-regulated mucin-like protein 1 [Q6UWI2] (H...)

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Reset

Search

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# Example Results: Prostate-specific Antigen

Positive and negative data for T cell assays outcomes with MHC Class I restriction in human host

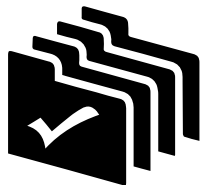
The screenshot displays the CEDAR (Cancer Epitope Database and Analysis Resource) interface. At the top, navigation links include Home, Specialized Searches, and Analysis Resource. The main content area is divided into several sections:

- Pending Filters:** A sidebar on the left with a 'Reset' and 'Search' button, and a 'Filter Options' section where 'T Cell' is selected.
- Current Filters:** A horizontal bar at the top of the results area showing active filters: 'Antigen: Prostate-specific antigen [P07288] (Homo sapiens (human))', 'Immune Exposure: Naturally occurring disease', 'Include Positive Assays', 'Include Negative Assays', 'No B cell assays', 'No MHC assays', and 'MHC Restriction Type: Class I'. A red box highlights this area.
- Summary:** A row of tabs for 'Epitopes (22)', 'Antigens (2)', 'Assays (129)', 'Receptors (0)', and 'References (20)'. A red box highlights this row.
- Table:** A table with 22 records found, showing columns for Details, Epitope, Antigen, Organism, # References, and # Assays. The table lists various epitopes and their corresponding antigens and organisms (all Homo sapiens (human)).
- Navigation:** 'Go To Records Starting At 1200' and 'Page 1 of 1' are visible at the bottom of the table.

Below the screenshot, a red arrow points to the 'Filter Options' sidebar, accompanied by the text: 'Query can be refined further on the 'Results' page via our 'Filter Options''.

Query can be refined further on the 'Results' page via our 'Filter Options'

2



**Curate literature epitope data, relevant to cancer immunology**

## 2 Curation of cancer-related epitope data

### PubMed / PDB

- Complex query
- Bi-weekly

240K retrieved

### Classifier

- Content based categories
- Retrained annually

151K epitope related

### Abstract Review

- Manual scan
- Confirmation of classification

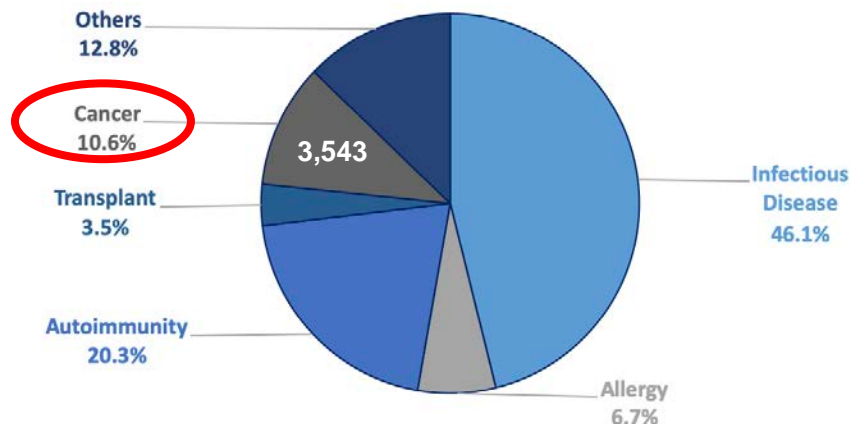
44K likely curatable

### Manual Curation

- Assigned to curators
- Peer review

23K curated

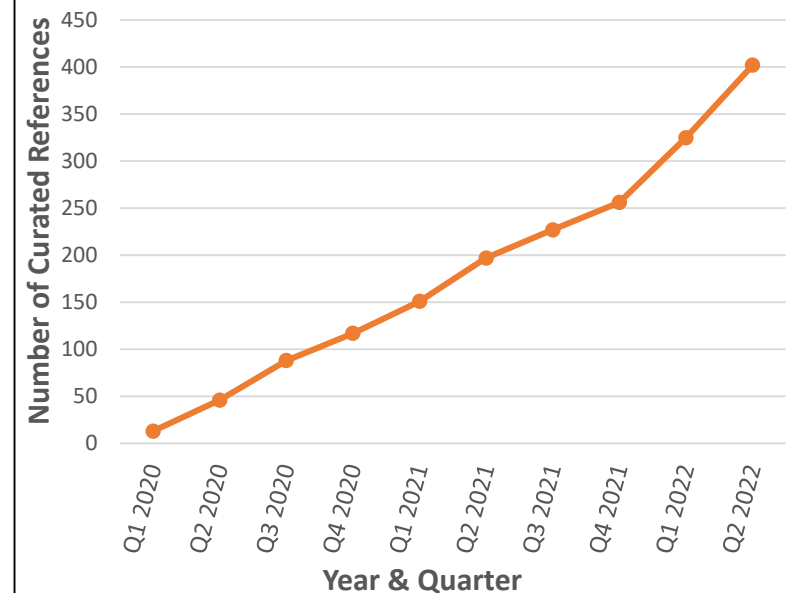
### Breakdown of Classified and Curatable References



