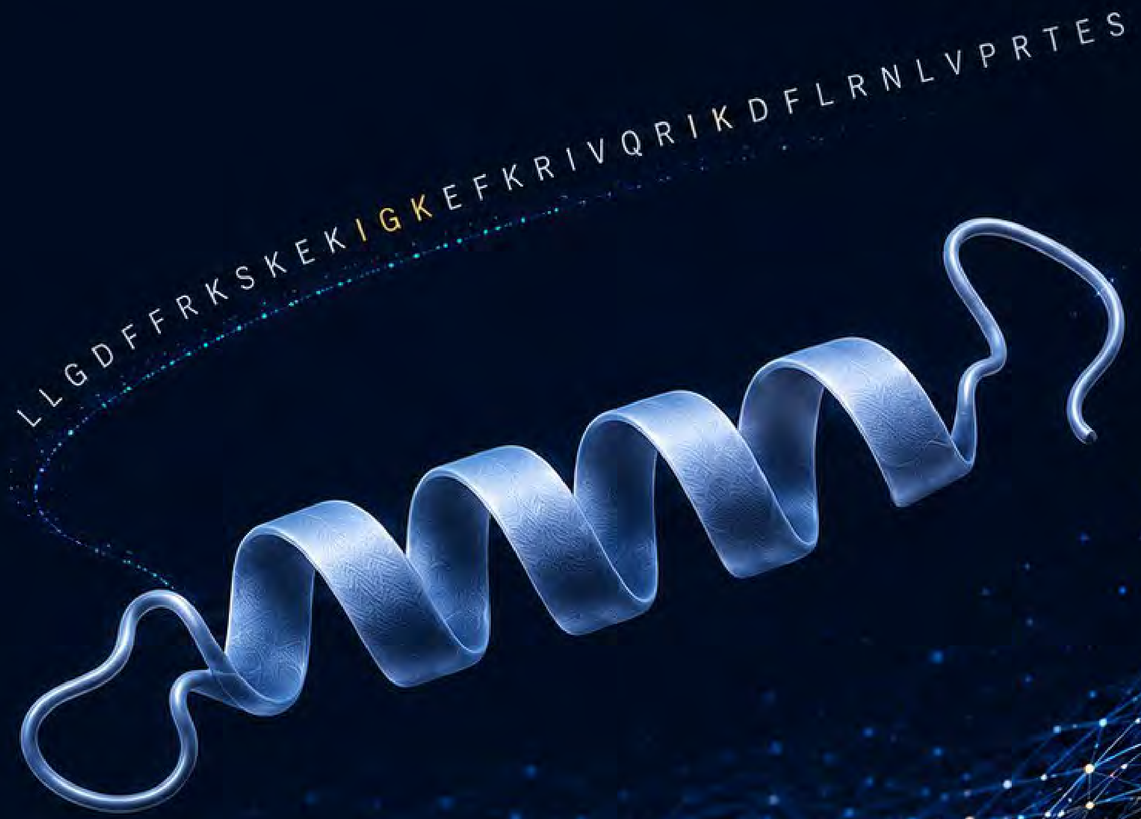
Can machines discover function in the code of life?

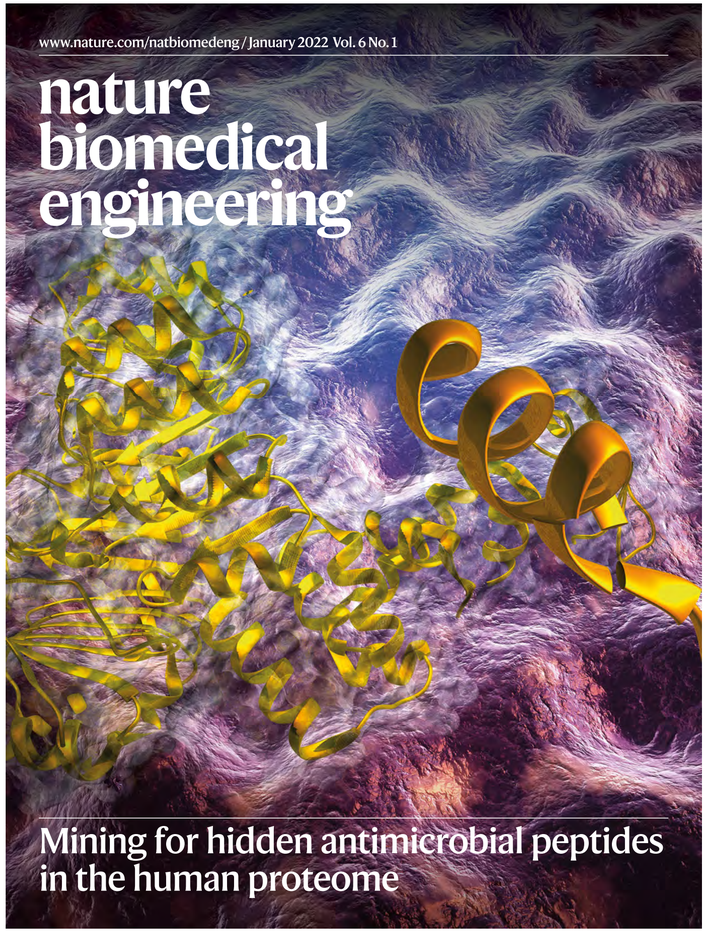


Prof. César de la Fuente, Ph.D., FRSB, AIMBE Fellow

Presidential Associate Professor

Director, Machine Biology Group · University of Pennsylvania

The human proteome contains hidden antibiotics



We realized we could scale to entire proteomes

Algorithmic search used length, net charge and average hydrophobicity to scan proteome-scale sequence space

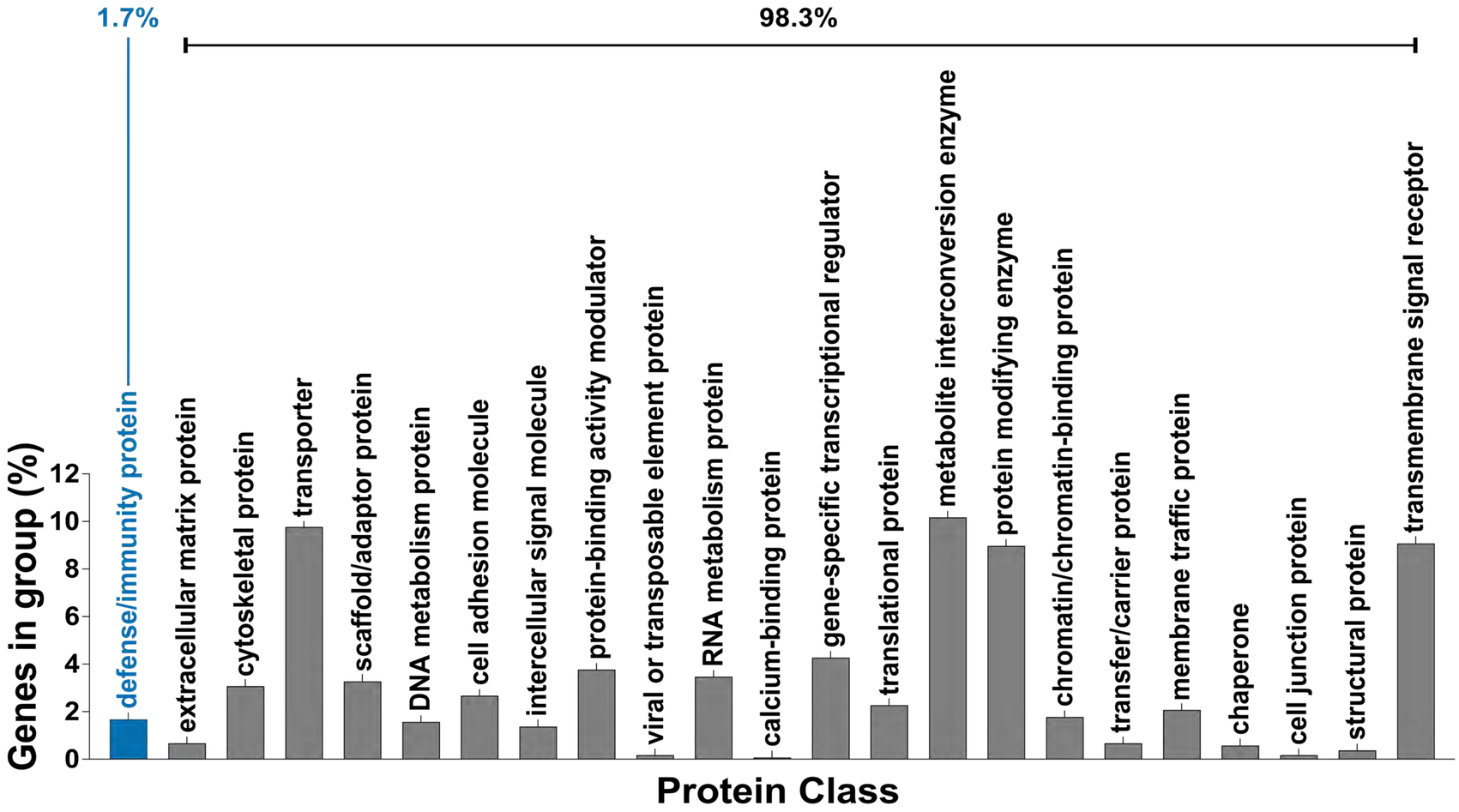
Human proteome: ~20,000 proteins; ~42,000 isoforms; ~100M candidate peptides

