

Pertussis Vaccination

CMI-PB Project

Barry Grant
UC San Diego

<http://thegrantlab.org>

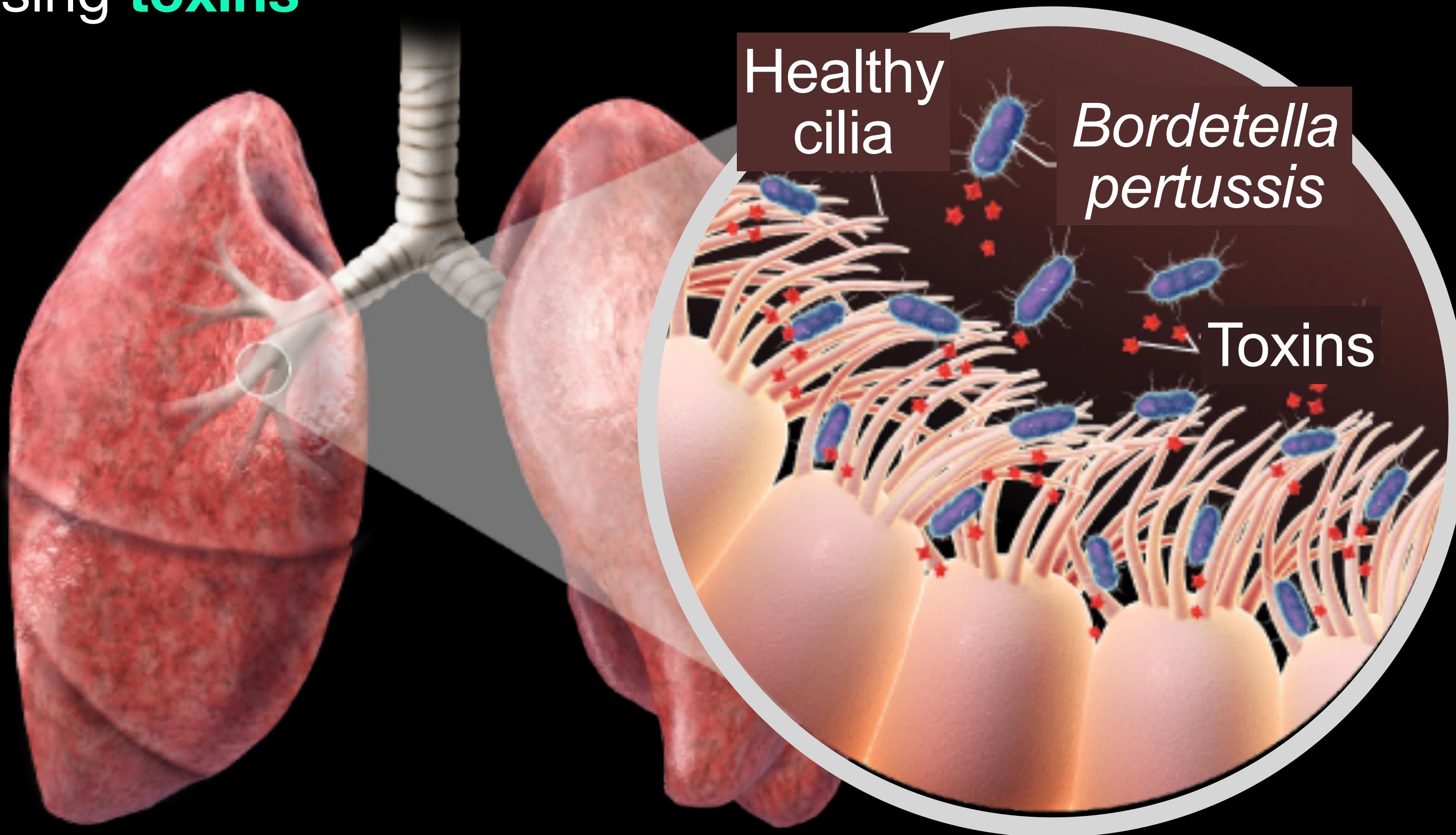
Pertussis is a leading causes of vaccine-preventable deaths

Pertussis, or **whooping cough**, is a highly contagious lung infection caused by the bacteria *Bordetella pertussis*.

- Estimated 16 million cases and 200,000 associated infant deaths annually.
- Can infect people of all ages but is most severe and life threatening for infants under a year old
- Transmission occurs primarily through bacteria laden **respiratory droplets** produced when an infected individual coughs and sneezes

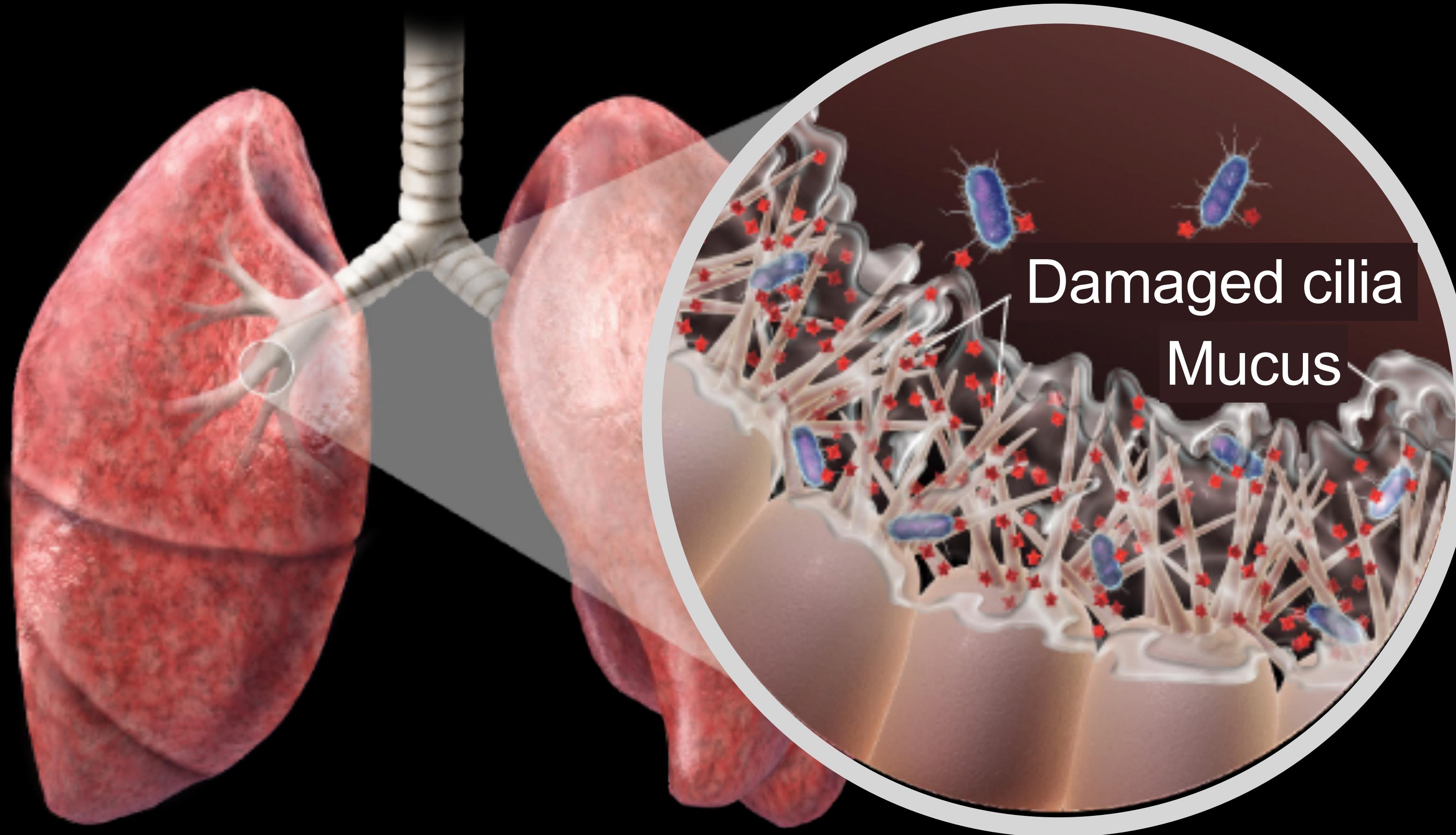
Bordetella pertussis attacks cells lining the airways

The bacteria use adhesive proteins to stick to **ciliated cells** whilst releasing **toxins**

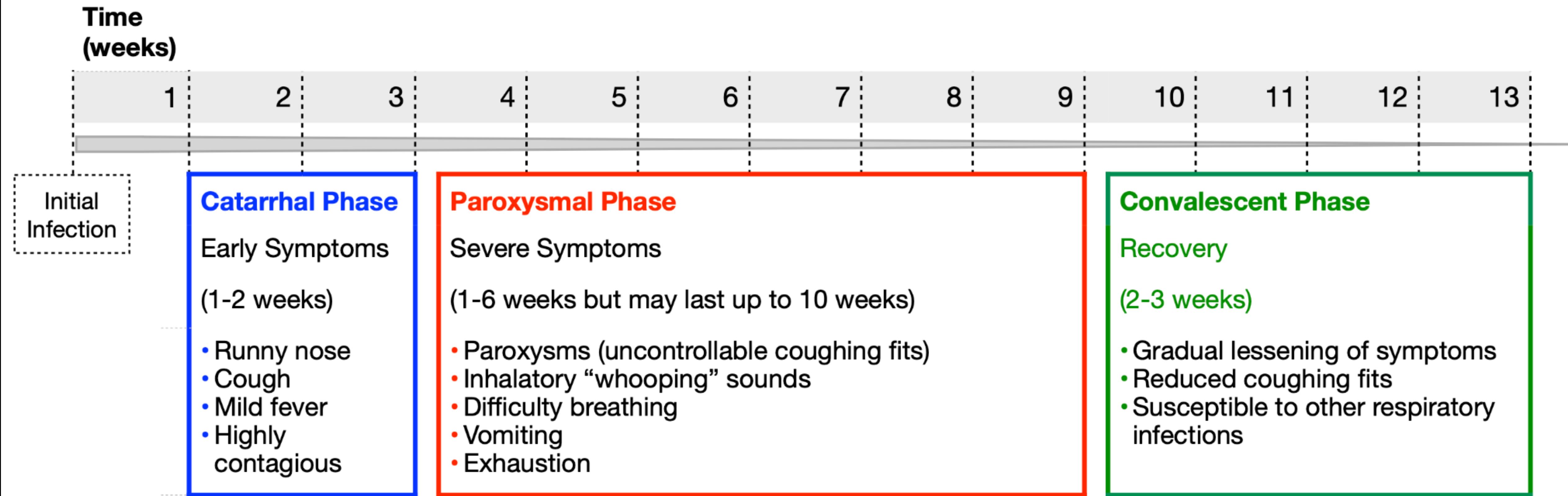


Bacterial toxins damage cells

Damaged cilia can no longer effectively transport mucus and foreign particles out of the lungs.

