

# *New approaches to hepatitis B and D using AI tools*

Amalio Telenti, MD PhD

Managing Director

Trail Biomed

# Discussion points



**CURRENT DIRECTIONS IN AI  
RESEARCH AND DEVELOPMENT**



**A CLOSER LOOK AT CO-SCIENTISTS**



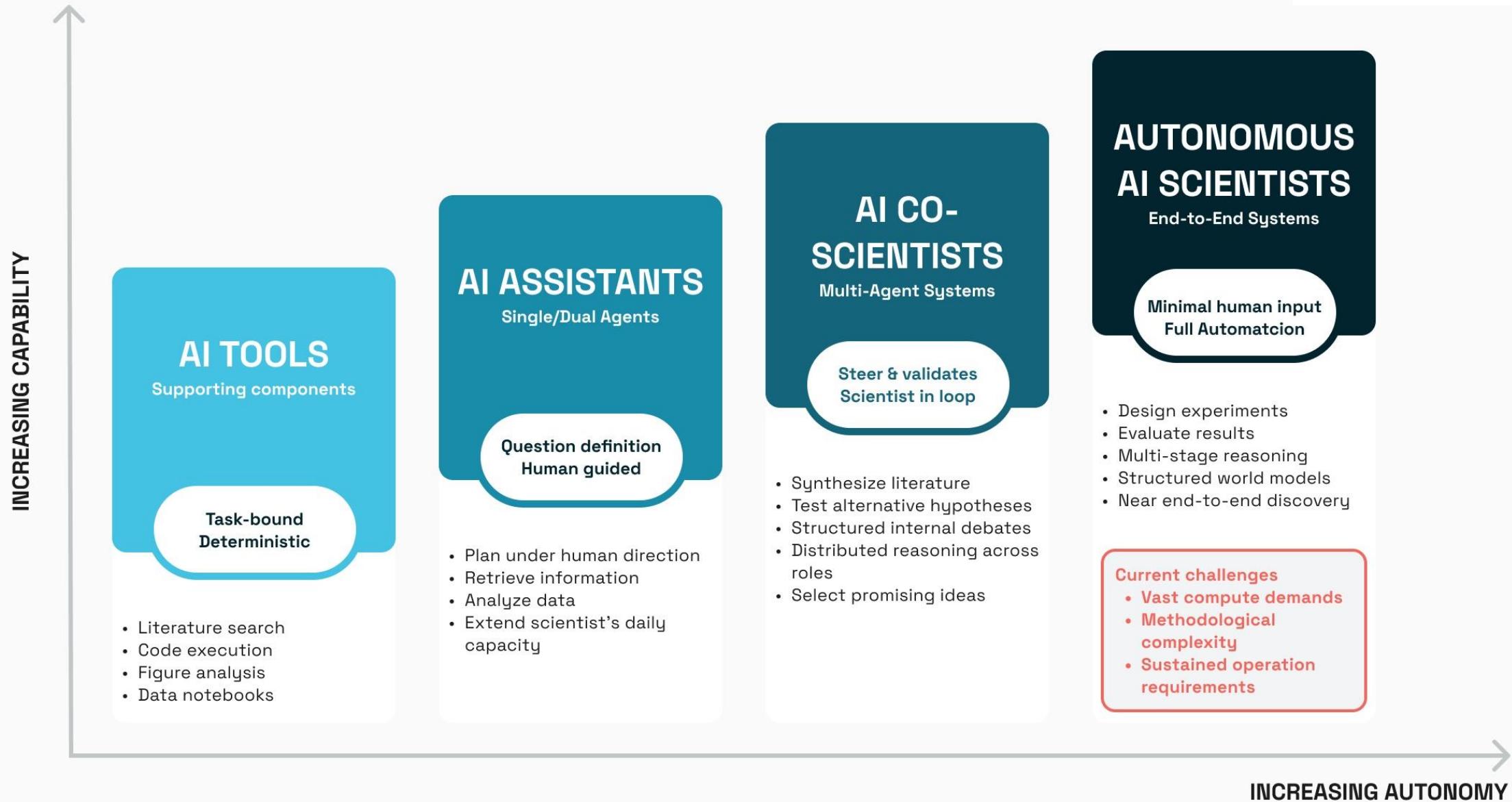
**ADDRESSING HEPATITIS RESEARCH  
AND CLINICAL PRACTICE**

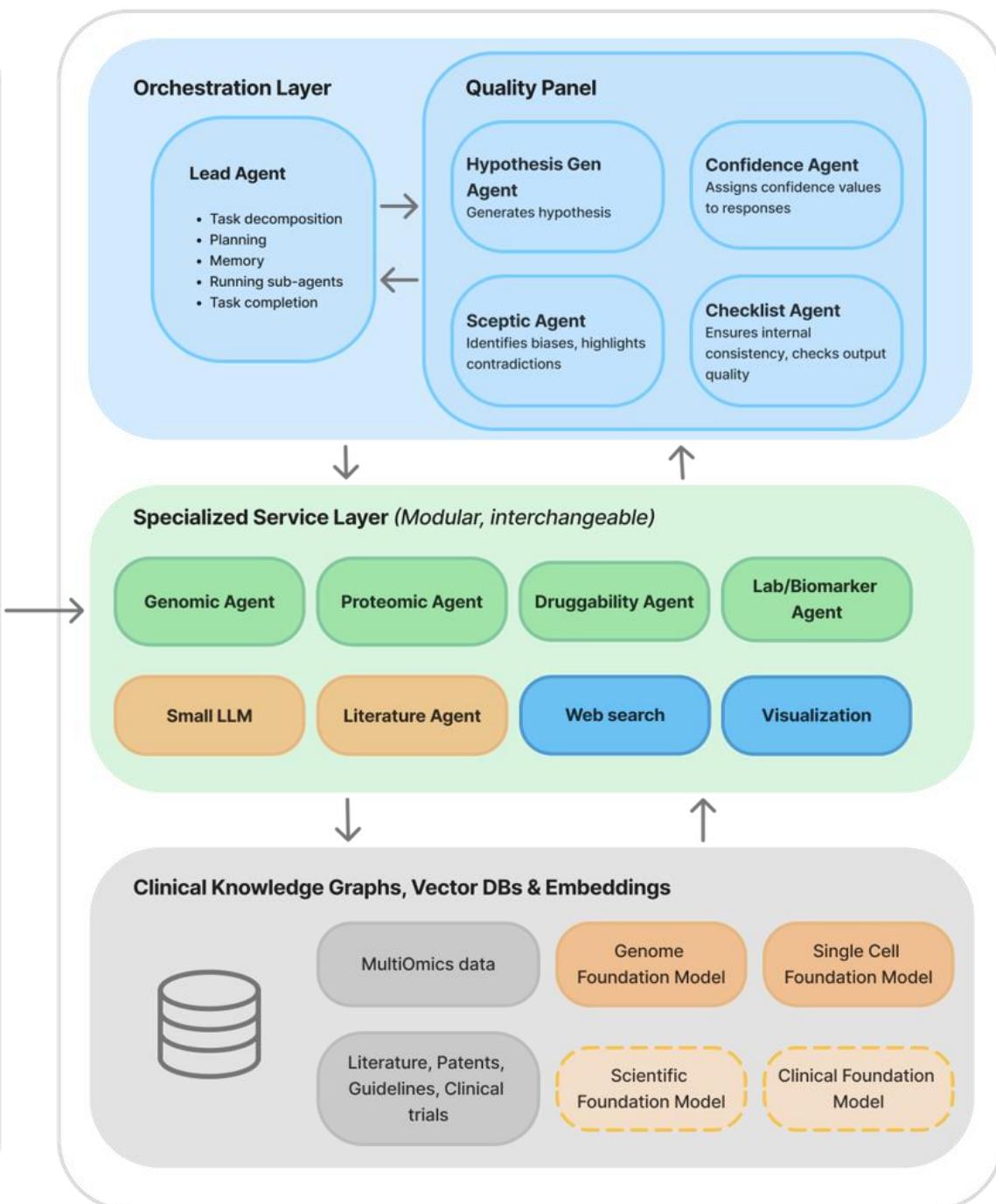
# Current directions in AI research and development



- LLMs, coding agents and co-scientists
- Foundation models of science

# THE SPECTRUM OF AI SCIENTISTS





# What for?

- ★★★ • Brainstorming and exploration
- ★★ • Literature and evidence synthesis
- ★★★ • Flexible data retrieval and review
- ★★ • Guided analysis and workflow planning
- ★ • Hypothesis generation
- ★★ • Reasoning and critique
- ★★ • Experimental planning

# Current directions in AI research and development



- LLMs, coding agents and co-scientists
- Foundation models of science

# Foundation Models in Biology

## Cellular Analysis Models

- **Virtual-cell / single-cell models** (scGPT, Geneformer, scFoundation)

## Genomic Sequence Modeling

- **Genomic sequence models** (Nucleotide Transformer, DNABERT-2, Evo)

## Protein and Molecular Insights

- **Protein foundation models** (ESM family, AlphaFold-class models)