Mined the human proteome at computational speed:
~1 hour to mine the human proteome on 48 CPUs

Revealed a new class of antibiotic molecules (encrypted peptides)

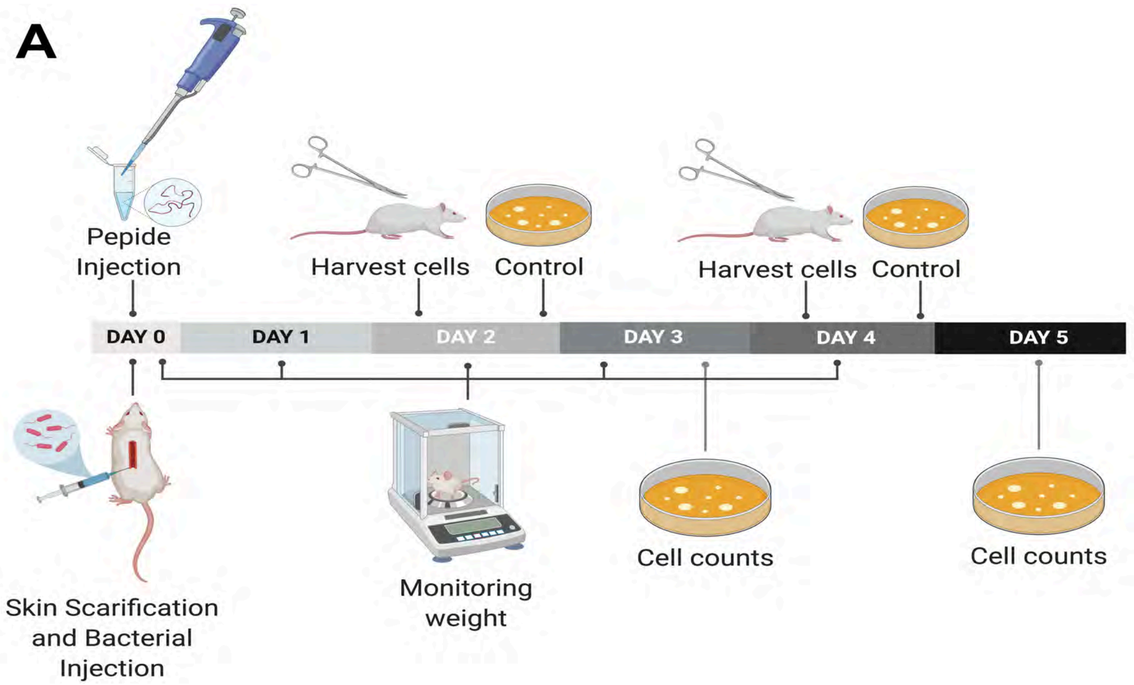
Torres et al. Nature Biomedical Engineering, 2022
Cesaro et al. ACS Nano, 2022

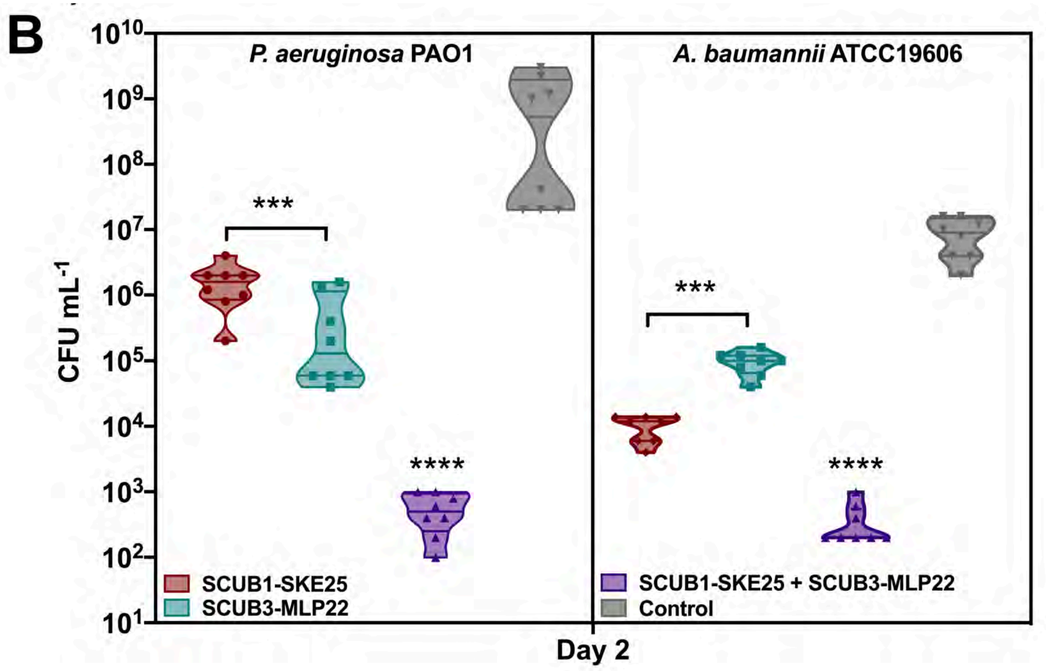
Encrypted immunity



Torres et al. Nature Biomedical Engineering, 2022
Cesaro et al. ACS Nano, 2022
Torres, Cesaro et al. Trends Biotech, 2024