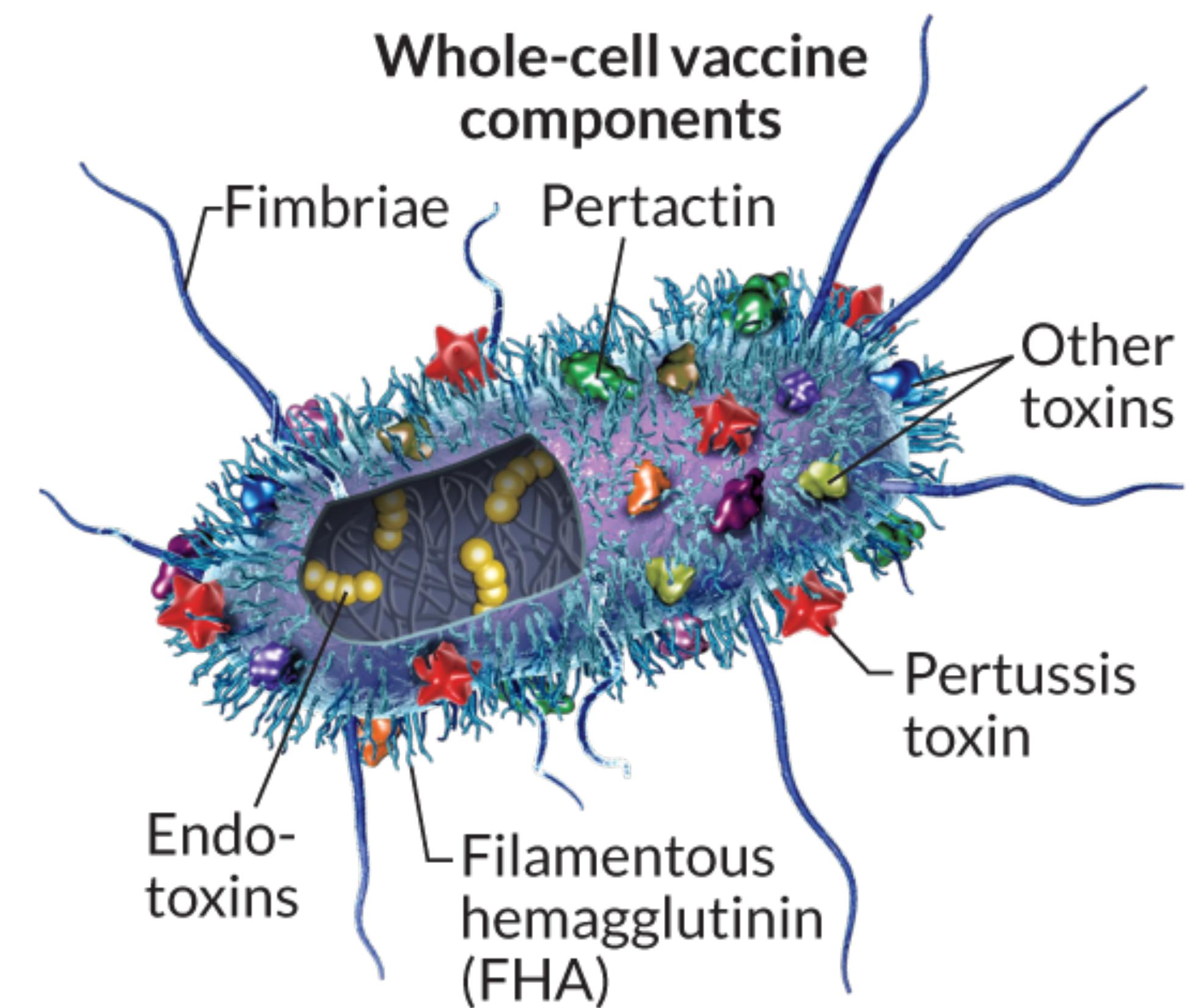


Pertussis Pathogenesis



HISTORY

FILE:///USERS/BARRY/DROPBOX/PERTUSSIS/TIMELINE/OUR_HISTORY_TIMELINE.HTML



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cdc.gov

CDC Pertussis Surveillance: Cases by Year | CDC

Español | Other Languages

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Pertussis (Whooping Cough)

CDC > Pertussis Home > Surveillance & Reporting

[Pertussis Home](#)

About Pertussis

Vaccination

Pregnancy & Whooping Cough

Outbreaks

Clinicians

Public Health Professionals

Surveillance & Reporting

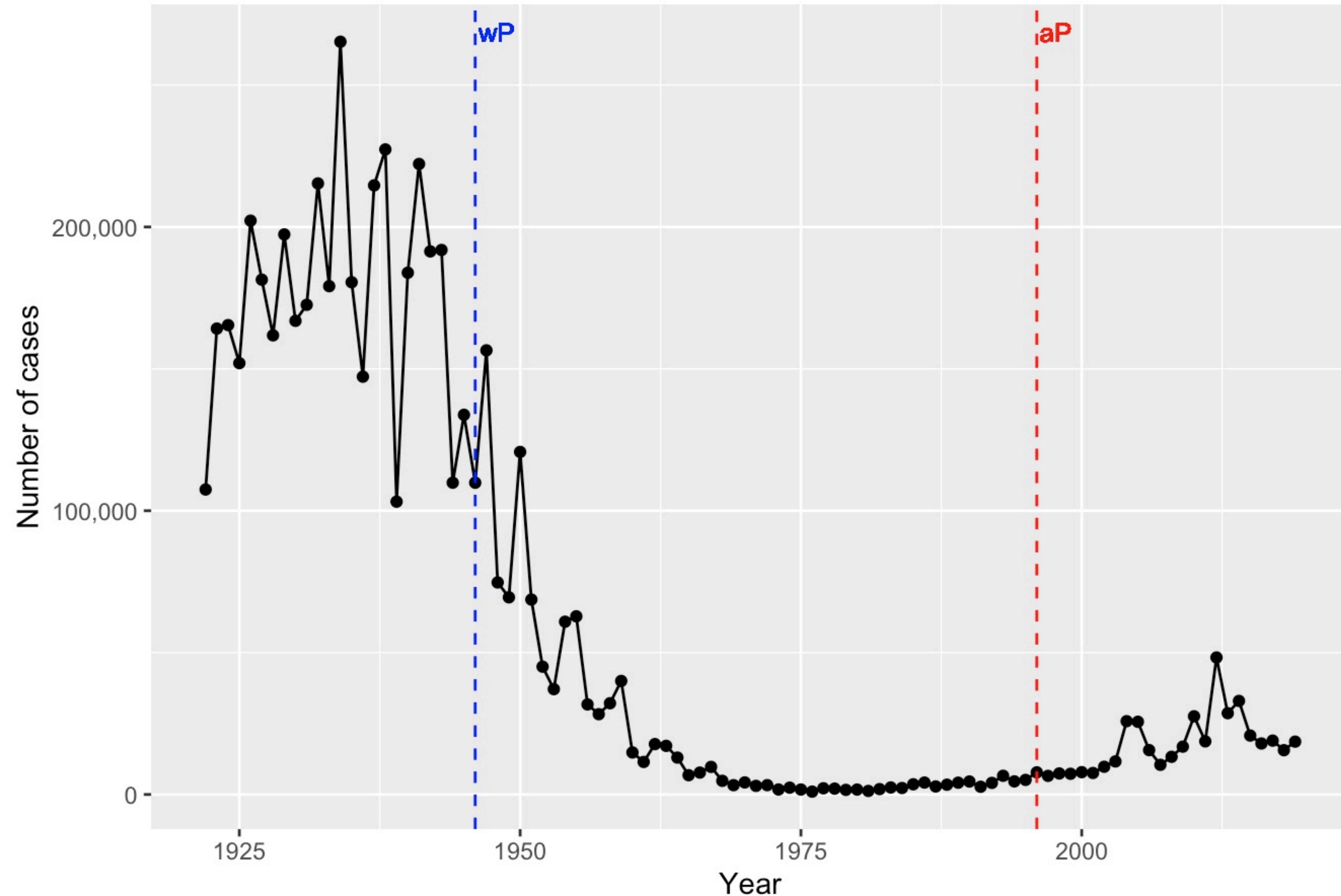
Pertussis Cases by Year (1922-2019)

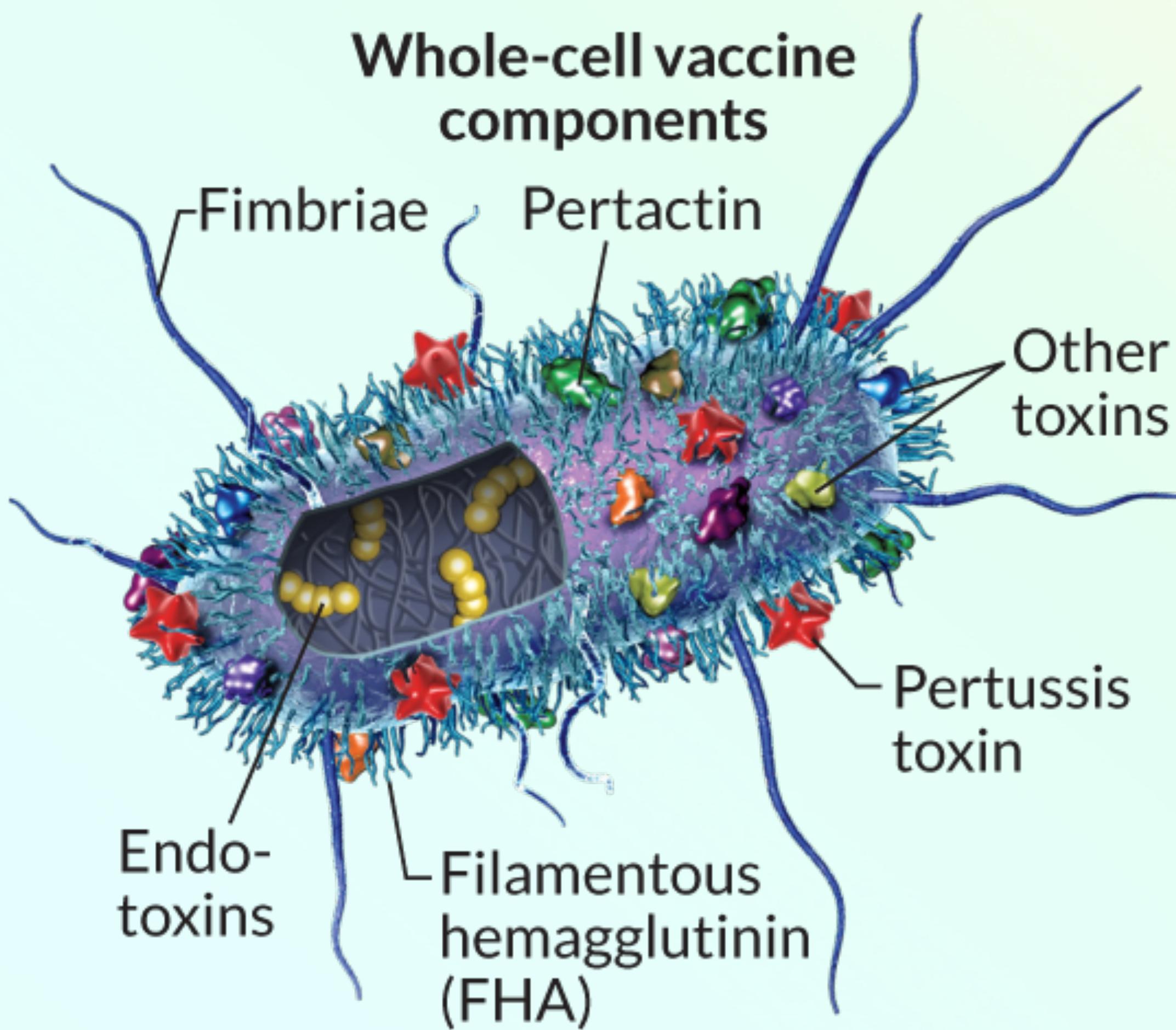
[Print](#)

This table shows reported pertussis cases in the United States since 1922. The related trend charts can be found on the [Surveillance and Reporting](#) page.

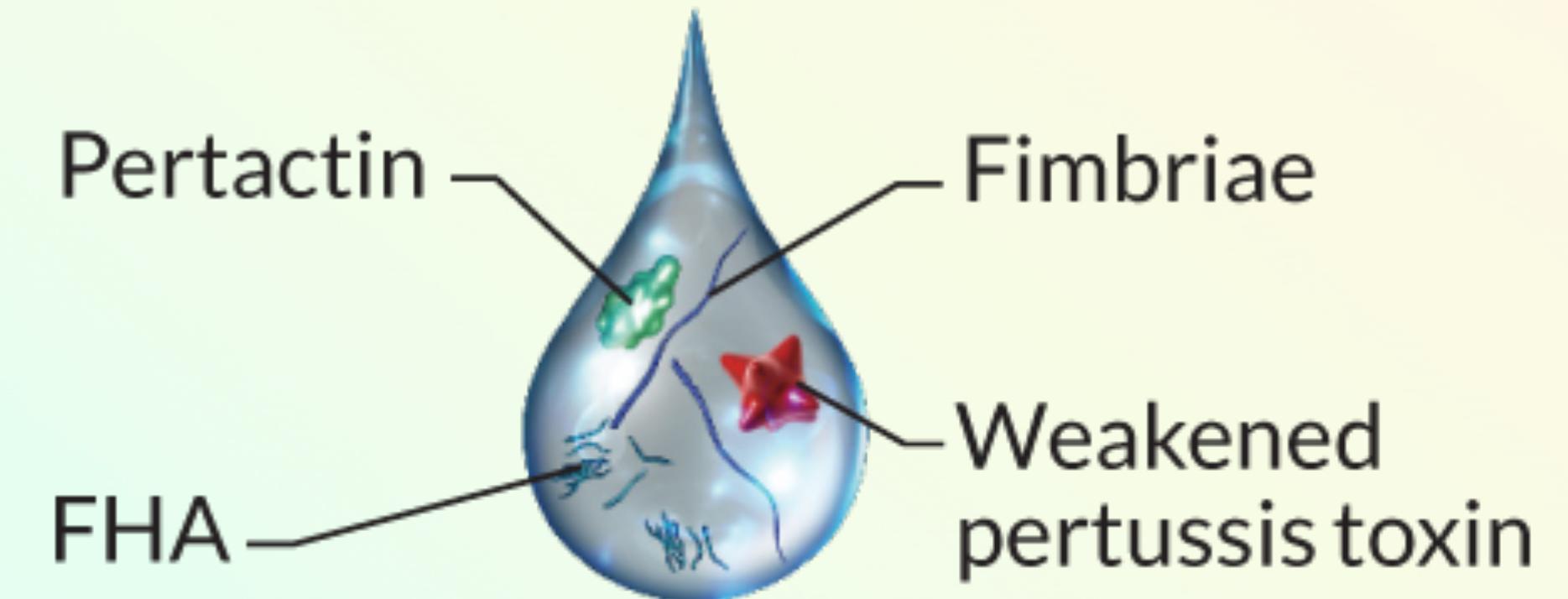
Year	No. Reported Pertussis Cases
1922	107,473
1923	164,191
1924	165,418
1925	152,003
1926	202,210