3,543 papers identified as cancer relevant

- Internal queue for curation: started with neopeptides and prostate antigens

### Curated Cancer References by Quarter



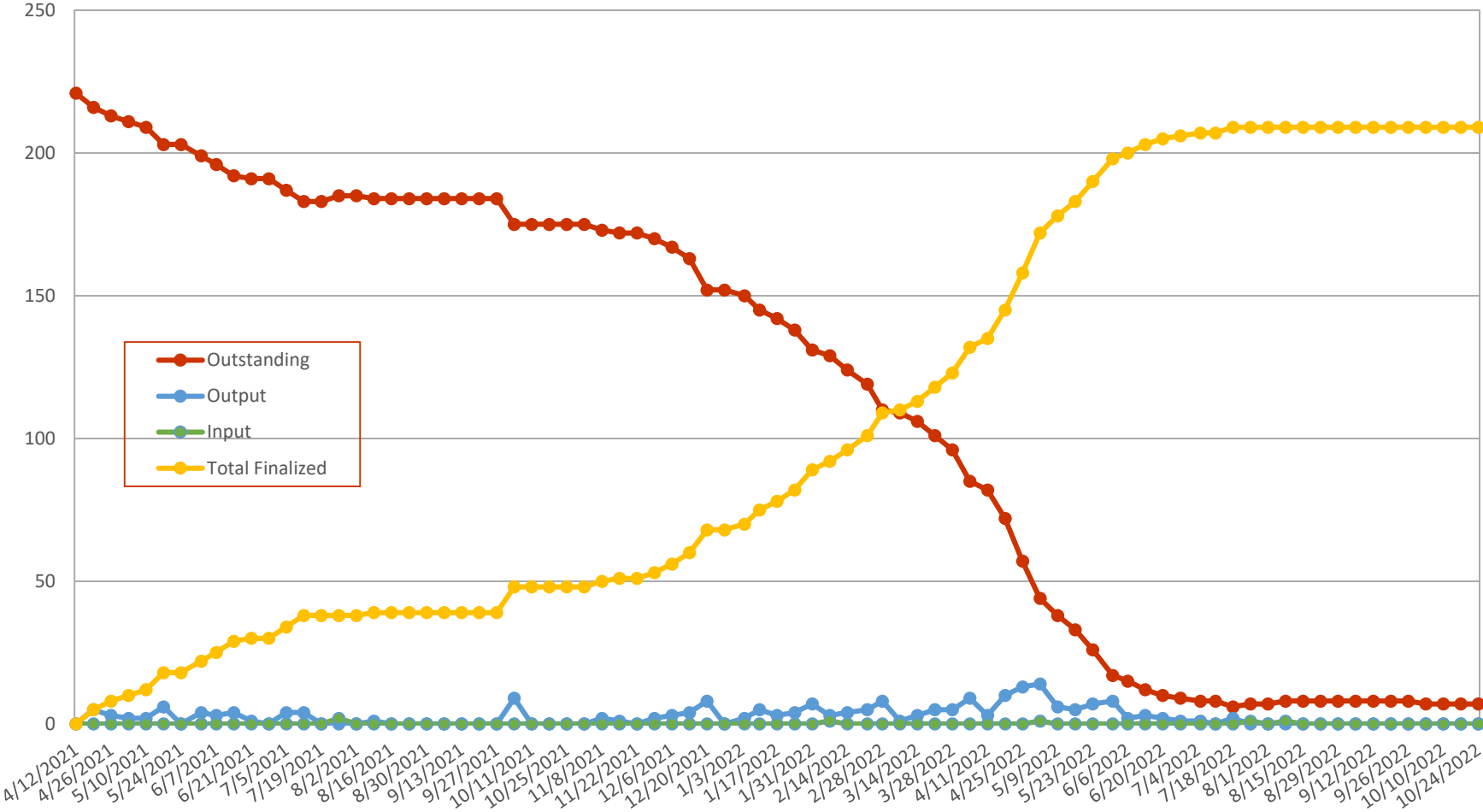
# 2

## Prostate Cancer Curation

**Neopeptide Category:**

- In progress – 74% completion

- 209 references finalized (as at October 24)
- ~97% complete with this category
- Category maintenance with 7 references in progress