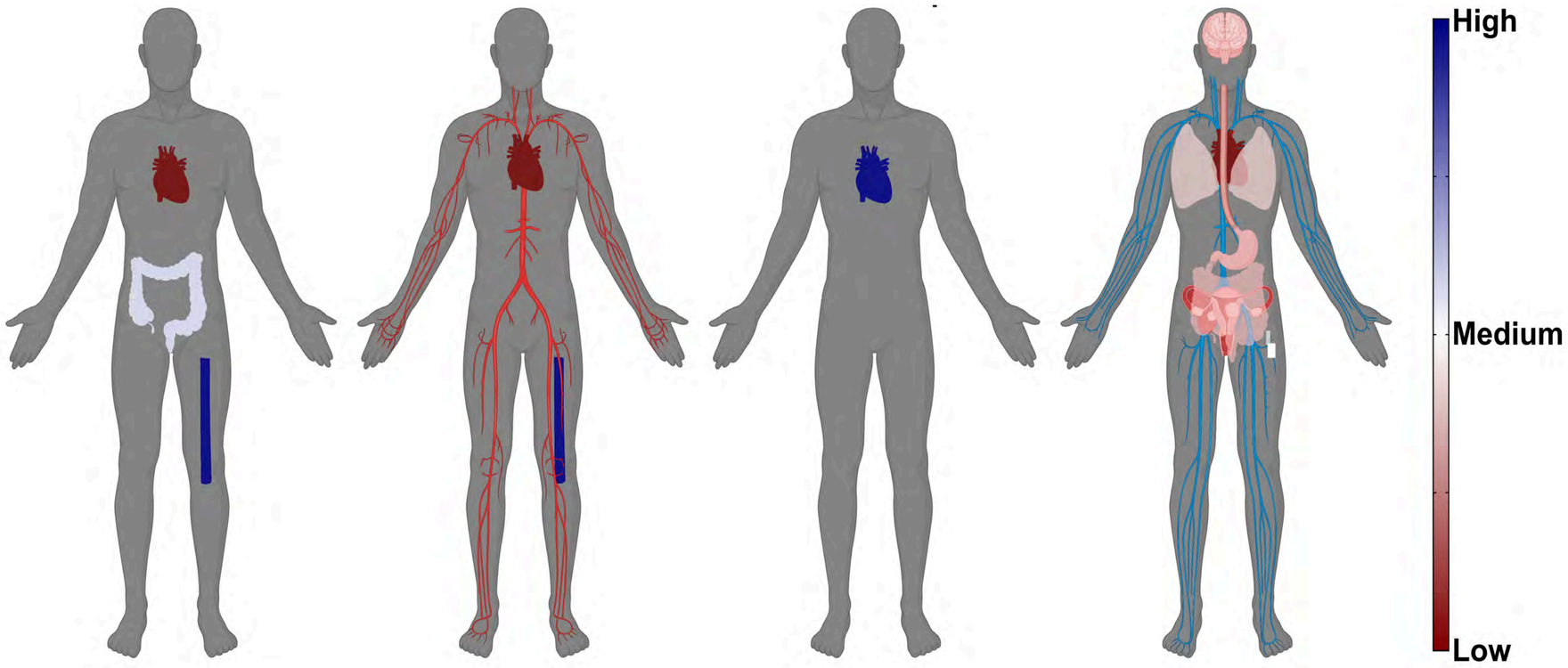
Encrypted peptides work in preclinical infection models





Torres et al. Nature Biomedical Engineering, 2022

Hidden peptides reveal a broader architecture of host immunity



Torres et al. Nature Biomedical Engineering, 2022
Cesaro et al. ACS Nano, 2022
Torres, Cesaro et al. Trends Biotech, 2024

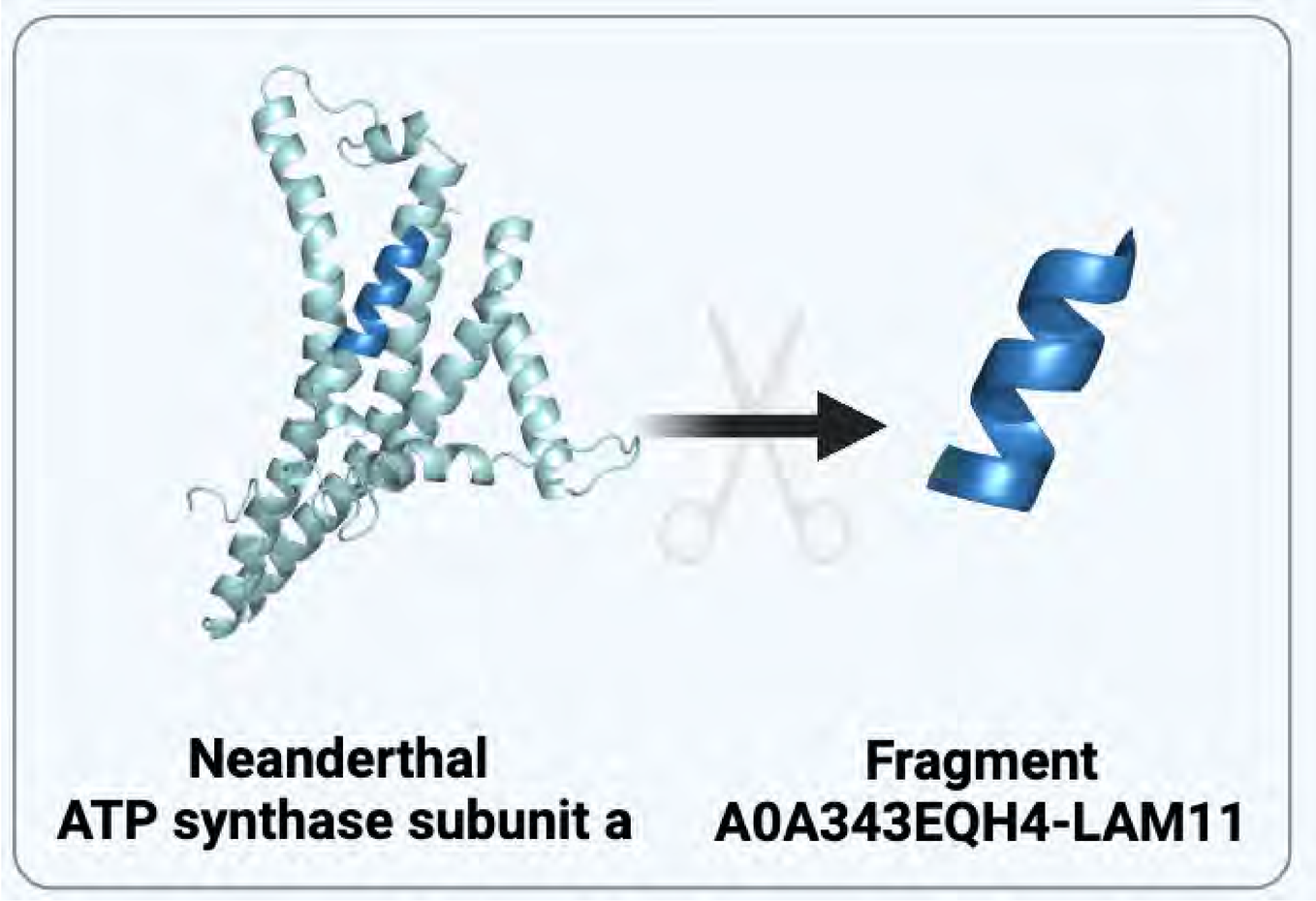
Evolutionary history is a searchable molecular archive





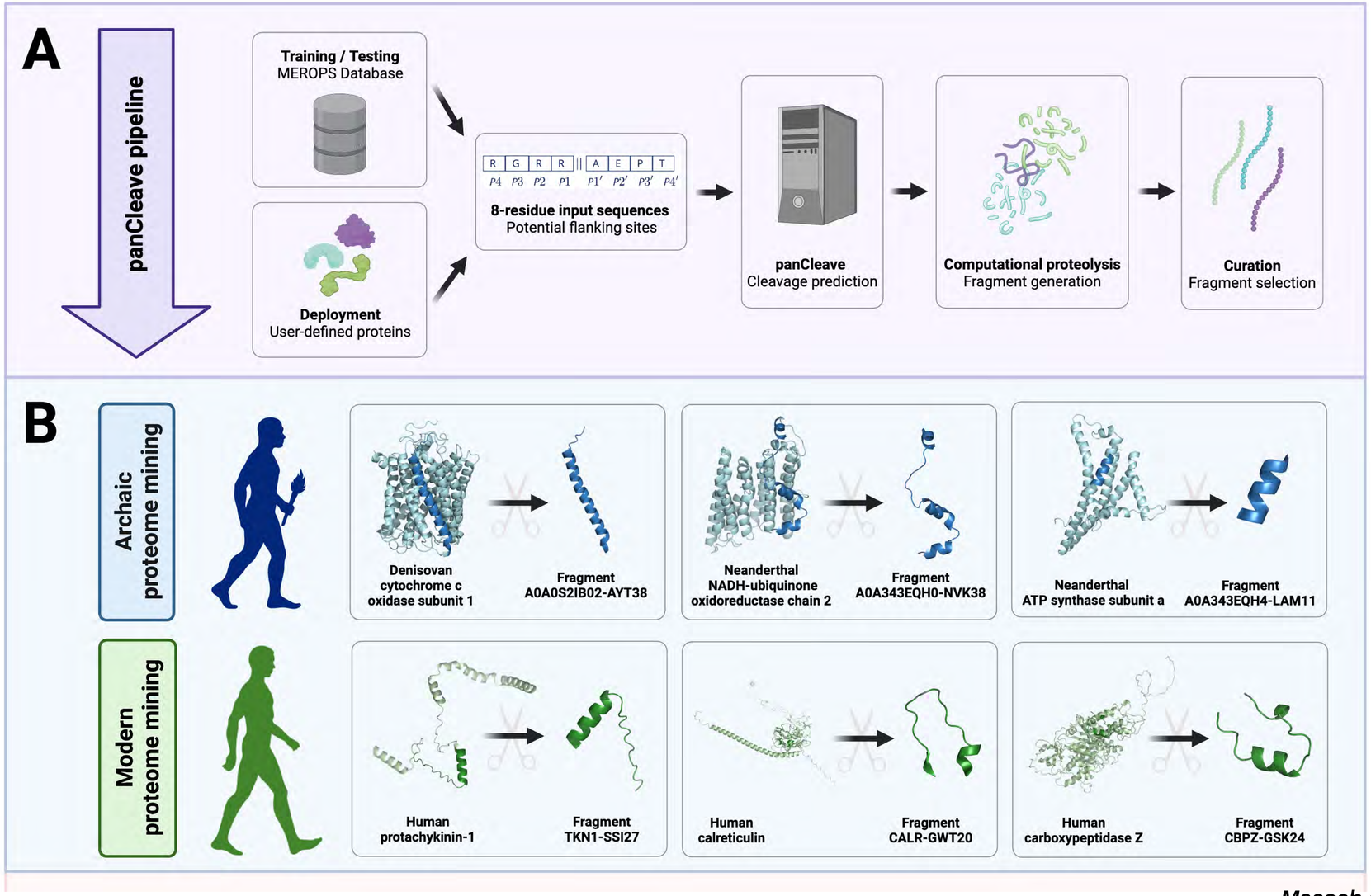
Maasch et al. Cell Host & Microbe 2023
Maasch et al. bioRxiv, 2022