Pertussis Cases by Year (1922-2019)





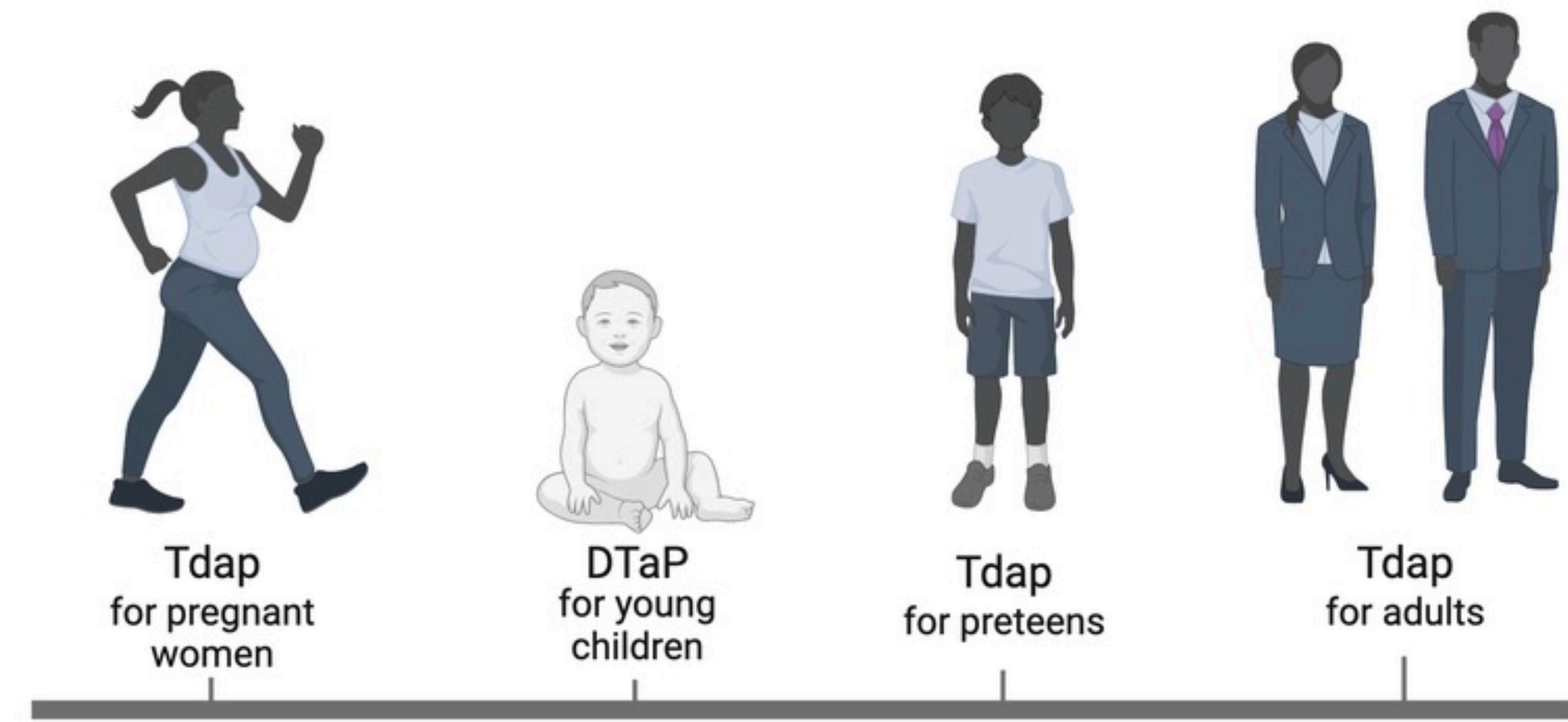
Acellular vaccine components



Major aP vaccines (US)

Vaccine	Trade Name	Manufacturers	Components (Concentrations)
DTaP	Daptacel, Infanrix	Sanofi Pasteur, GlaxoSmithKline	Inactivated PT: 10-20 µg, FHA: 5-20 µg, PRN: 3-5 µg, FIM 2+3: 5-10 µg
Tdap	Adacel, Boostrix	Sanofi Pasteur, GlaxoSmithKline	Inactivated PT: 2.5-8 µg, FHA: 5-8 µg, PRN: 3-5 µg, FIM 2+3: 5-8 µg

Major aP vaccines (US)



- During the 27-36th week of each pregnancy

- 2, 4 and 6 months
- 15 through 18 months
- 4 through 6 years

- 11 through 12 years

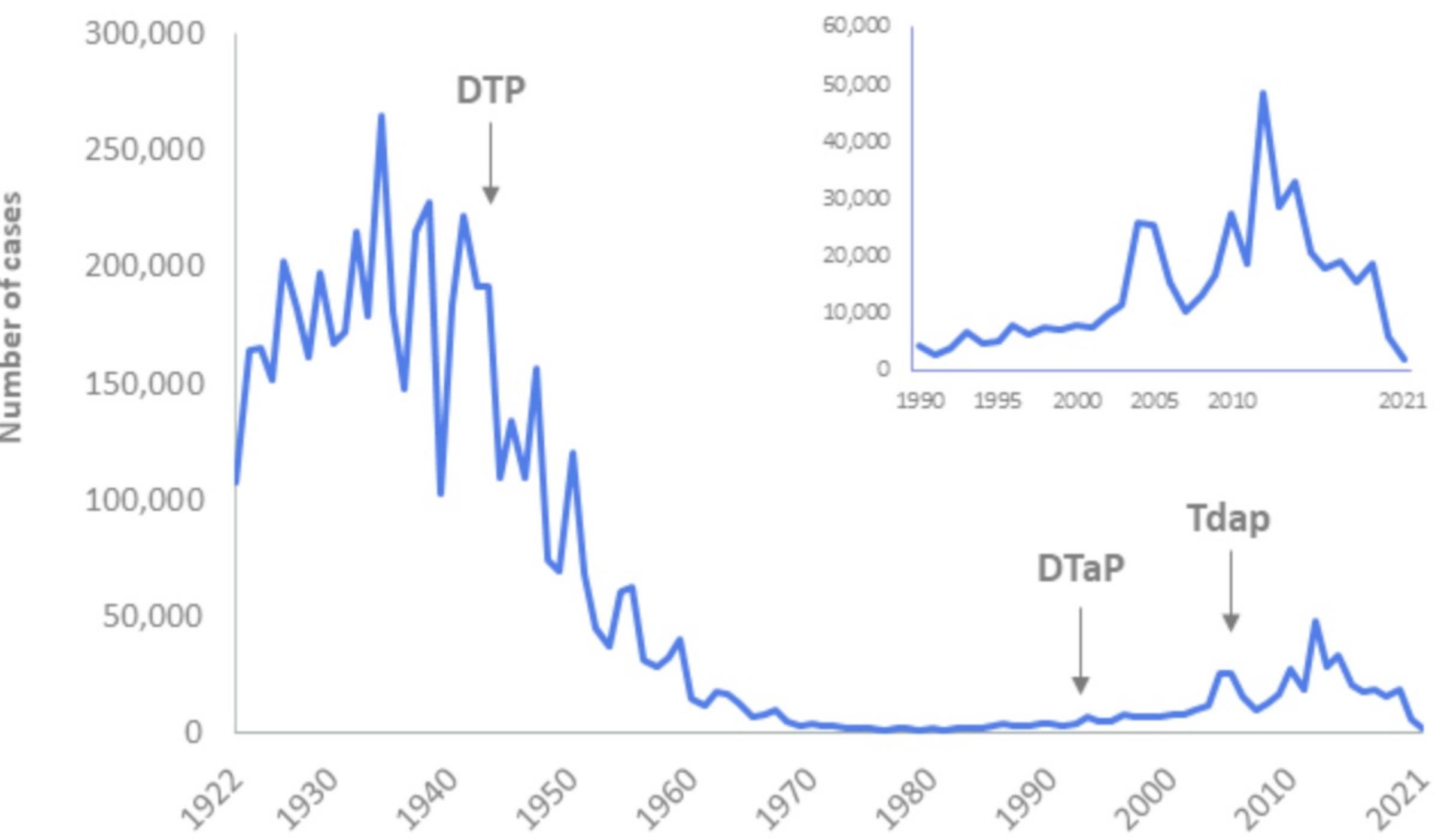
- Anytime for those who have never received it
- Subsequent boosters at 10 year intervals following initial vaccine

Source: Centers for Disease Control

Waning Immunity from aP pertussis vaccination

- 1940s: Introduction of an inactivated whole bacteria PT vaccine (**wP**) dramatically decreased cases
- 1995: Vaccine-related side effects led to a replacement with the acellular PT vaccine (**aP**) in the USA
- aP induced protection wanes faster than wP → Why?

Reported NNDSS pertussis cases: 1922-2021



Source: National Notifiable Diseases Surveillance System, CDC

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cmi-pb.org https://www.cmi-pb.org

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PERTUSSIS BOOST

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Ab titer

The mission of CMI-PB is to provide the scientific community with a comprehensive, high-quality and freely accessible resource of Pertussis booster vaccination.

LEARN ABOUT THE PROJECT



The NIH funded CMI network
What is pertussis vaccination?
What are the open scientific questions?
The CMI-PB approach: A community

UNDERSTAND THE DATA



How do we measure immune responses?
What data is available?
Our approach to data standardization
Browse our terminology

ACCESS THE DATA



Data statistics
Use the API in your programs
Download all data (SFTP)
More ...

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https://www.cmi-pb.org

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Ab titer **Search**

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UNDERSTAND THE DATA



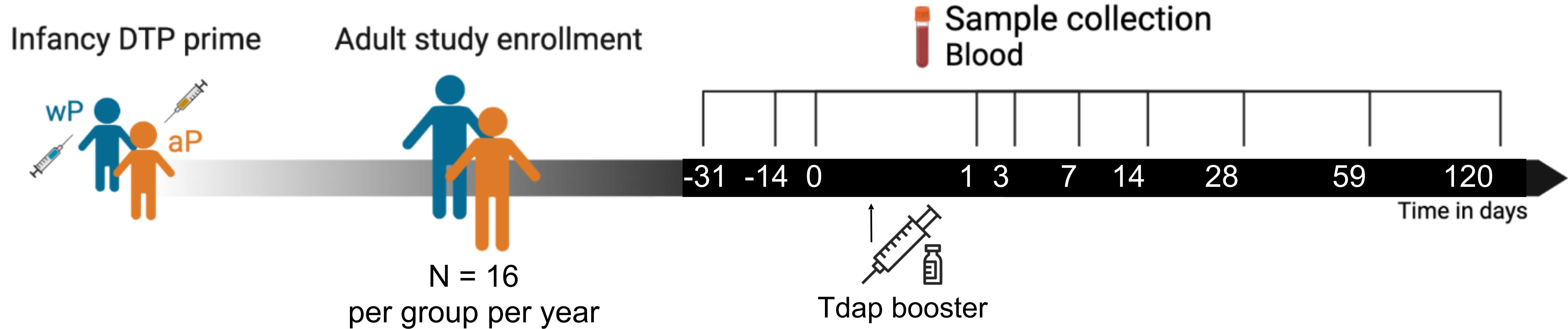
How do we measure immune responses?
What data is available?
Our approach to data standardization
Browse our terminology

ACCESS THE DATA

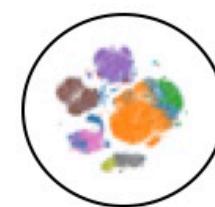


Data statistics Data statistics
Use the API in your programs
Download all data (SFTP)
More ...