## Metabolome Insights

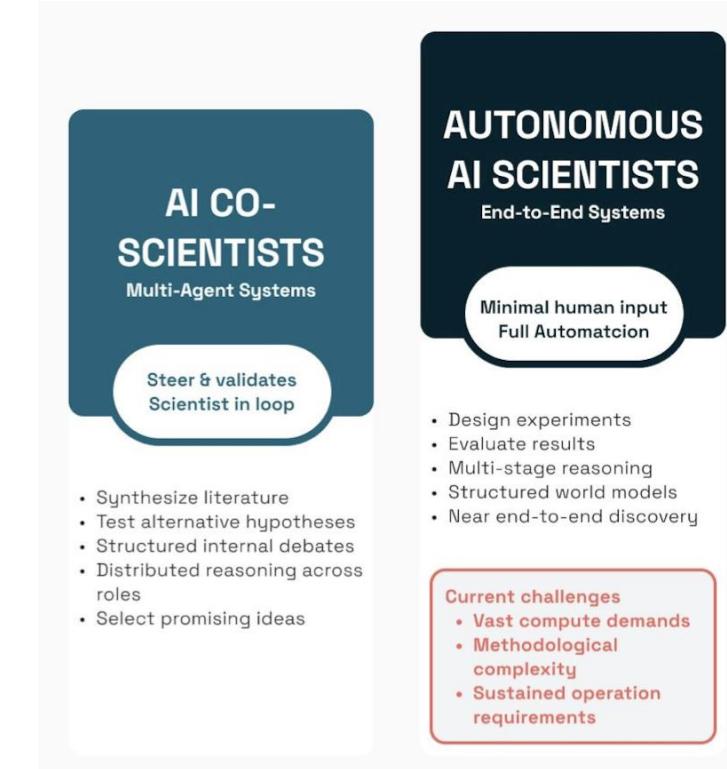
- **Metabolomics & MS foundation models** (MetaboFM, MS encoders)



# A closer look at co-scientists



- A comparison of offers
- Deep loops
- Lab-in-the-loop



# A closer look at co-scientists



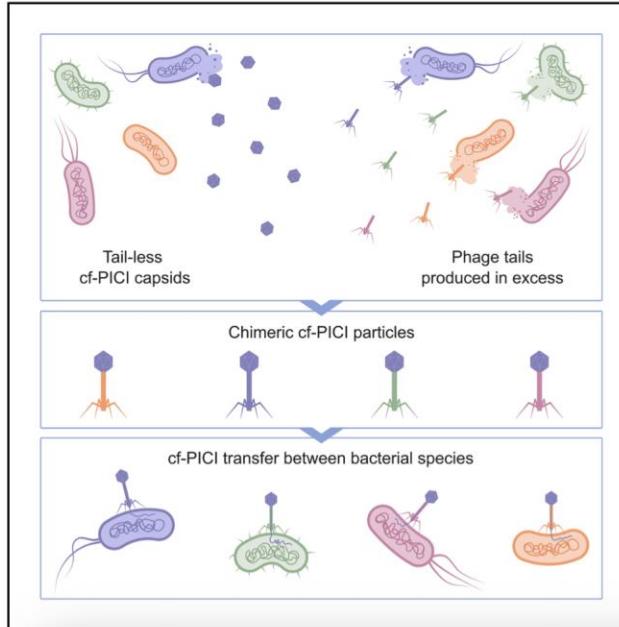
- **Biomni**  
<https://biomni.stanford.edu/>
- **FutureHouse Kosmos**  
<https://edisonscientific.com/>
- **ToolUniverse**  
<https://arxiv.org/abs/2509.23426>)

# Deeper loops

## Cell

### Chimeric infective particles expand species boundaries in phage-inducible chromosomal island mobilization

#### Graphical abstract



#### Authors

Lingchen He, Jonasz B. Patkowski, Jinlong Wang, ..., Alfred Fillol-Salom, Tiago R.D. Costa, José R. Penadés

#### Correspondence

t.costa@imperial.ac.uk (T.R.D.C.), j.penades@imperial.ac.uk (J.R.P.)