Molecular de-extinction resurrects functional matter



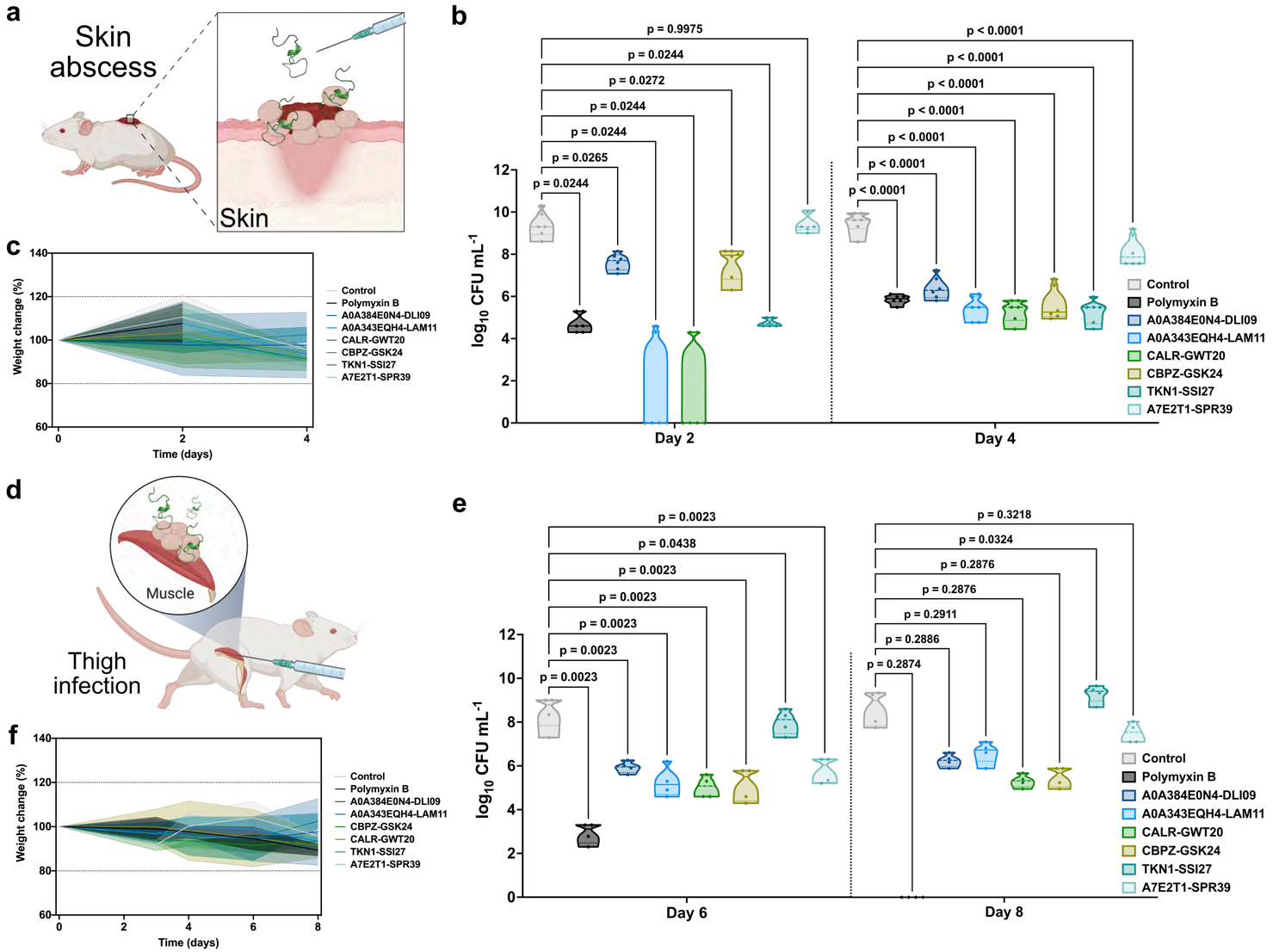
Maasch et al. Cell Host & Microbe 2023
Maasch et al. bioRxiv, 2022