Recruitment Strategy



Characterizing immune responses - Multiomics approach



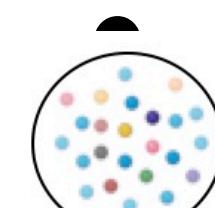
PBMC cell frequencies by flow cytometry

- Total of 37 distinct cell populations



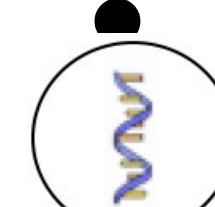
Plasma antigen-specific antibody titers by Luminex

- Antibody Isotypes: IgG, IgG1, IgG2, IgG3, IgG4
- Vaccine Antigens
 - Pertussis Toxin (PT), PRN, FHA, FIM2/3
 - Tetanus Toxoids (TT)
 - Diphtheria Toxoids (DT)
 - OVA (irrelevant control)



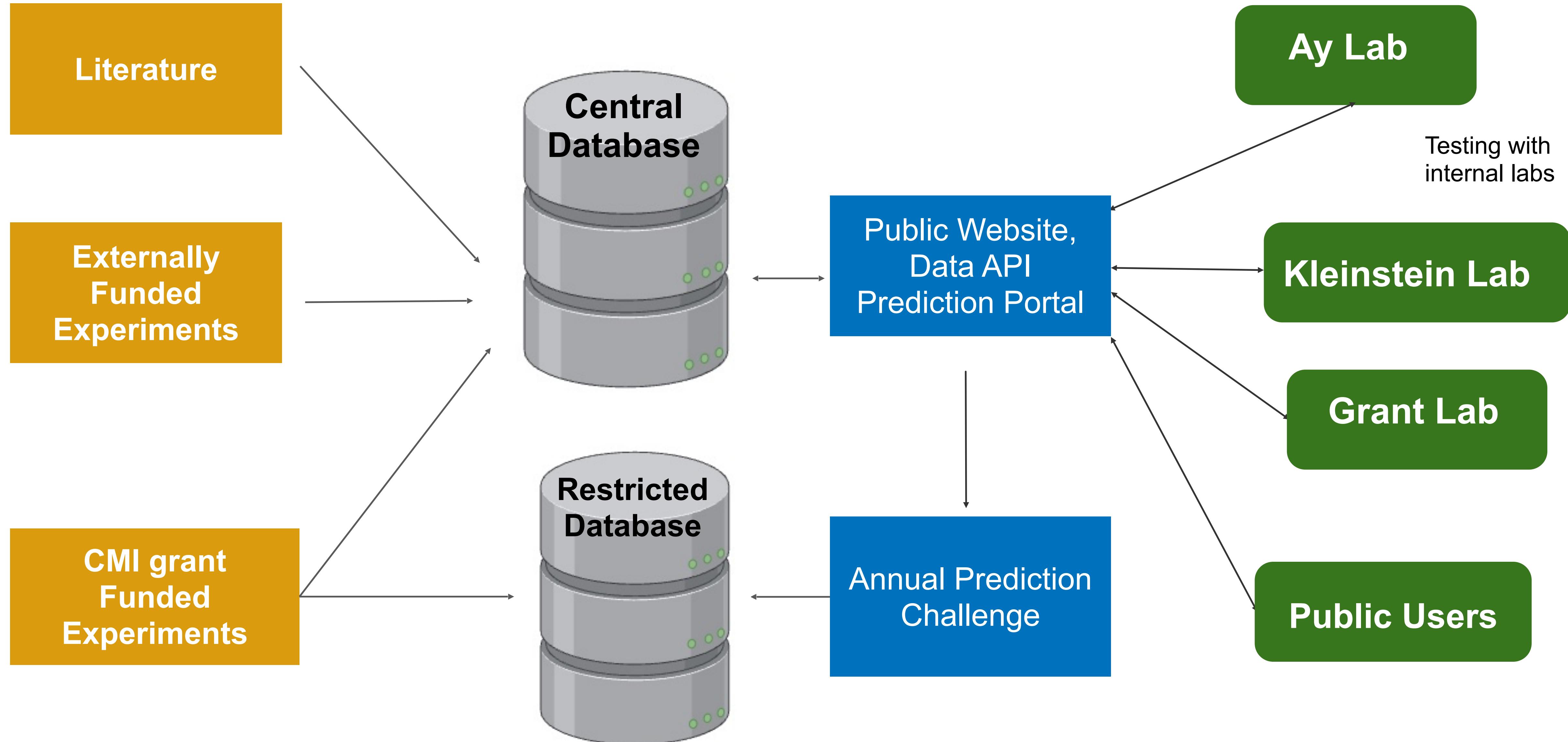
Plasma proteomics by Olink

- Concentration of 45 cytokines

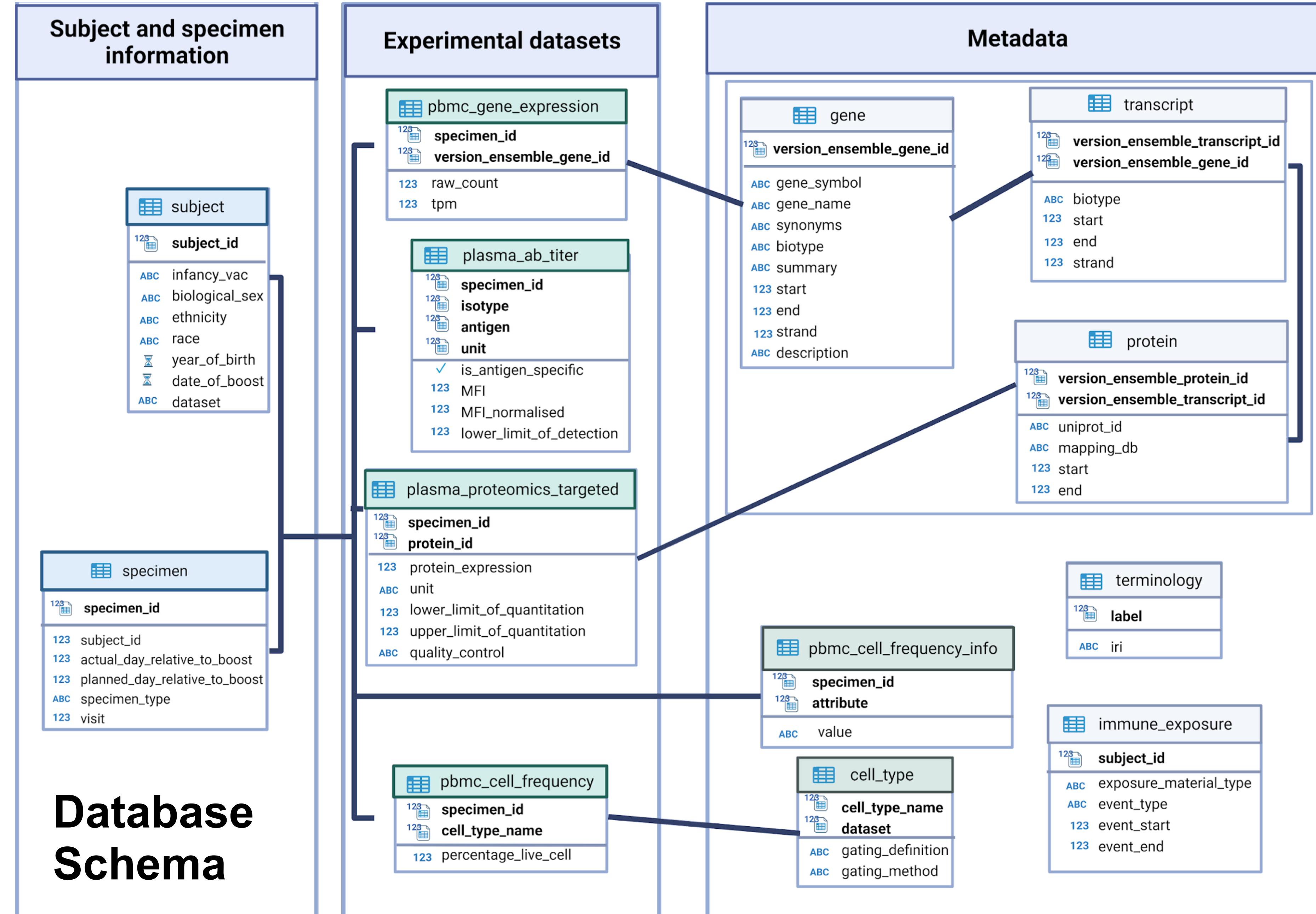


Transcriptomics by bulk RNA-Seq

d. Databases, Model building, and Prediction Challenge



e. Providing access to experimental data in a standardized format



INFORMATION TABLES

SUBJECT
subject_id
infancy_vac
biological_sex
ethnicity
race
year_of_birth
date_of_boost
dataset

SPECIMEN
specimen_id
subject_id
actual_day_relative_to_boost
planned_day_relative_to_boost
specimen_type
visit

DPLYR *_JOIN() FUNCTIONS...

inner_join(x, y)

1	x1
2	x2
3	x3

1	y1
2	y2
4	y4

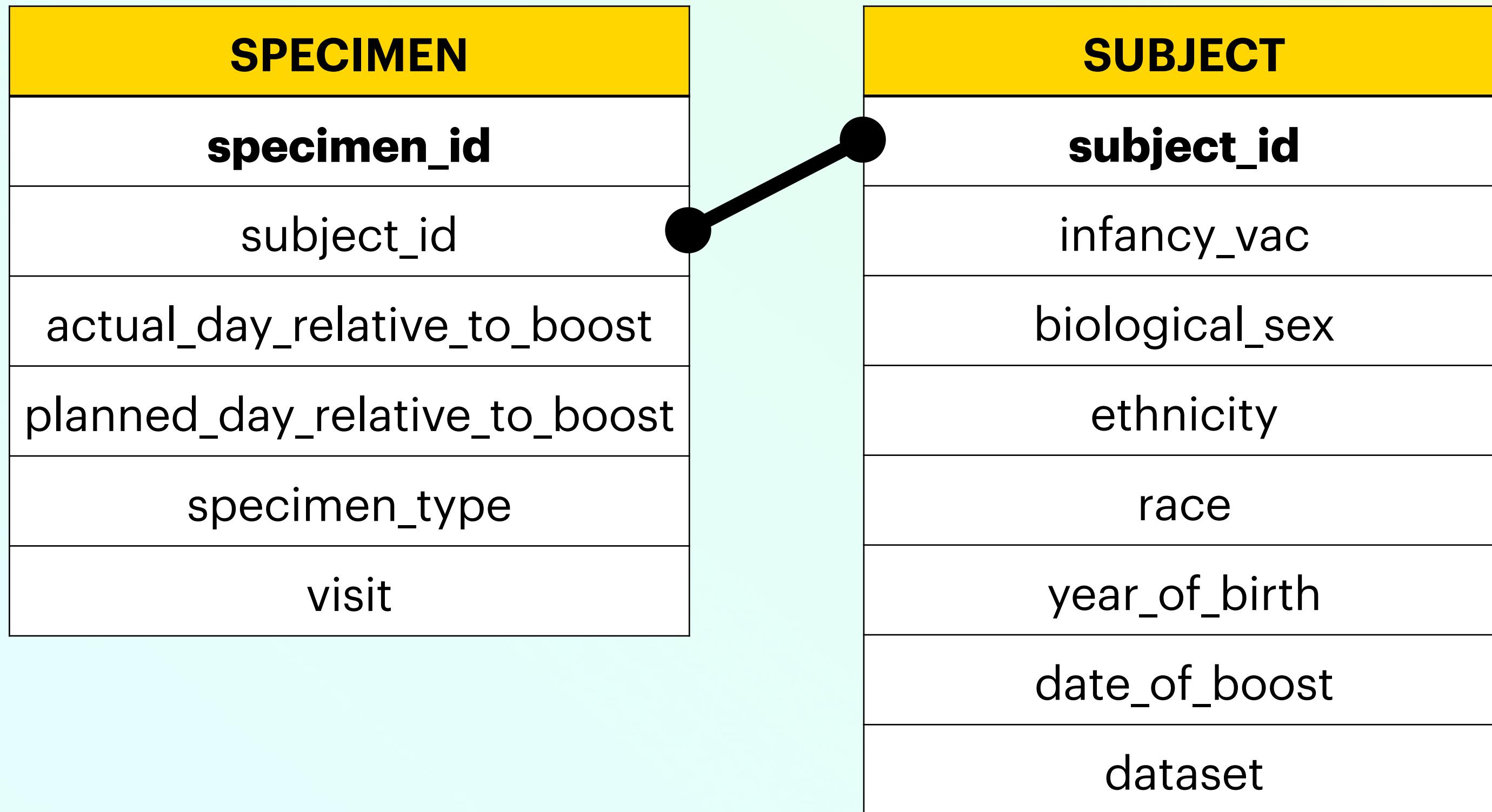
full_join(x, y)