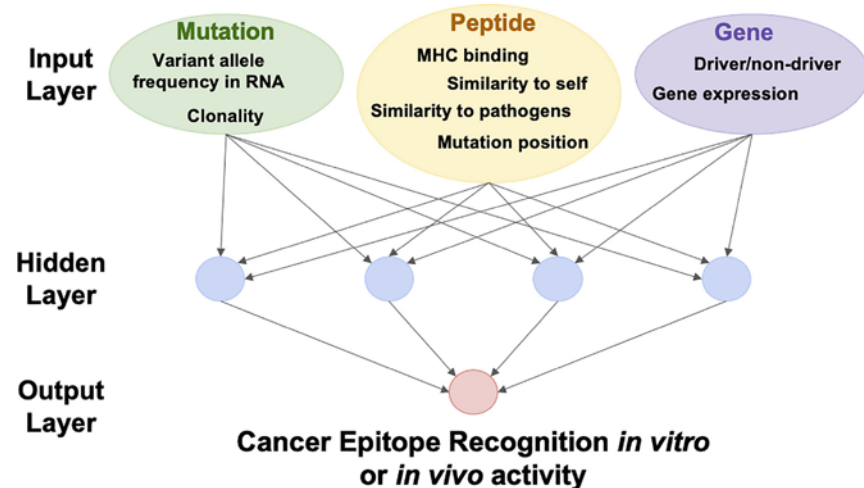
3



**Provide a validated set of cancer epitope prediction and analysis tools**

### 3 Overarching Analysis Resource Goals

- Provide prediction tools tailored to the needs of cancer immunologists
  - what neoepitopes are generated by a given mutation?
  - side-by-side predictions for mutant and wild-type peptides
- Develop novel prediction tools for cancer epitopes
  - combined assessment of expression and binding
  - include additional features when predicting epitopes



# 3 Overarching Analysis Resource Goals

- Provide web-implementations for published but hard to access cancer-epitope related tools in CEDAR
- Prioritize tools to implement in CEDAR based on cost-benefit analysis

Cell

Resource

## Key Parameters of Tumor Epitope Immunogenicity Revealed Through a Consortium Approach Improve Neoantigen Prediction

Graphical Abstract



Authors

Daniel K. Wells, Marit M. van Buuren, Kristen K. Dang, ..., Ton N. Schumacher, Pia Kvistborg, Nadine A. Defranoux

nature  
biotechnology

ARTICLES

<https://doi.org/10.1038/s41587-019-0322-9>

## A large peptidome dataset improves HLA class I epitope prediction across most of the human population

Siranush Sarkizova<sup>1,2,13</sup>, Susan Klaeger<sup>2,13</sup>, Phuong M. Le<sup>3</sup>, Letitia W. Li<sup>3</sup>, Giacomo Oliveira<sup>3</sup>, Hasmik Keshishian<sup>2</sup>, Christina R. Hartigan<sup>2</sup>, Wandi Zhang<sup>3</sup>, David A. Braun<sup>2,3,4,5</sup>, Keith L. Ligon<sup>2,4,6,7</sup>, Pavan Bachireddy<sup>2,3,5</sup>, Ioannis K. Zervantonakis<sup>8</sup>, Jennifer M. Rosenbluth<sup>8</sup>, Tamara Ouspenskaia<sup>2</sup>, Travis Law<sup>2</sup>, Sune Justesen<sup>9</sup>, Jonathan Stevens<sup>10</sup>, William J. Lane<sup>4,10</sup>, Thomas Eisenhaure<sup>2</sup>, Guang Lan Zhang<sup>3,4,11</sup>, Karl R. Clauser<sup>2</sup>, Nir Hacohen<sup>2,3,12\*</sup>, Steven A. Carr<sup>2\*</sup>, Catherine J. Wu<sup>2,3,4,5\*</sup> and Derin B. Keskin<sup>2,3,4,5,11\*</sup>

LETTER

doi:10.1038/nature24473

## A neoantigen fitness model predicts tumour response to checkpoint blockade immunotherapy

Marta Luksza<sup>1</sup>, Nadeem Riaz<sup>2,3</sup>, Vladimir Makarov<sup>3,4</sup>, Vinod P. Balachandran<sup>5,6,7</sup>, Matthew D. Hellmann<sup>7,8,9</sup>, Alexander Solovyyov<sup>10,11,12,13</sup>, Naiyer A. Rizvi<sup>14</sup>, Taha Merghoub<sup>7,15,16</sup>, Arnold J. Levine<sup>1</sup>, Timothy A. Chan<sup>2,3,4,7</sup>, Jedd D. Wolchok<sup>7,8,15,16</sup> & Benjamin D. Greenbaum<sup>10,11,12,13</sup>