Ancient human proteomes revealed antimicrobial function



Maasch et al. Cell Host & Microbe 2023
Maasch et al. bioRxiv, 2022

Ancient antibiotics retained anti-infective activity



Neanderthalin-1

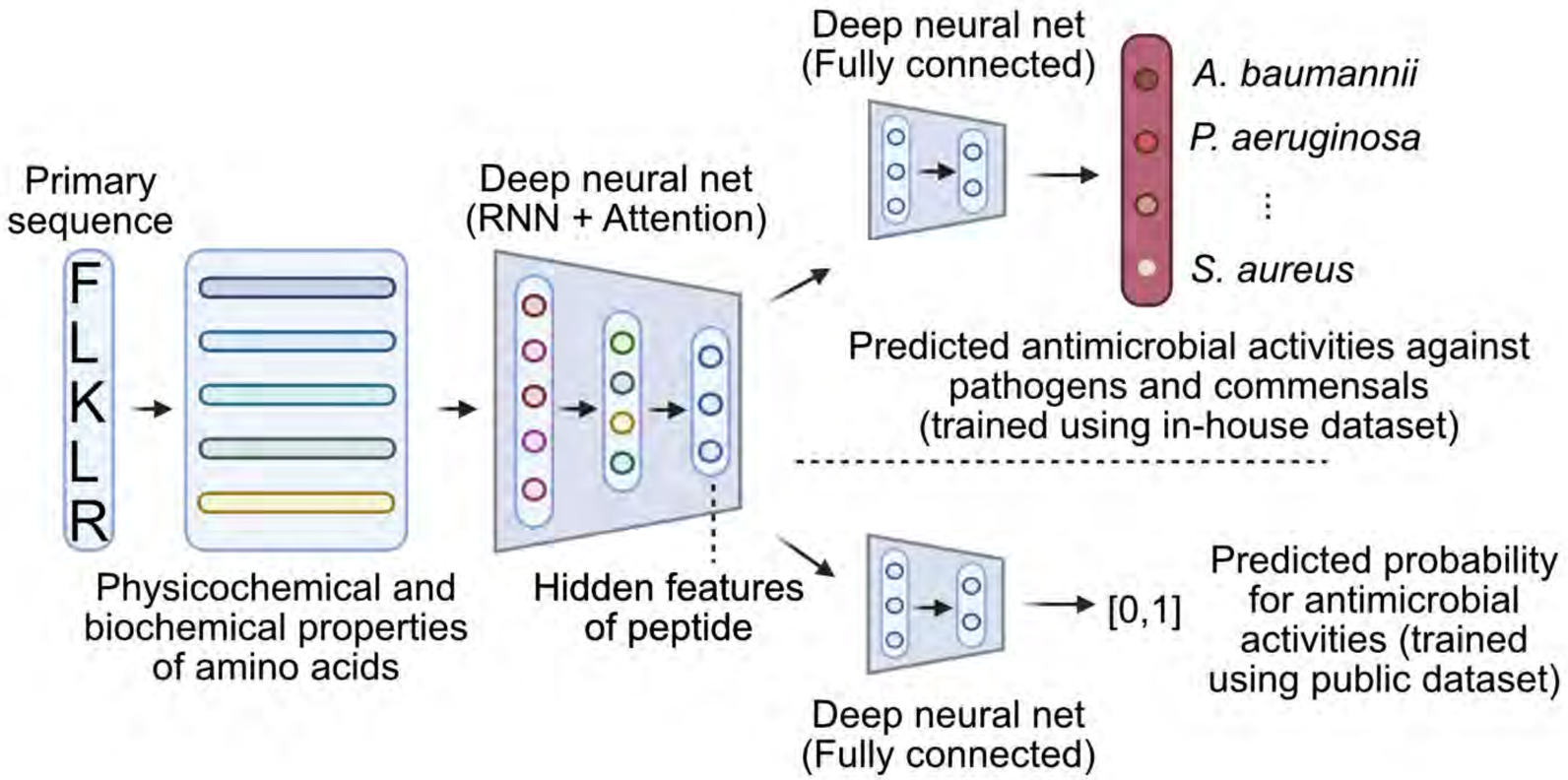
Maasch et al. Cell Host & Microbe 2023
Maasch et al. bioRxiv, 2022

The real test was generalization

Can high-quality data let machines learn organizing principles of functional antibiotic matter?

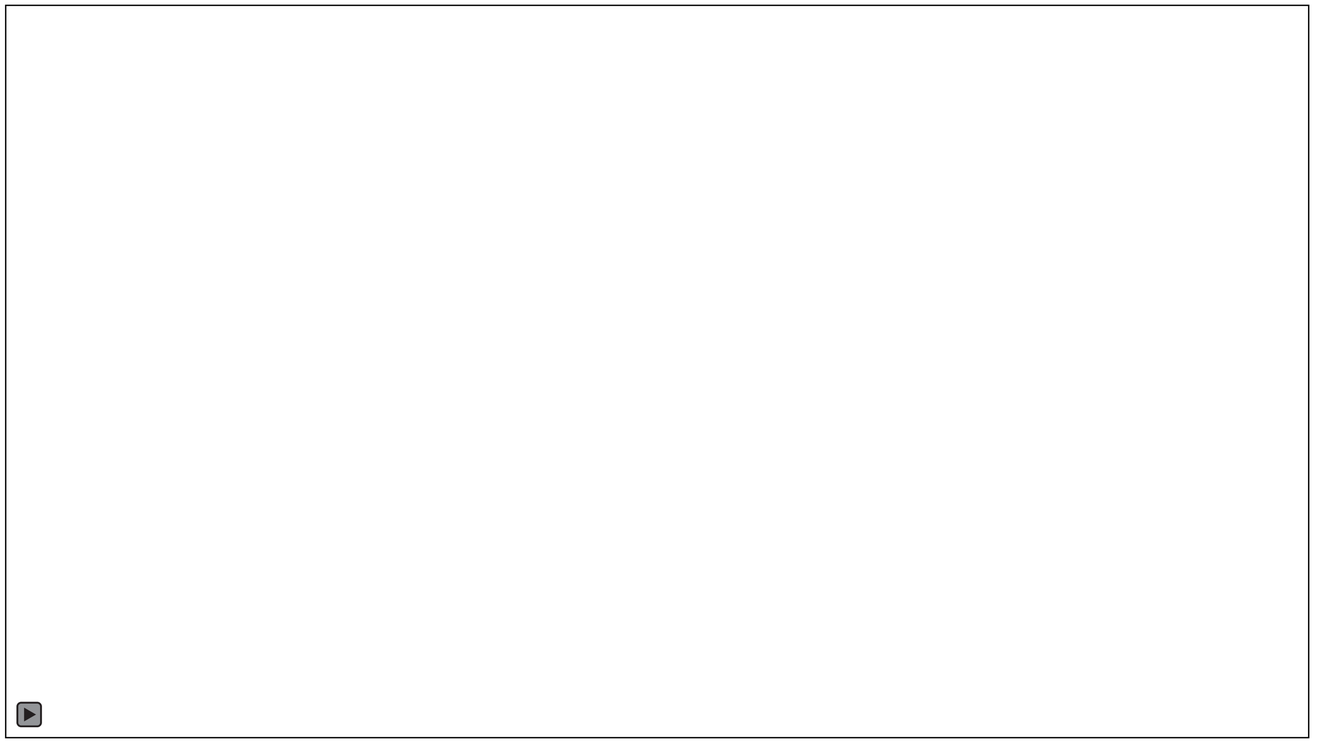
If yes, models should work beyond familiar sequences, organisms, and evolutionary contexts