1	x1
2	x2
3	x3

1	y1
2	y2
4	y4

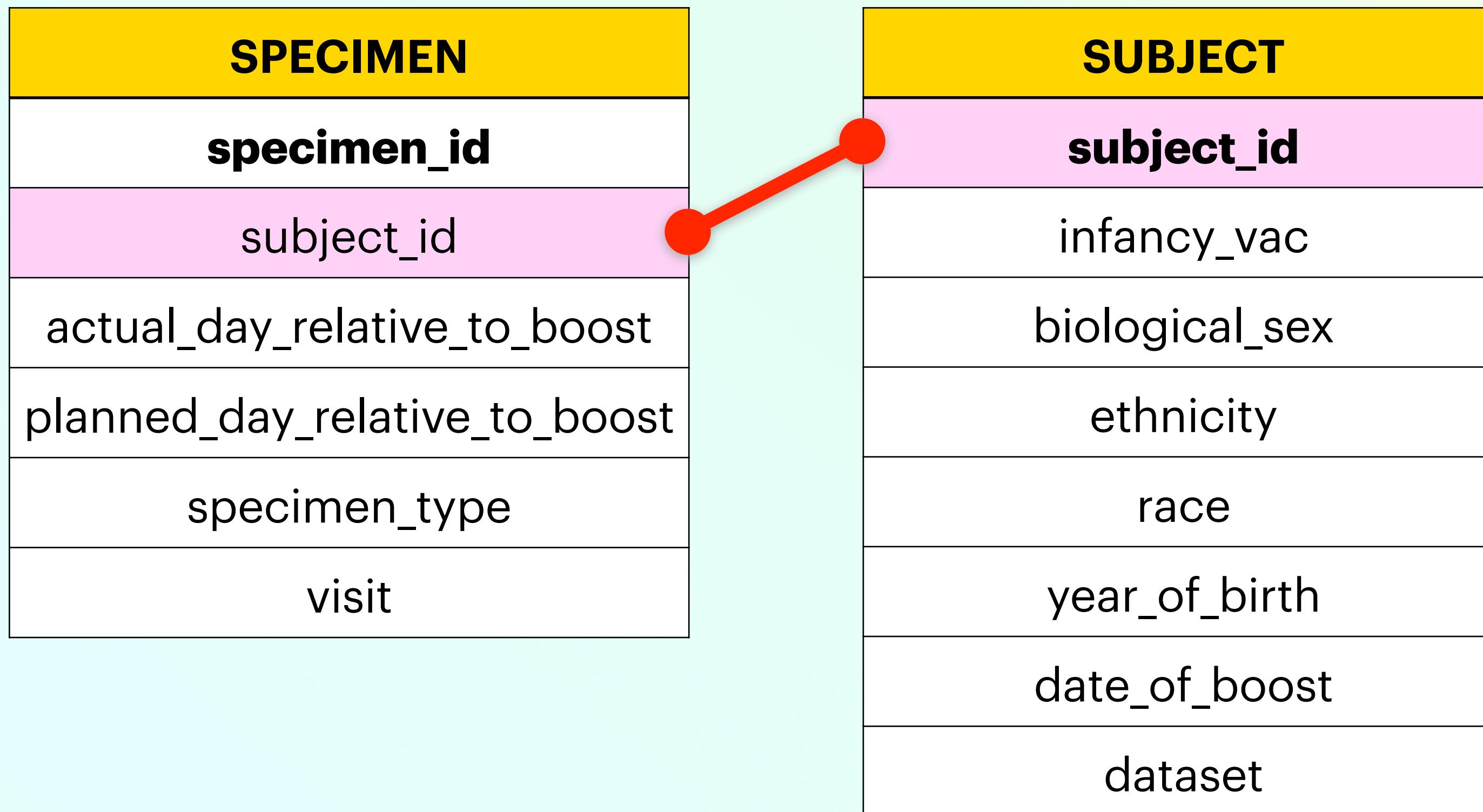
INFORMATION TABLES

CAN BE LINKED BY “**SUBJECT_ID**”



INFORMATION TABLES

CAN BE LINKED BY “**SUBJECT_ID**”



WE WANT ONE META TABLE

USE DPLYR `*_JOIN()` FUNCTIONS...

SPECIMEN
specimen_id
subject_id
actual_day_relative_to_boost
planned_day_relative_to_boost
specimen_type
visit

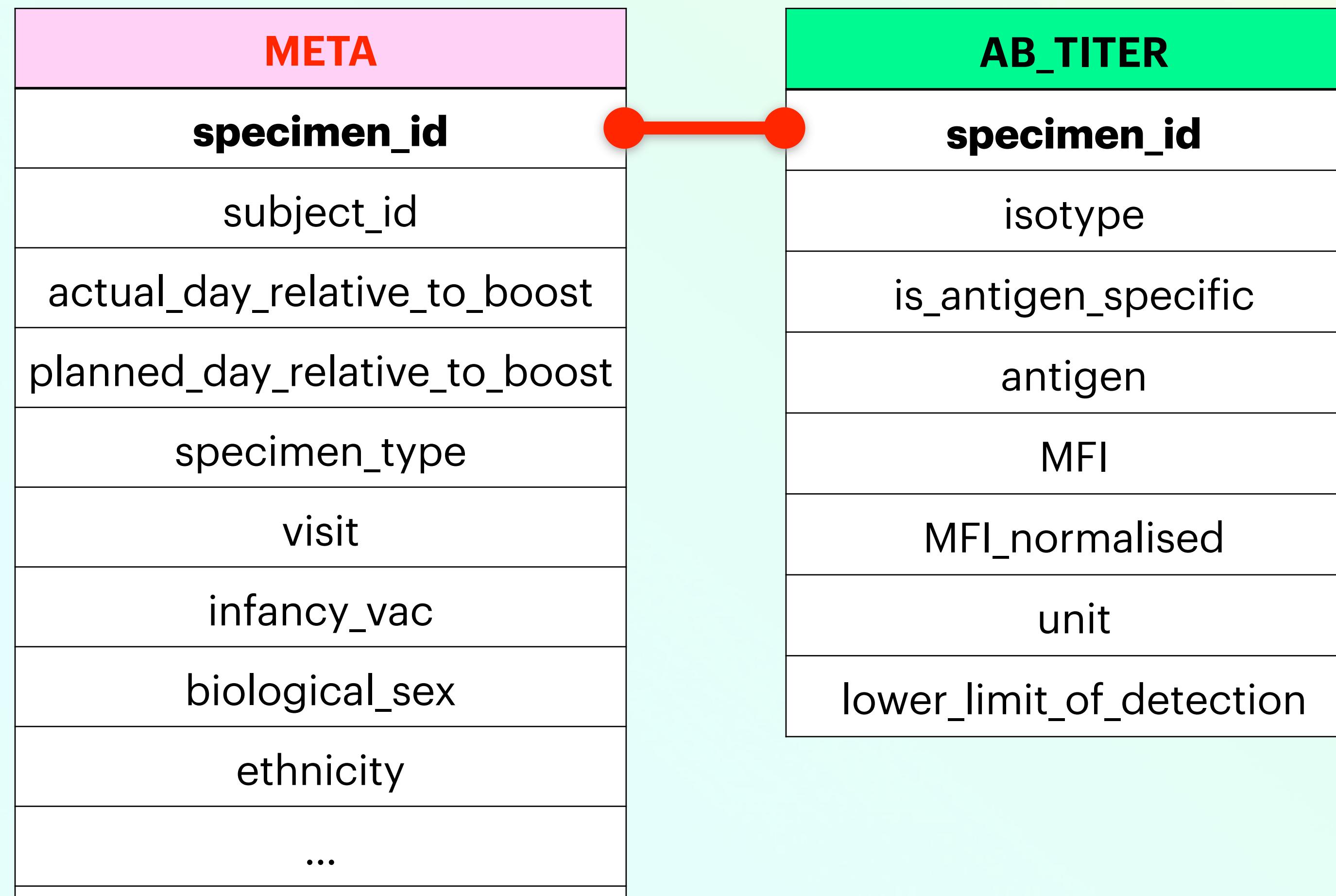
SUBJECT
subject_id
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ethnicity
race
year_of_birth
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dataset

=

META
specimen_id
subject_id
actual_day_relative_to_boost
planned_day_relative_to_boost
specimen_type
visit
infancy_vac
biological_sex
ethnicity
race
year_of_birth
date_of_boost
dataset

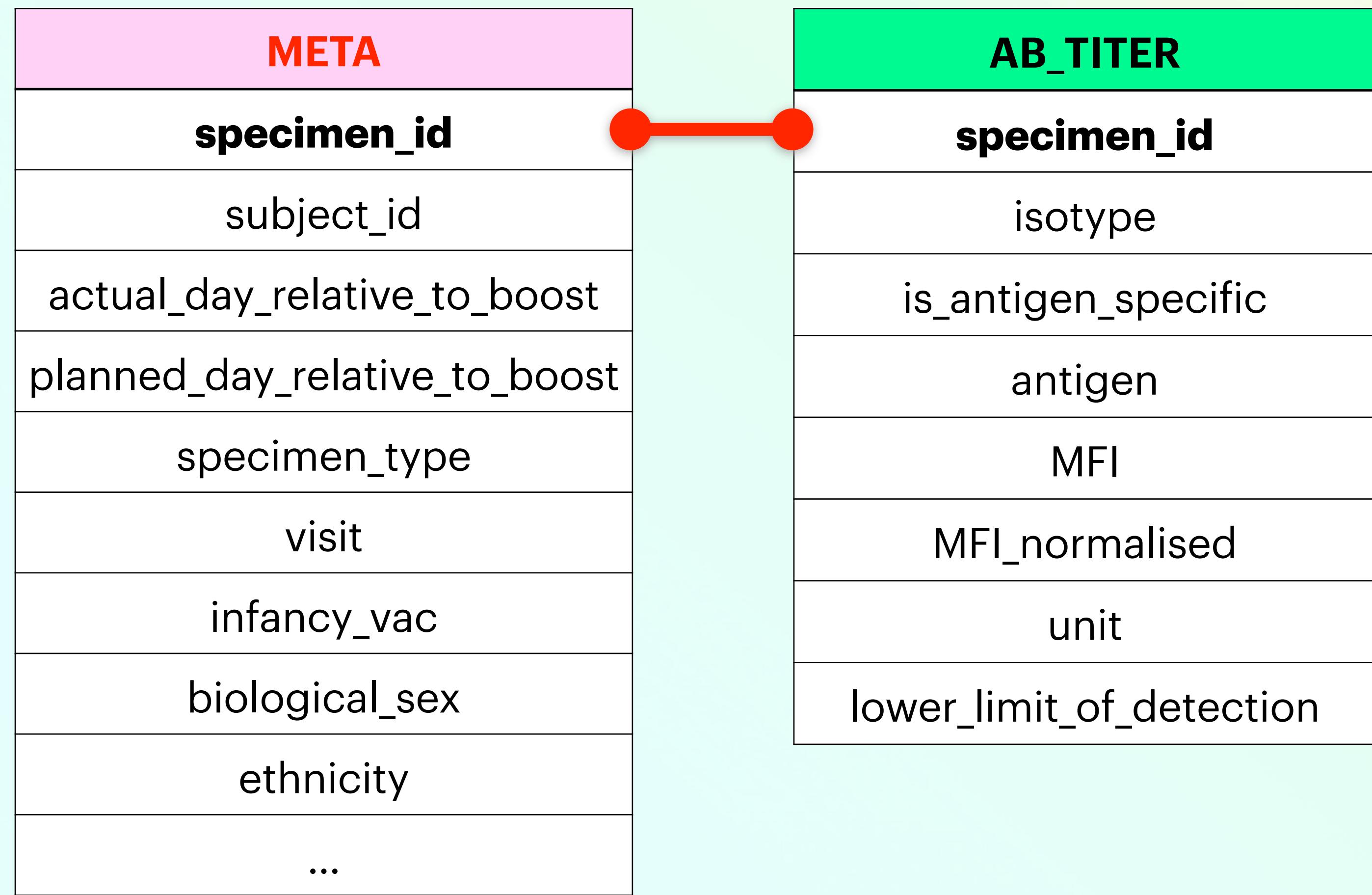
JOIN WITH EXPERIMENT TABLES

USE DPLYR ***_JOIN()** FUNCTIONS...