#### In brief

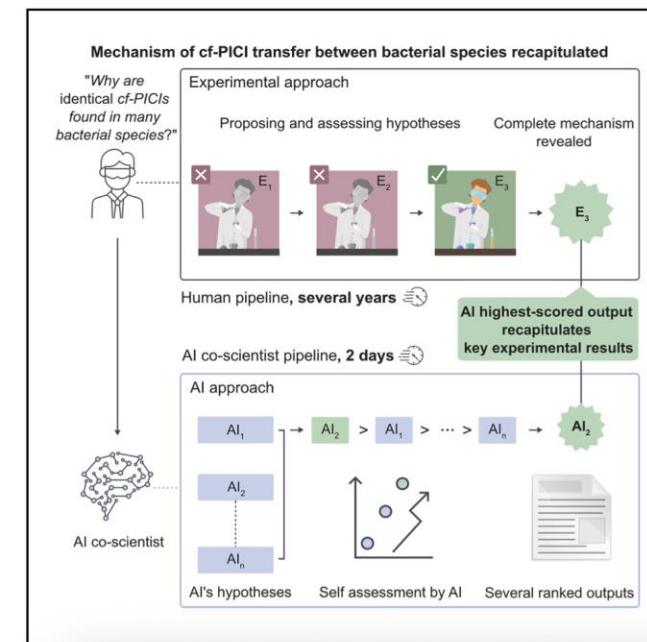
Capsid-forming PICIs (cf-PICIs) produce their own capsids and exploit phage tails from unrelated species to transfer their DNA across bacterial hosts. This tail piracy enables broad dissemination and reveals a new mechanism of horizontal gene transfer with major implications for bacterial evolution and pathogenesis.

## Article

## Cell

### AI mirrors experimental science to uncover a mechanism of gene transfer crucial to bacterial evolution

#### Graphical abstract



#### Authors

José R. Penadés, Juraj Gottweis, Lingchen He, ..., Vivek Natarajan, Alan Karthikesalingam, Tiago R.D. Costa

#### Correspondence

j.penades@imperial.ac.uk (J.R.P.), natviv@google.com (V.N.), alankarthi@google.com (A.K.), t.costa@imperial.ac.uk (T.R.D.C.)

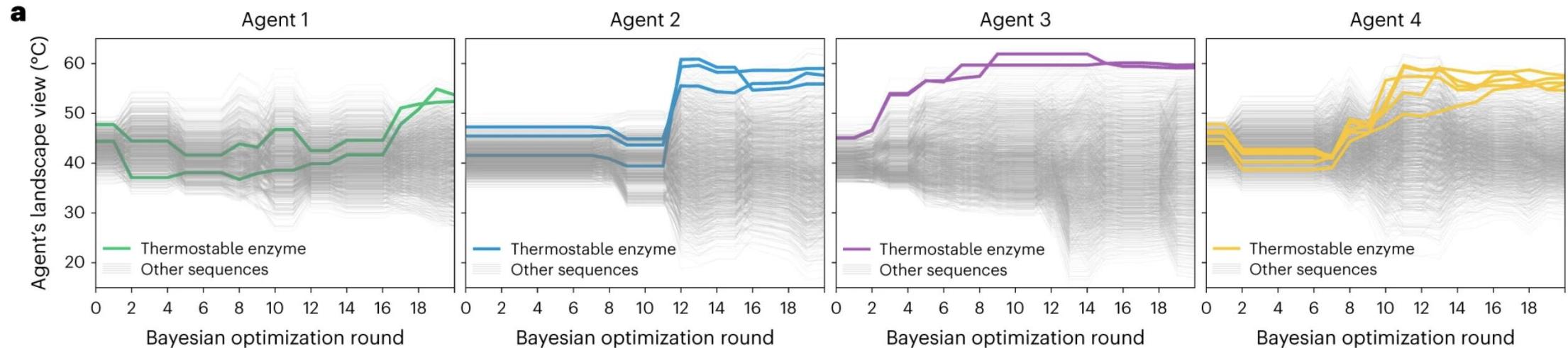
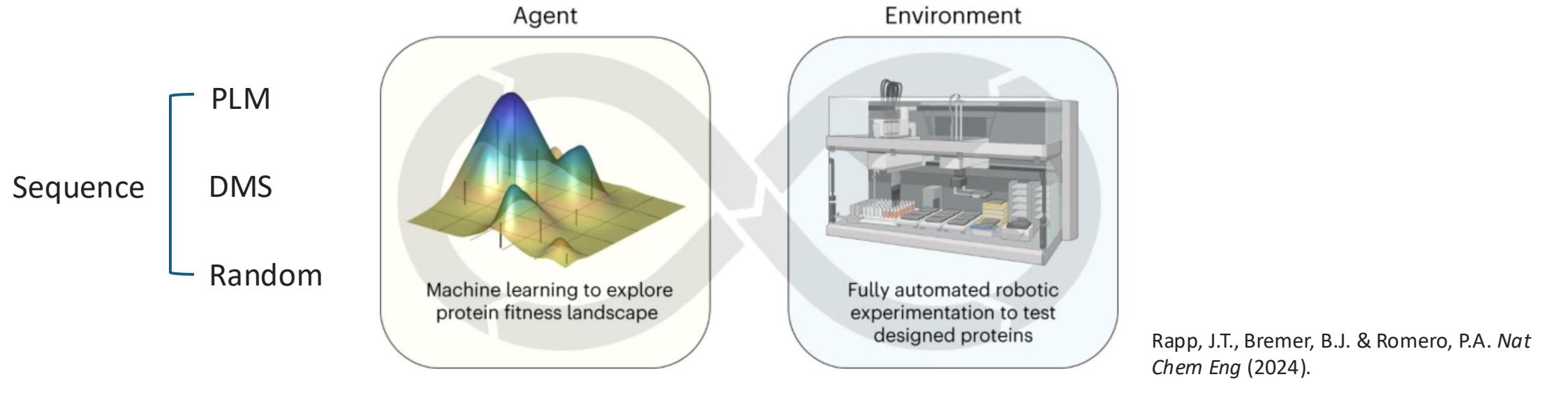
#### In brief