APEX learned sequence-to-function relationships

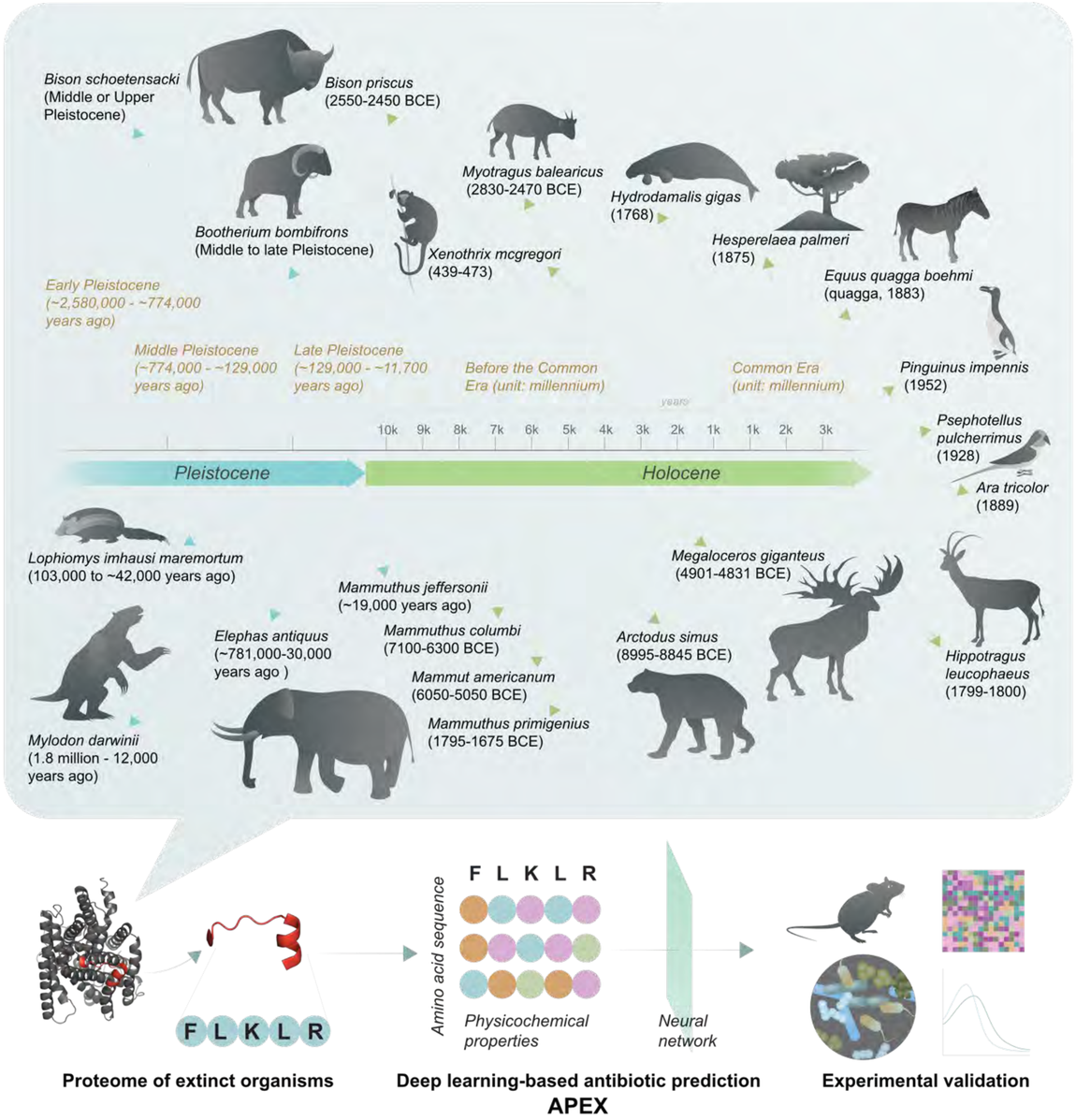


Can we design function directly from sequence?