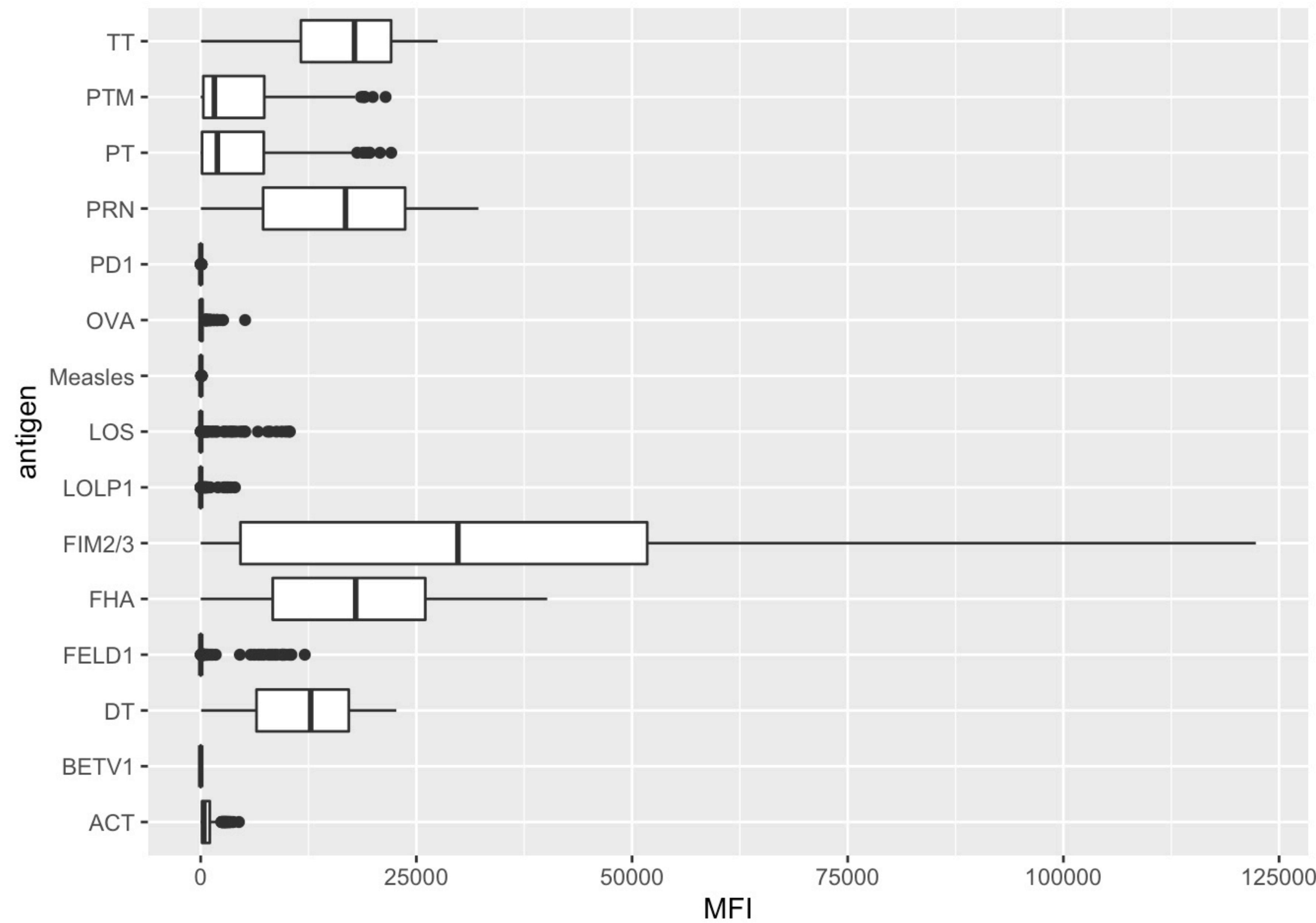


META + EXPERIMENT

HAS EVERYTHING WE NEED FOR FURTHER ANALYSIS...



ABDATA	
specimen_id	
subject_id	
actual_day_relative_to_boost	
planned_day_relative_to_boost	
specimen_type	
visit	
infancy_vac	
biological_sex	
ethnicity	
race	
year_of_birth	
date_of_boost	
dataset	
isotype	
is_antigen_specific	
antigen	
MFI	
MFI_normalised	
unit	
lower_limit_of_detection	



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https://www.cmi-pb.org/terminology/uniprot:Q5I8X0

fim2 - Fimbrial protein - *Bordetella pertussis* | UniProtKB | UniProt



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Terminology ▾ FIMbrial protein Search

Terminology Browser uniprot:Q5I8X0

Fimbrial prote...

<https://www.uniprot.org/uniprot/Q5I8X0>

Ontology

Class

material entity

molecular entity

protein

Fimbrial protein

Annotation Property

Data Property

Object Property

Individual

Datatype

Fimbrial protein

Fimbrial protein Fim3

Mixture of Fim2 and Fim3

uniprot:Q5I8X0

- label
 - Fimbrial protein
- CMI-PB alternative term
 - fim2
- type
 - Class
- subclass of
 - protein

uniprot.org

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https://www.cmi-pb.org/terminology/uniprot:Q5I8X0

fim2 - Fimbrial protein - Bordetella pertussis | UniProtKB | UniProt

UniProt BLAST Align Peptide search ID mapping SPARQL UniProtKB Advanced List Search Help

Function Q5I8X0 · Q5I8X0_BORPT

Names & Taxonomy

Proteinⁱ Fimbrial protein

Statusⁱ UniProtKB unreviewed (TrEMBL)

Organismⁱ Bordetella pertussis

Geneⁱ fim2

Amino acids 207

Protein existenceⁱ Predicted

Annotation scoreⁱ 1/5

Subcellular Location

Phenotypes & Variants

PTM/Processing

Expression

Interaction

Structure

Family & Domains

Sequence

Similar Proteins

Entry Feature viewer Publications External links History

BLAST Align Download Add Add a publication Entry feedback

Feedback

Help

Functionⁱ

GO Annotationsⁱ

Slimming set:

generic

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https://www.cmi-pb.org/terminology/uniprot:Q5I8X0

fim2 - Fimbrial protein - Bordetella pertussis | UniProtKB | UniProt

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BLAST Align Download Add Add a publication Entry feedback

Functionⁱ

GO Annotationsⁱ

Slimming set: generic

metabolic process, precursor metabolites and energy, cellular process, DNA repair, recombination, organization, transcription, folding, template, RNA, protein, glycosylation, acid, metabolic, amino, acid, modification, transport, compound, protein, lipid, vitamin, metabolic, process, sulfur, compound, metabolic, process, intracellular, protein, transport, autophagy, topoplasmic, response, mitochondrial, organization, nucleotide, based, movement, peroxisome, organization, lysosome, organization, establishment, or, maintenance, of, cell, polarity, inflammatory, response, cytoskeleton, organization, aging, programmed, cell, death, photosynthesis, vesicle, mediated, transport, reproductive, system, process, signaling, differentiation, process, rna, catabolic, process, extracellular, matrix, organization, gene, silencing, telomere, organization, protein, modification, process, wound, healing, cell, junction, organization, ribosome, biogenesis, cilium, organization, endocrine, process, nervous, system, process, metal, ion, maturation, transmembrane, transport, nucleobase, transmembrane, hepaticobilis, membranous

Cell color indicative of number of GO terms

ASPECT	TERM
Cellular Component	pilus Source:InterPro
Biological Process	cell adhesion Source:InterPro

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Expand table

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fim2 - Fimbrial protein - Bordetella pertussis | UniProtKB | UniProt

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UniProt Annotation GO Annotation

📍 pilus ↗

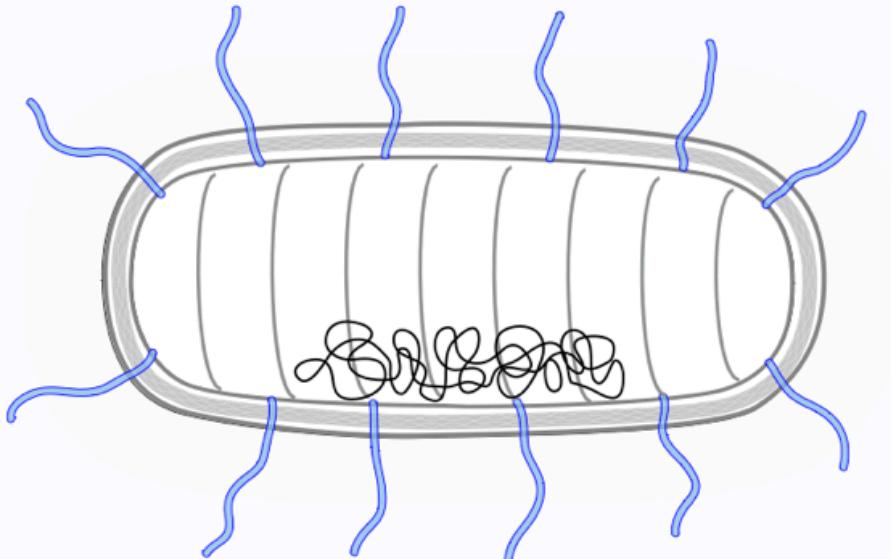
Complete GO annotation on QuickGO ↗

SIB

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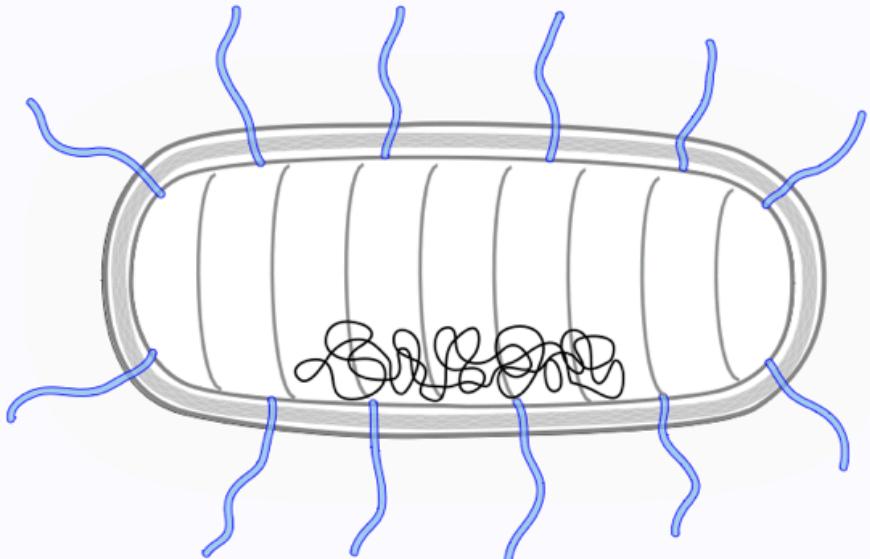
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Subcellular Locationⁱ

UniProt Annotation GO Annotation



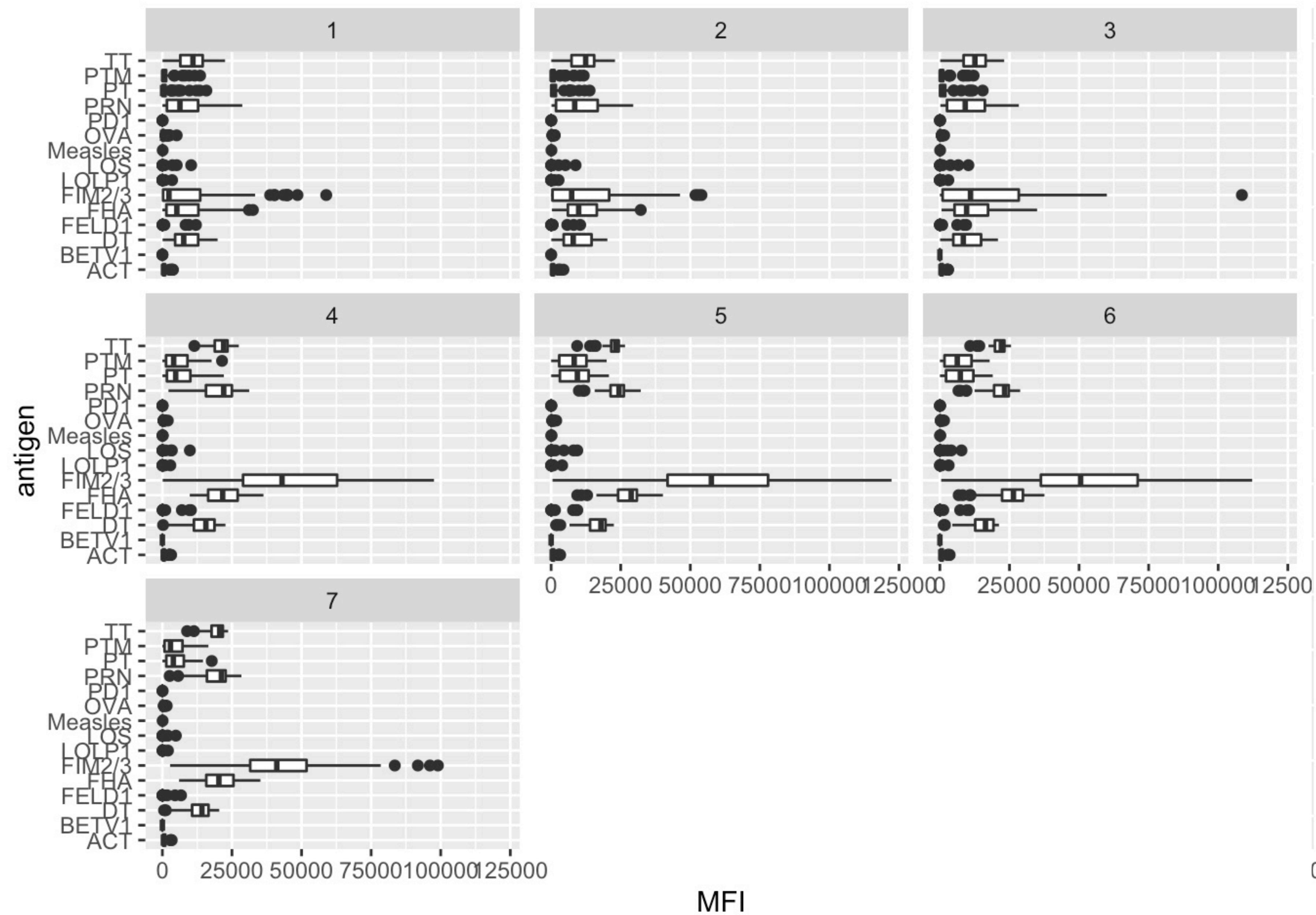
pilus

Complete GO annotation on QuickGO

Fimbrium
A fimbrium or pilus is a hair-like, non-flagellar, polymeric filamentous appendage that extend from the bacterial or archaeal cell surface, such as type 1 pili, P-pili, type IV pili or curli. Pili perform a variety of functions, including surface adhesion, motility, cell-cell interactions, biofilm formation, conjugation, DNA uptake, and twitching motility.