## 3

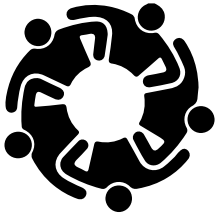
## Use curated cancer epitope datasets to benchmark epitope prediction tools

- Assemble comprehensive sets of cancer epitope data
- Make available in simple format for bioinformaticians for tool training and testing
- Conduct benchmarks of prediction tools on cancer epitope datasets
  - Manual compile and run benchmarks (initially)
  - Automated benchmarks of all tools implemented in CEDAR, using newly curated data

### Examples of benchmark targets for prediction tools

- What peptides in a tumor sample are processed and presented on MHC
- What neo-epitopes are recognized by T cells from a cancer patient?

4



**Implement a multifaceted outreach program to engage the cancer research community**

# 4 Community Outreach

## 2 CEDAR-Specific Manuscripts Published To-Date

ORIGINAL RESEARCH article

Front. Immunol., 24 August 2021 | <https://doi.org/10.3389/fimmu.2021.735609>

### The Cancer Epitope Database and Analysis Resource: A Blueprint for the Establishment of a New Bioinformatics Resource for Use by the Cancer Immunology Community

Zeynep Koşaloğlu-Yalçın<sup>1</sup>, Nina Blazeska<sup>1</sup>, Hannah Carter<sup>2,3</sup>, Morten Nielsen<sup>4,5</sup>, Ezra Cohen<sup>6</sup>, Donald Kufe<sup>7</sup>, Jose Conejo-García<sup>8</sup>, Paul Robbins<sup>9</sup>, Stephen P. Schoenberger<sup>6</sup>, Bjoern Peters<sup>10</sup> and Alessandro Sette<sup>11</sup>

### 1 The Cancer Epitope Database and Analysis Resource (CEDAR).

Koşaloğlu-Yalçın Z<sup>1</sup>, Blazeska N<sup>1</sup>, Vita R<sup>1</sup>, Carter H<sup>2</sup>, Nielsen M<sup>3</sup>, Schoenberger S<sup>4</sup>, Sette A<sup>1</sup>, Peters B<sup>1</sup>

Author information ▶

Nucleic Acids Research, 17 Oct 2022, :gkac902  
DOI: 10.1093/nar/gkac902 PMID: 36250634

### 2

## 2 Conference Booths Held



## 9 Presentations or Posters Completed To-Date

#	Presentation Title	Presenter	Event	Date
1	Talk: The Cancer Epitope Database & Analysis Resource	Sette & Peters	NCI Cancer Moonshot IOTN WG Meeting	July 15, 2021
2	Talk: The Cancer Epitope Database & Analysis Resource	Sette & Peters	Bioinformatics and Computational Biology WG	July 23, 2021
3	Talk: The Cancer Epitope Database & Analysis Resource	Sette & Peters	ITCR Annual Conference	September 21, 2021
4	Talk: The Cancer Epitope Database & Analysis Resource	Kosaloglu-Yalçın	2021 IEDB Virtual User Workshop	October 28, 2021
5	Talk: Recent Progress Within Immunopeptidome Prediction	Nielsen	5th Neoantigen Summit Europe	April 28, 2022
6	Poster: The Cancer Epitope Database & Analysis Resource	Kosaloglu-Yalçın	RECOMB-CCB 2022	May 20, 2022
7	Talk: The Cancer Epitope Database & Analysis Resource	Kosaloglu-Yalçın	Dynamics of Immune Repertoires	July 14, 2022
8	Poster: The Cancer Epitope Database & Analysis Resource	Kosaloglu-Yalçın	SIXTH CRI-ENCI-AACR INTERNATIONAL CANCER IMMUNOTHERAPY CONFERENCE	September 28-October 1, 2022
9	Talk: The Cancer Epitope Database & Analysis Resource	Kosaloglu-Yalçın	2022 ITCR Investigators Meeting	September 12-14

1. AACR Annual Meeting: April 8-13, 2022
2. FOCIS 2022: June 21-24, 2022



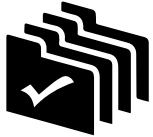
# Summary

*CEDAR is an extension of the IEDB, containing cancer-related epitope data and tools*



1

[cedar.iedb.org](https://cedar.iedb.org) is a working prototype cancer epitope database



2

Literature curation is moving rapidly, with prostate cancer category completed and neoepitope category 74% complete



3

Existing tools will be adapted to the needs of cancer researchers and novel cancer-specific tools will be developed. Cancer benchmark datasets are being assembled.



4

Community engagement has been initiated and will increase as we have more to show

# Looking forward...

## Improved style and functionality!



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