MGLSDGEWQLVLNVWGKV
EADIPGHGQEVLIRLFKSH

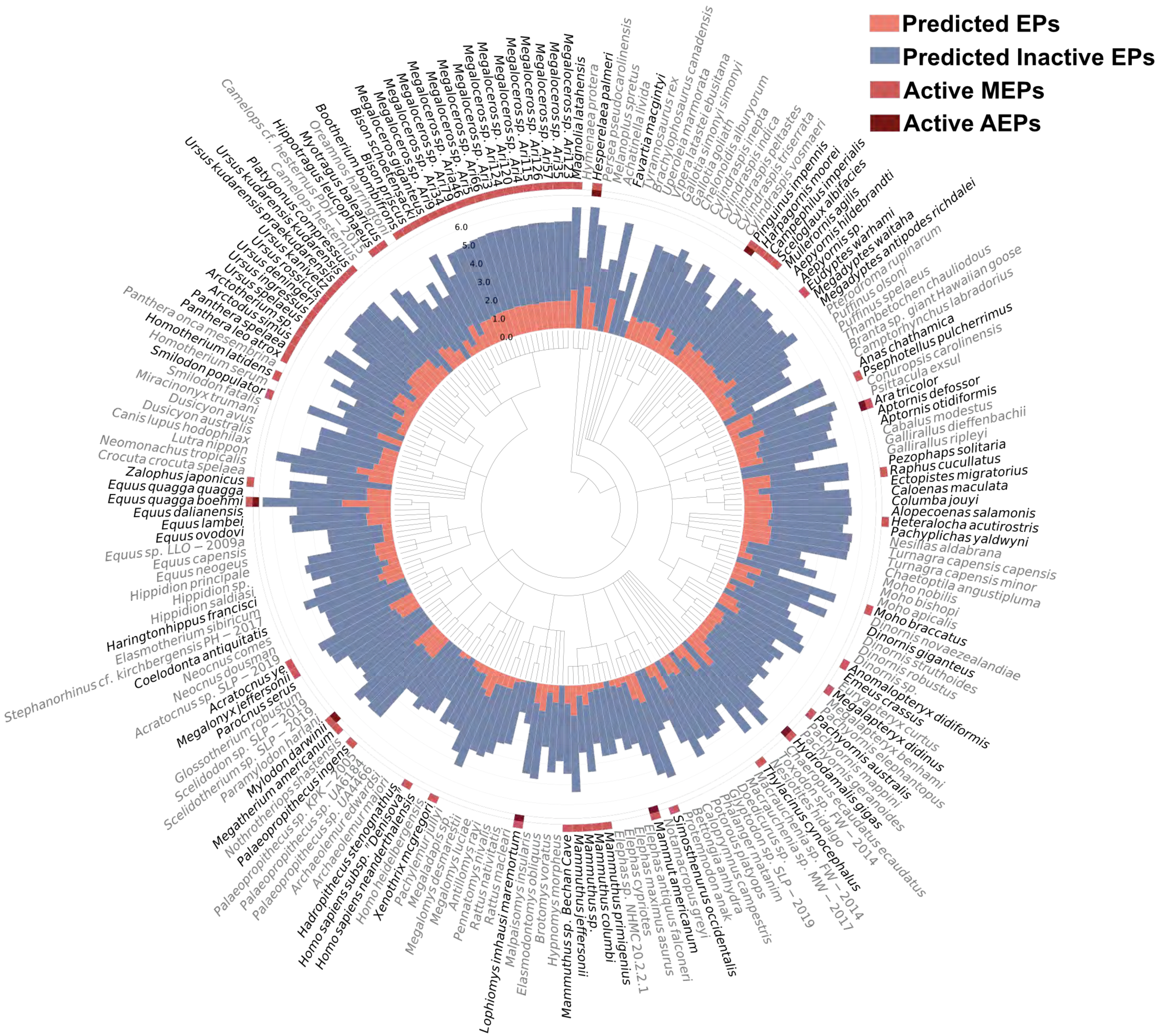


Ancient biology expanded the antibiotic search space

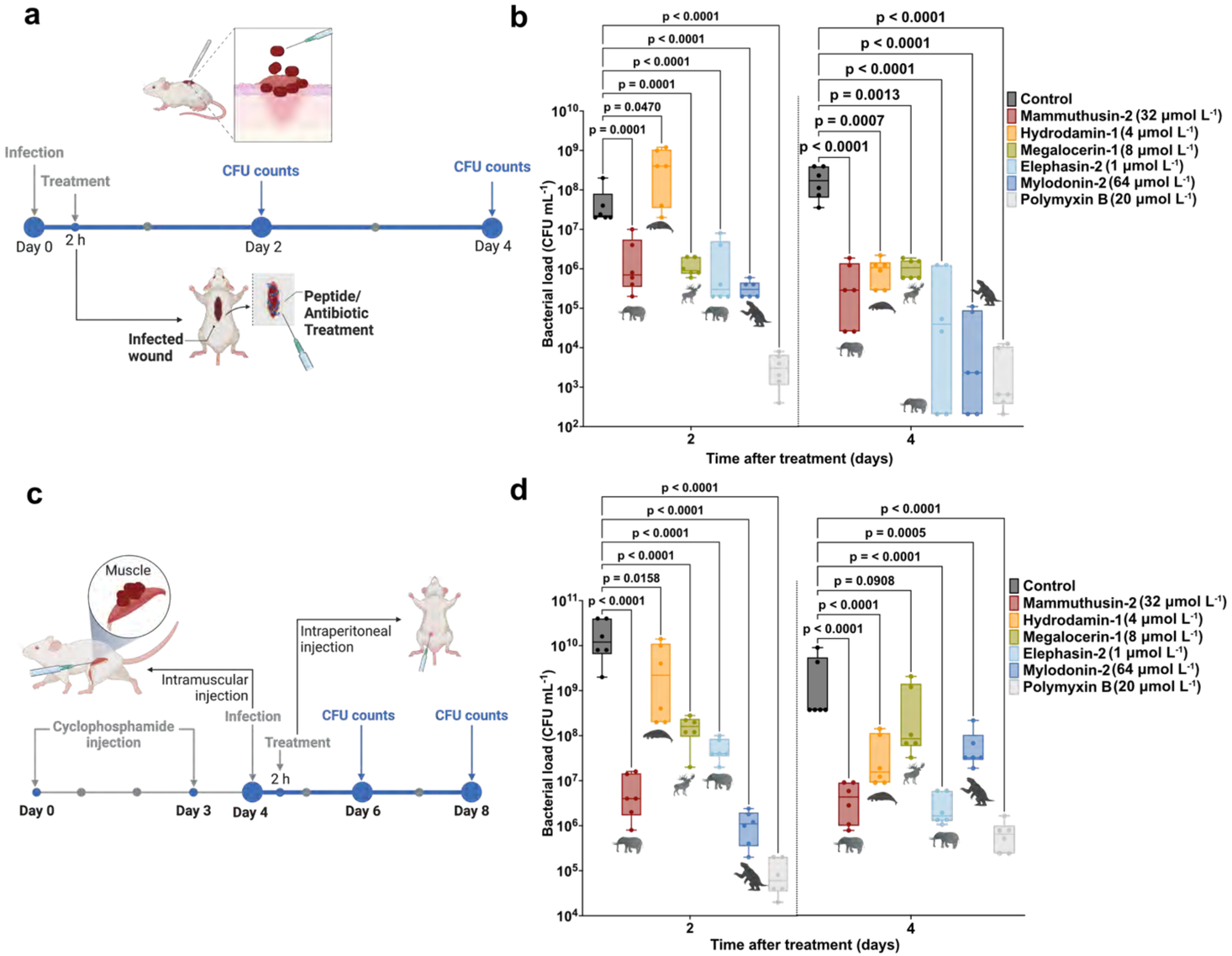


Wan et al. Nature Biomedical Engineering, 2024
Wan et al. bioRxiv, 2023

Ancient biology expands the searchable space of life



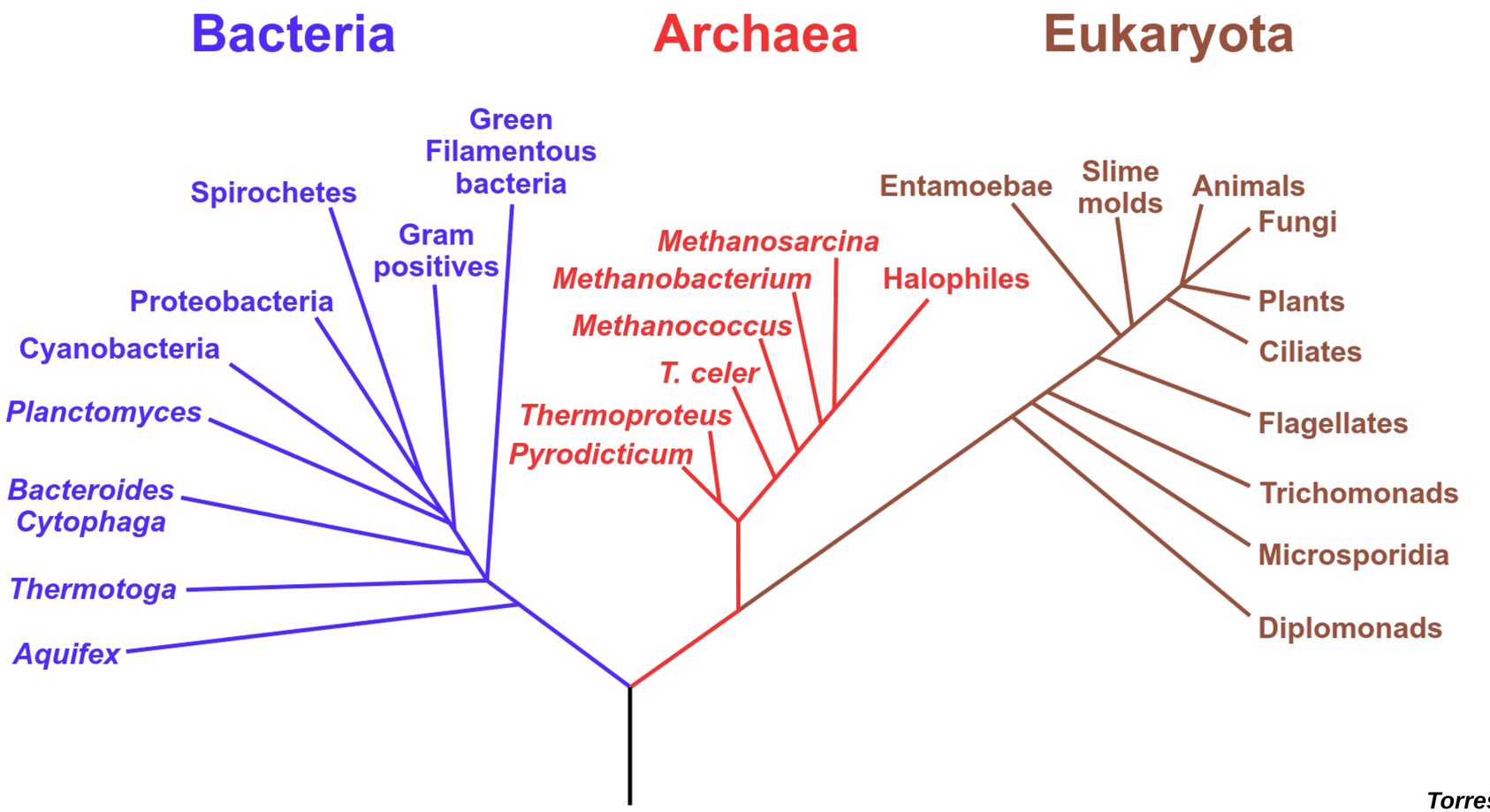
Antibiotics from extinct organisms worked in infection models



Discovered antibiotic molecules in the woolly mammoth (e.g., mammuthusin-2), ancient sea cow, giant sloth, and extinct giant elk with efficacy in preclinical infection models

Wan et al. Nature Biomedical Engineering, 2024
Wan et al. bioRxiv, 2023

The Tree of Life is an antibiotic search space



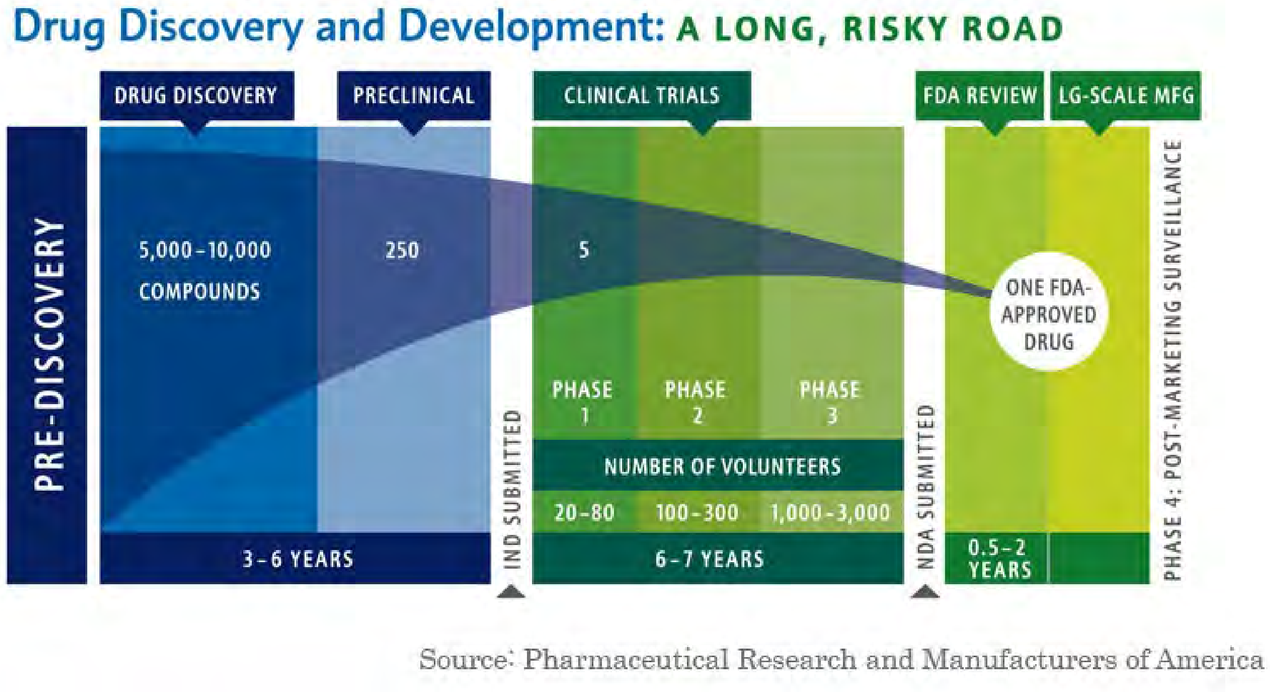
Torres et al. Nature Microbiology 2025
Torres et al. bioRxiv, 2024