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a. Past and future CMI-PB annual prediction challenges



	Annual prediction challenge title	Contestants	Training datasets
1	First Challenge: Internal dry run	CMI-PB consortium	60 (28 aP + 32 v)
2	Second Challenge: Invited challenge	Invited contestants	96 (47 aP + 49 v)
3	Third Challenge: Open Challenge 1	Public	118 (60 aP + 58 v)
4	Fourth Challenge: Open Challenge 2	Public	150 (76 aP + 74 v)

b. Prediction challenge outline

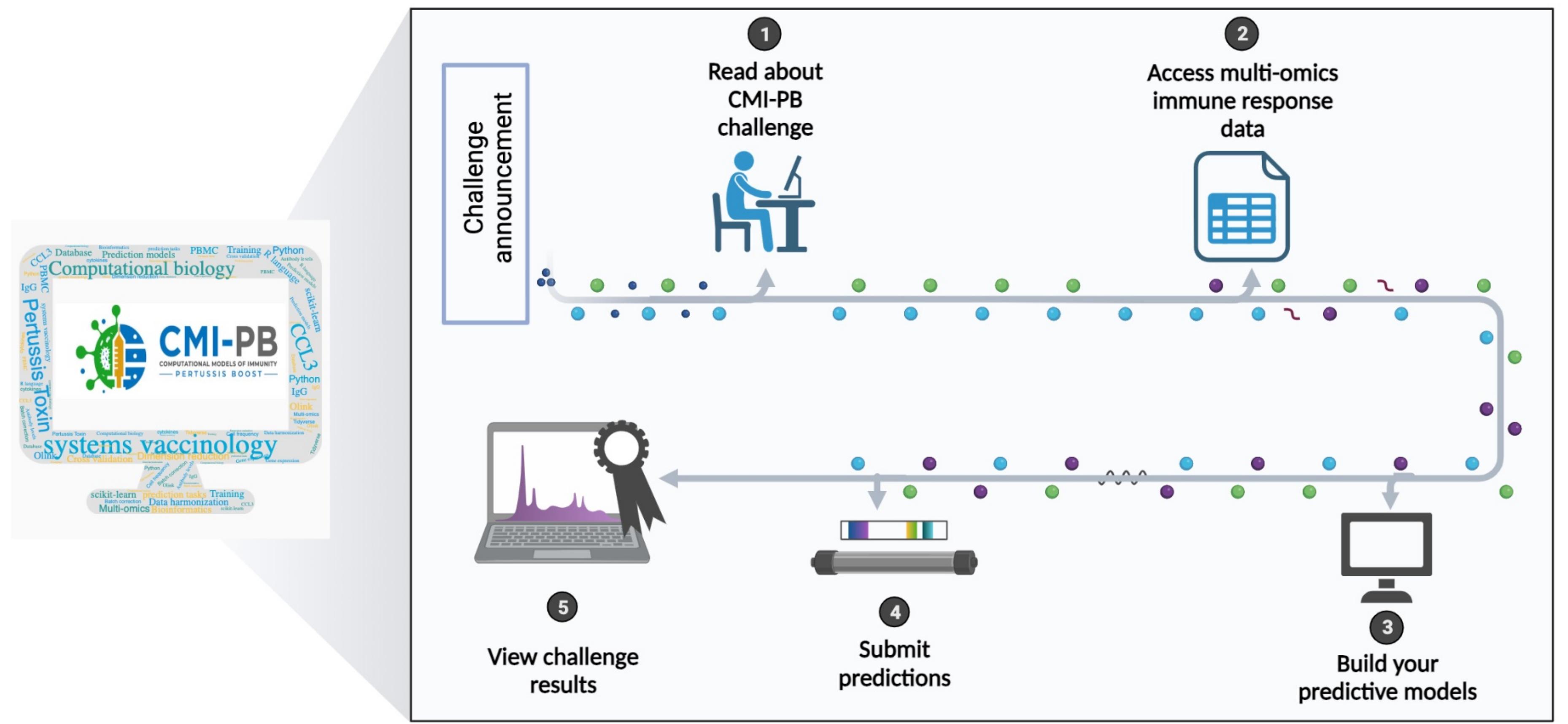


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2nd CMI-PB Prediction Challenge Outline

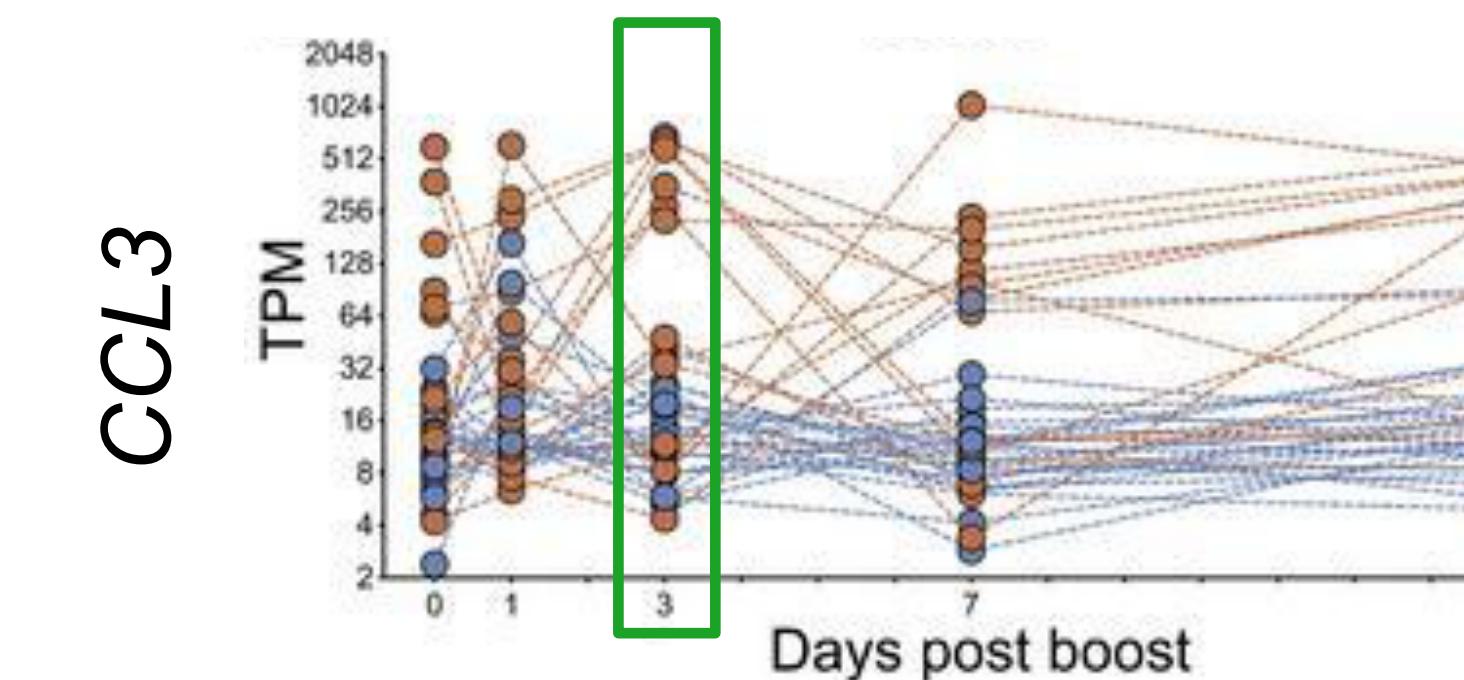
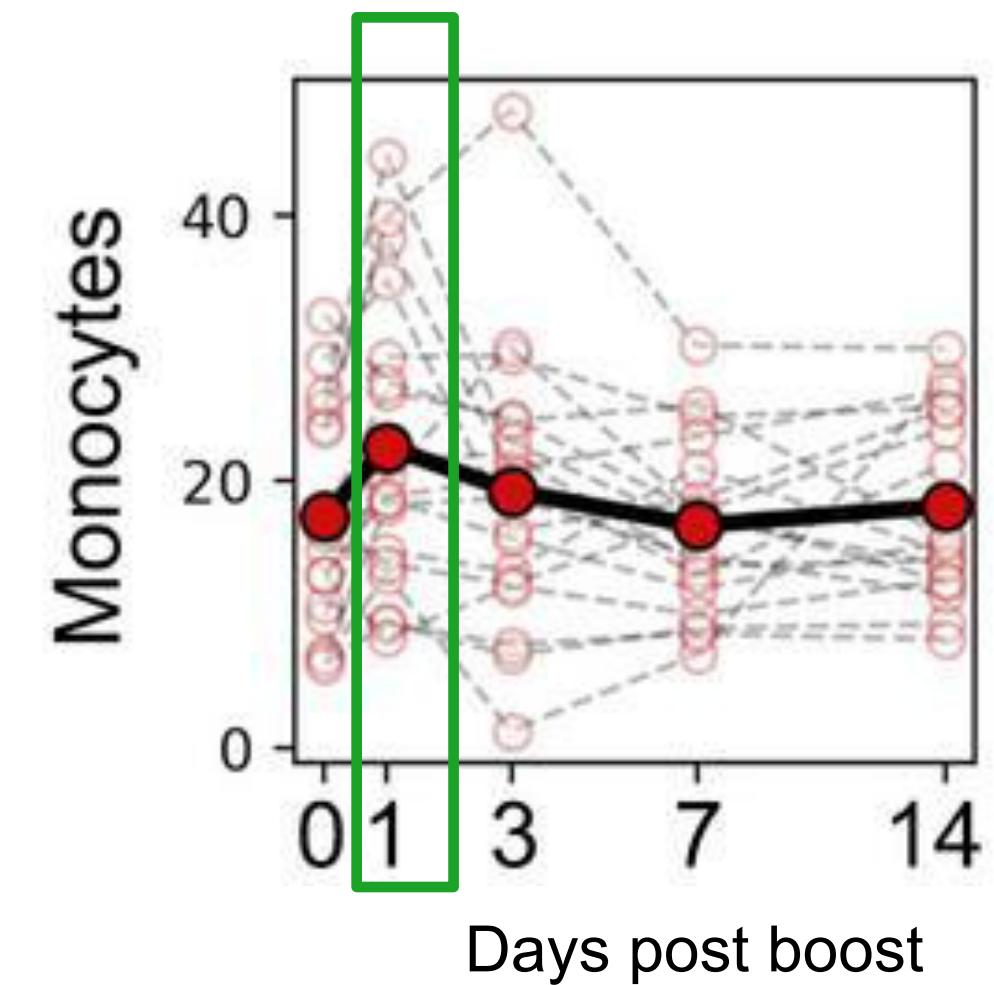
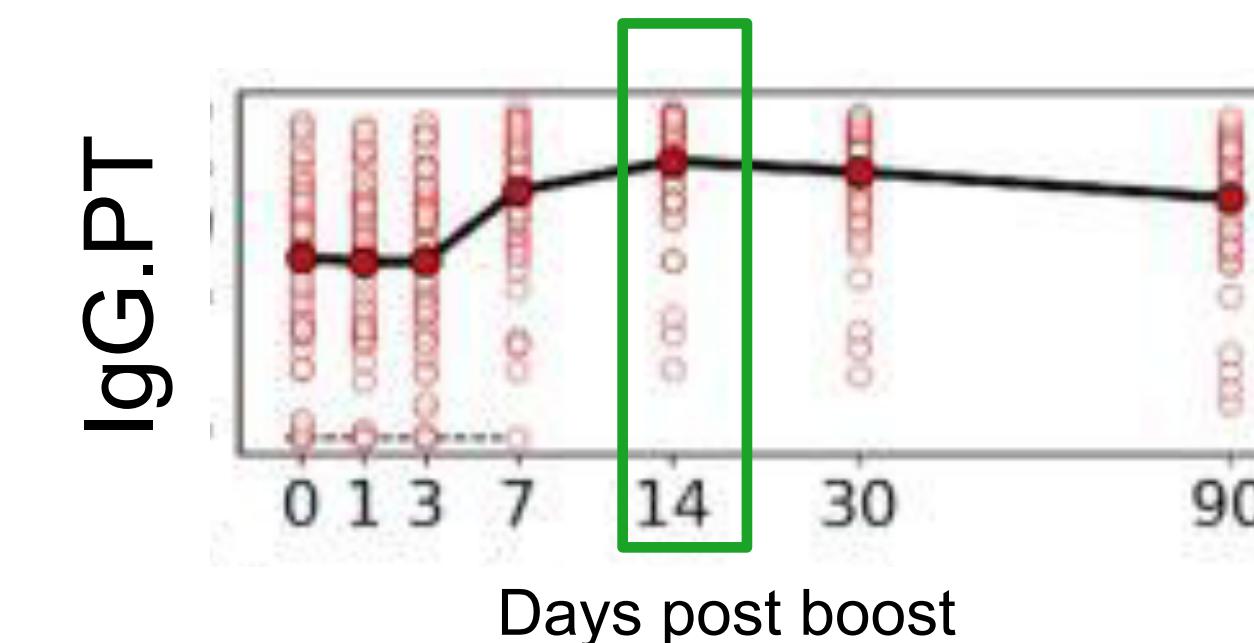
Revolutionizing computational modelling approaches for immune response prediction



c. Formulating prediction tasks for CMI-PB Challenge



- Previously identified **vaccine responses** are formulated as prediction tasks*
- General vaccine responses:**
 - Plasma IgG levels increased at day 14 post-booster vaccination compared to baseline
 - Increase in the percentage of monocytes on day 1 post-booster than baseline
- aP/wP specific vaccine responses:**
 - A subset of aP-primed individuals showed an increased expression of proinflammatory genes, including CCL3 at day 3 post-booster vaccination