Santos-Júnior et al. Cell, 2024
Santos-Júnior et al. bioRxiv, 2023

Torres et al. Cell, 2024
Torres et al. bioRxiv, 2023

https://organismalbio.biosci.gatech.edu/biodiversity/prokaryotes-bacteria-archaea-2/

Antibiotic discovery now moves at digital speed



Source: Pharmaceutical Research and Manufacturers of America

In a few hours, we can discover hundreds of thousands of candidates

Can go from discovery to synthesis and testing within 1 week

Nature Machine Intelligence, 2026

Leyva et al. Nature Machine Intelligence, 2025

Torres, Wan et al. Nature Microbiology, 2025

Guan et al. Nature Comm, 2025

Torres, Chen et al. Cell Biomaterials, 2025

Santos-Júnior et al. Cell, 2024

Wan et al. Nature Biomedical Engineering, 2024

Torrance and de la Fuente-Nunez. Nature Biotech, 2024

Torres et al. Cell, 2024

Wan et al. Nature Rev. Bioengineering, 2024

de la Fuente-Nunez. PLOS Biology, 2024

Torres, Cesaro et al. Trends Biotech, 2024

Wong et al. Science, 2023

Santos-Júnior et al. bioRxiv, 2023

Torres et al. bioRxiv, 2023

Wan et al. bioRxiv, 2023

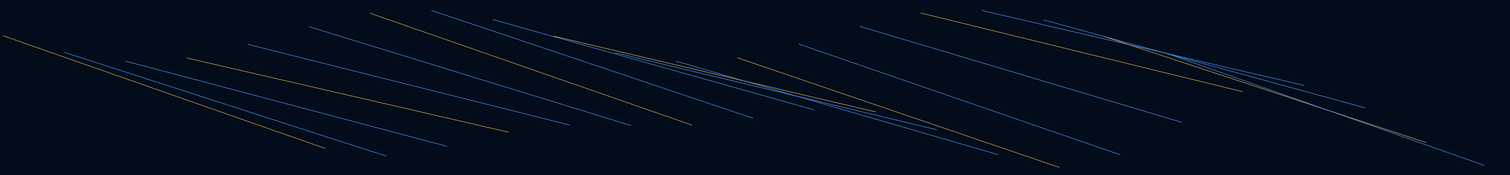
Maasch et al. Cell Host & Microbe, 2023

Maasch et al. bioRxiv, 2022

Torres et al. Nature Biomedical Engineering, 2022

Porto et al. Nature Communications, 2018

From discovering function to generating it



ApexGO generates and optimizes antibiotic candidates

First ground-truth experimental validation of generative Bayesian optimization in any setting

Generative AI framework integrates a transformer-based variational autoencoder with Bayesian optimization to design and optimize antibiotics

85% hit rate

72% success rate enhancing antimicrobial activity

Collaboration with Jake Gardner Lab

Nature Machine Intelligence, 2026
Torres et al. bioRxiv, 2024

ApexGO candidates are active in preclinical models

Nature Machine Intelligence, 2026
Torres et al. bioRxiv, 2024

Can AI anticipate future pathogens?

ApexOracle tests whether AI can anticipate future pathogens

Combines pathogen genomes and literature with molecular embeddings for unified prediction and generation

Leng et al. bioRxiv, 2025

ApexOracle simulated a future superbug outbreak

Two WHO-priority multidrug-resistant strains never seen during training

***E. coli* AR-0349** *Colistin-resistant*

Colistin is often the last-resort antibiotic. Resistance to it represents one of the most dangerous forms of antimicrobial resistance.

***P. aeruginosa* PA5257** *Fluoroquinolone / Carbapenem-resistant*

Resistant to two major antibiotic classes. WHO categorizes this pathogen as a critical-priority threat for new antibiotic development

Task: design new agents and identify existing molecules active against strains the model had never seen

ApexOracle generated multiple therapeutic modalities

Strain-Selective Linear Peptide

ApexOracle-3

P. aeruginosa PA5257

Selective activity against the target strain among a broad panel of bacteria

Generated

D-Amino Acid Containing Peptide

ApexOracle-12

P. aeruginosa PA5257

First AI de novo designed antimicrobial peptide incorporating D-amino acids

Generated

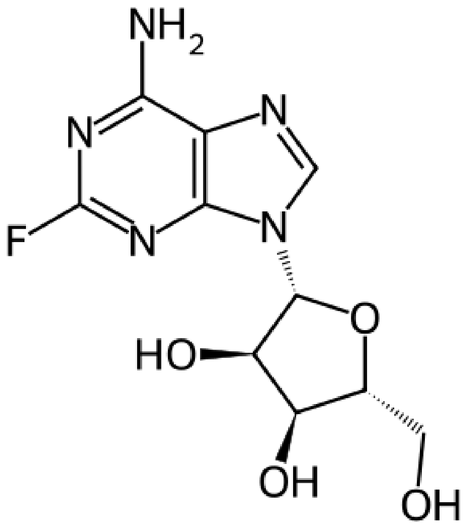
Potent Cyclic Peptide

ApexOracle-23

E. coli AR-0349

Experimental MIC = 8 µmol/L — first AI de novo designed antimicrobial cyclic peptide

Generated



Small Molecule Inhibitor

2-Fluoroadenosine

E. coli AR-0349

Identified using model trained exclusively on peptide data — cross-modal generalization

Predicted

Conflict of Interest Disclosure

CO-FOUNDER + SCIENTIFIC ADVISOR

Peptaris, Inc.
Co-founder and scientific advisor

CONSULTING SERVICES

Invaio Sciences
Consulting services

SCIENTIFIC ADVISORY BOARDS

- Basecamp Research
- Intera Bio
- Nowture S.L.
- Peptidus
- European Biotech Venture Builder
- Peptide Drug Hunting Consortium (PDHC)
- ePhective Therapeutics, Inc.
- Phare Bio

Acknowledgments



Illustration by Jianing Bai

delafuentelab.seas.upenn.edu

cfuente@upenn.edu

@delafuentelab

@delafuentelab.bsky.social

OUR TEAM

Angela Cesaro
Marcelo Torres
Fangping Wan
Ajay Yagati
Erik Hartman
Hyun-Su Lee
Jenny Bai
John Connolly
Hanqun Cao
Changge Guan
Rakesh Krishnan
Ben Sprung
Xiaoqiong Xia
Anlan Zhao
Anna Crysler
Tianang Leng
Shiyu Ji
Abdullah Ali
Yiming Wang
Madeline Calvert

COLLABORATORS

Jake Gardner — Penn
Squire Booker — Penn
Michel Koo — Penn
Jorge Henao-Mejía — Penn
Ravi Radhakrishnan — Penn
Kate Stebe — Penn
Hydar Ali — Penn
Norbert Pardi — Penn
Sarah Tishkoff — Penn
Ben Abella — Penn
Ronald Collman — Penn
Henry Daniell — Penn
Flavia Vitale — Penn
Payel Das — IBM
Samuel Sánchez — IBEC
Joe Zackular — Penn
Harvey Friedman — Penn
Gary Cohen — Penn
Sita Awasthi — Penn
Christoph Thaiss — Penn
Ami Bhatt — Stanford
Ewa Szczurek — Warsaw/HMGU
Jiangning Song — Monash
Luis Pedro Coelho — QUT
Octavio Franco — UCDB
Carlos Brizuela — CICESE
William Araujo — UNICAMP
Ennio Notomista — U. Naples
Renee Fleeman — UCF
Angela Arciello — U. Naples
Lefteris Mylonakis — Houston
Pranam Chatterjee — Duke
Vani X. Oliveira Jr. — UFABC
Olalla Vázquez — Marburg
Fabien Plisson — CINVESTAV
Sandra Muñoz Bonilla — CSIC
Robert Vácha — Masaryk
Guangyong Chen — CUHK
Igor Iatsenko — MPI Infection

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