* A system-view of *Bordetella pertussis* booster vaccine responses in adults primed with whole-cell versus acellular vaccine in infancy

c. Formulating prediction tasks for CMI-PB Challenge



List of tasks

1) Antibody titer tasks

1.1) Rank the individuals by IgG antibody titers against pertussis toxin (PT) that we detect in plasma 14 days post booster vaccinations.

predicted values

1.2) Rank the individuals by fold change of IgG antibody titers against pertussis toxin (PT) that we detect in plasma 14 days post booster vaccinations compared to titer values at day 0.

predicted fold-change values

2) Cell frequencies tasks

2.1) Rank the individuals by predicted frequency of Monocytes on day 1 post boost after vaccination.

2.2) Rank the individuals by fold change of predicted frequency of Monocytes on day 1 post booster vaccination compared to cell frequency values at day 0.

3) Gene expression tasks

3.1) Rank the individuals by predicted gene expression of CCL3 on day 3 post-booster vaccination.

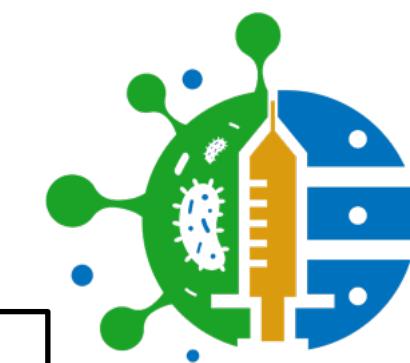
3.2) Rank the individuals by fold change of predicted gene expression of CCL3 on day 3 post booster vaccination compared to gene expression values at day 0.

Example of Rankings

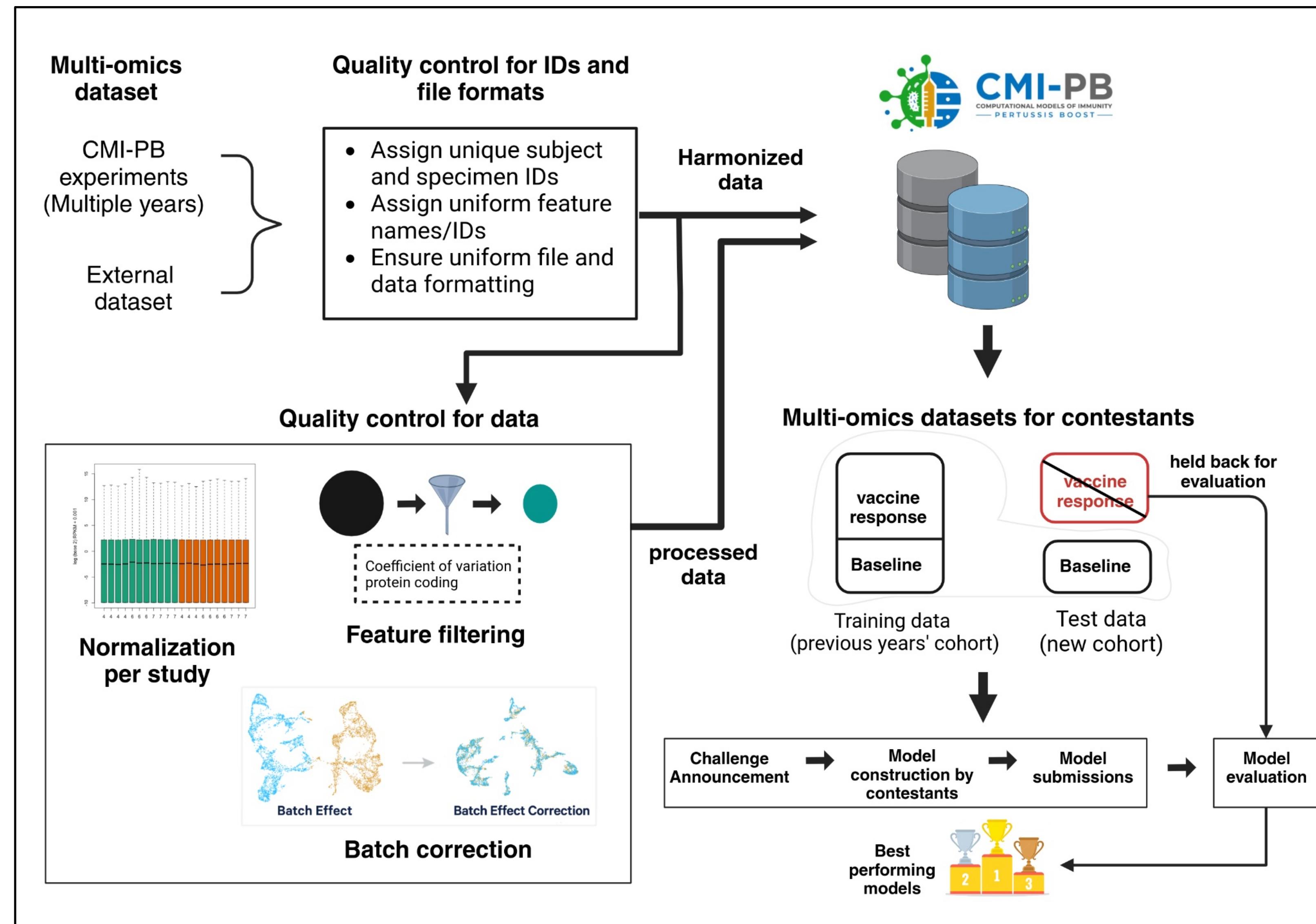
Subject ID	Predicted value	Rank
101	2.9	4
102	9.1	1
103	1.2	5
104	4.5	3
105	4.7	2

The ultimate goal is to model as many of the tasks as possible. However, contestants are not required to submit answers for all tasks.

d. Overview of the CMI-PB Challenge data



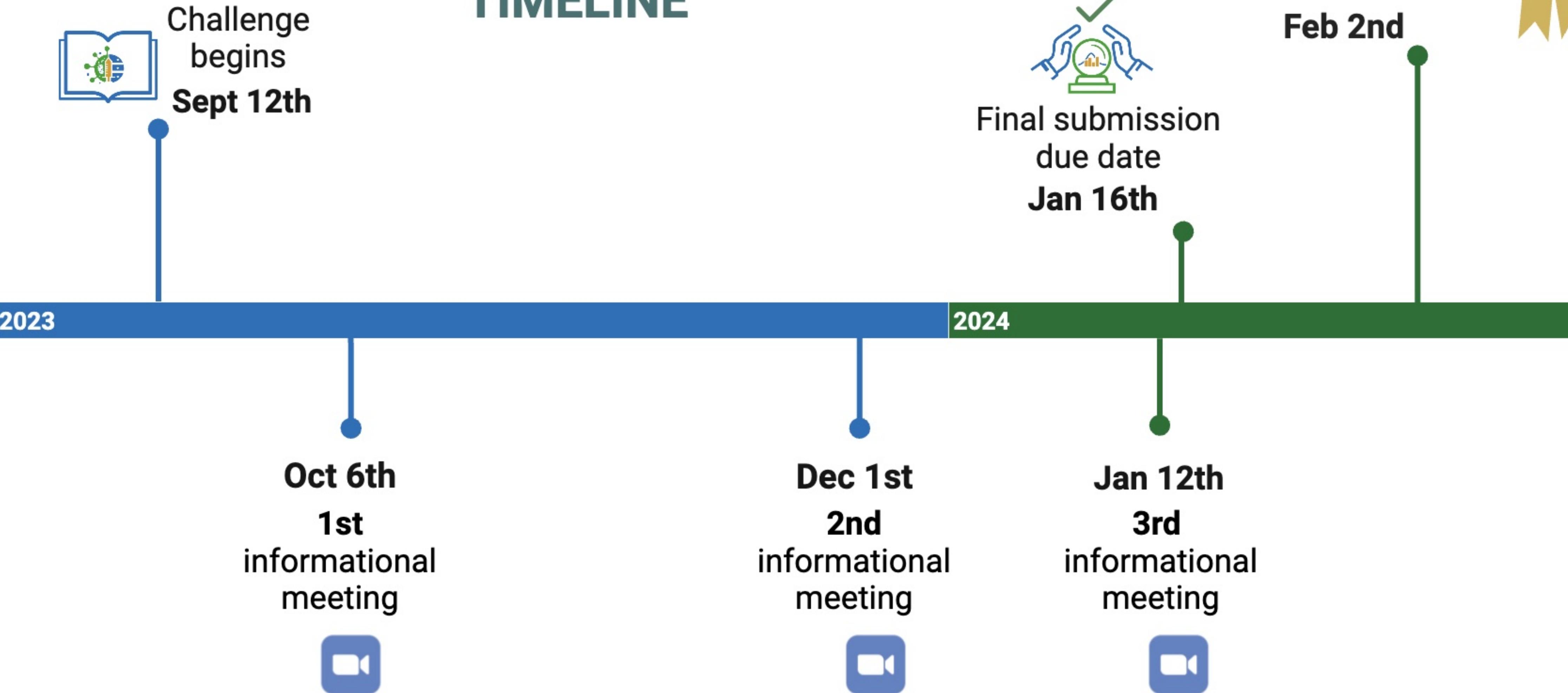
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Challenge related information and Data access is provided via the CMI-PB website



CMI-PB PREDICTION CHALLENGE TIMELINE



The CMI-PB team



Kleinstein Lab (Yale)



- Expertise: A combination of "big data" analysis and immunology domain.
- Collaborating on data and models being released to the community to support reproducibility and the prediction contest, and also participate in the prediction challenge.

Steven Kleinstein
Jeremy Gygi
Leying Guan
Anna Konstorum

Grant Lab (UCSD)



- Expertise: the use of computational approaches, based on both biophysics and bioinformatics, to study the structure, function and evolution of key biological macromolecules.
- Dr. Grant will engage and advise over 40 biology graduate students in the CMI-PB Prediction Challenge.

Barry Grant

Ay Lab (LJI)



- Expertise: Development of bioinformatics tools that utilize high-dimensional and high-throughput datasets to deduce insights into chromatin conformation, genetic variation, and the regulation of gene expression.
- The Ay lab is focused on developing predictive machine learning models, which will serve as examples and baselines for participants in the CMI-PB challenge.

Ferhat Ay
Joaquin Reyna

Peters Lab (LJI)



- Expertise: Both experimental and computational studies to better understand human immune responses in the context of infectious diseases, allergy, cancer and vaccines.
- The team is responsible for the generation of experimental data, making it accessible in a central and standardized fashion, and coordinating the creation and coordination of the prediction contest.

Bjoern Peters
Jason Greenbaum
James Overton
Brendan Ha

Pramod Shinde
Mari Kojima
Rasteh Haji Kazem Nili

Jiyeun Lee
Lisa Willemsen
Shelby Orfield

And thank you to the Sette Lab, Crotty lab, LJI Clinical Core, LJI Bioinformatics Core

The CMI-PB team members



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Bjoern Peters



Steven Kleinstein



Ferhat Ay



Barry Grant



Shane Crotty



Alessandro Sette



Pramod Shinde



Shelby Orfield



Lisa Willemsen



Leying Guan



Joaquin Reyna



Mari Kojima



Ferran Soldevila



Rasteh Nili



Jason Greenbaum



Brendan Ha



Jiyeun Lee



Ricardo De Silva Antunes



Jeremy Gygi



Anna Konstorum