By solving a previously unsolved biological question, the AI co-scientist predicted a complex mechanism of gene transfer and generated hypotheses that opened new research directions, illustrating AI's potential as a creative engine in discovery.

## Theory

# Lab-in-the-loop

train  
biomed



# Addressing hepatitis research and clinical practice



- Connect to a co-scientist
- Build/Restrict/Identify your resource

# Addressing hepatitis research



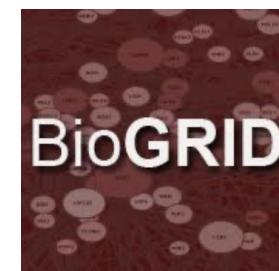
**ChatGPT:**  
"Identify hepatitis host factors"



**ChatGPT:**  
"Identify hepatitis host factors in CRISPR screens in BioGrid"



**Biomni:**  
"Identify hepatitis host factors in CRISPR screens in BioGrid"



# ChatGPT 5.2 ("Identify hepatitis host factors in CRISPR screens in BioGrid")



| Virus | Host Gene      | Functional Category    | Screen Phenotype | Viral Stage        | Evidence Type      |
|-------|----------------|------------------------|------------------|--------------------|--------------------|
| HAV   | UFM1           | UFMylation             | KO ↓ infection   | Translation        | Genome-wide CRISPR |
| HAV   | UBA5           | UFMylation E1          | KO ↓ infection   | Translation        | Genome-wide CRISPR |
| HAV   | UFC1           | UFMylation E2          | KO ↓ infection   | Translation        | Genome-wide CRISPR |
| HAV   | RPL26          | Ribosome / translation | KO ↓ infection   | Translation        | Genome-wide CRISPR |
| HAV   | PAPD7          | TRAMP-like RNA tailing | KO ↓ infection   | RNA metabolism     | Genome-wide CRISPR |
| HBV   | ZCCHC14        | RNA binding            | KO ↓ HBsAg       | Antigen production | Genome-wide CRISPR |
| HBV   | TENT4A (PAPD7) | RNA tailing            | KO ↓ HBsAg       | RNA stability      | Genome-wide CRISPR |
| HBV   | TENT4B (PAPD5) | RNA tailing            | KO ↓ HBsAg       | RNA stability      | Genome-wide CRISPR |
| HBV   | HSD17B12       | Lipid metabolism       | KO ↓ infection   | Replication        | Genome-wide CRISPR |
| HCV   | CD81           | Entry receptor         | KO ↓ infection   | Entry              | CRISPR screen      |
| HCV   | CLDN1          | Tight junction         | KO ↓ infection   | Entry              | CRISPR screen      |
| HCV   | OCLN           | Tight junction         | KO ↓ infection   | Entry              | CRISPR screen      |
| HCV   | TRIM26         | E3 ubiquitin ligase    | KO ↓ replication | Replication        | Genome-wide CRISPR |
| HCV   | SEC14L2        | Lipid transport        | KO ↓ replication | Replication        | CRISPR screen      |
| HEV   | RAB5A          | Early endosome         | KO ↓ replication | Replication        | Genome-wide CRISPR |
| HEV   | VPS45          | Vesicle trafficking    | KO ↓ replication | Replication        | Genome-wide CRISPR |
| HEV   | WDR81          | Endosomal maturation   | KO ↓ replication | Replication        | Genome-wide CRISPR |



# Biomni ("Identify hepatitis host factors in CRISPR screens in BioGrid")



## HBV Host Factors (5 factors):

- ZCCHC14 - RNA-binding protein required for HBsAg production [1]
- TENT4A (PAPD5) - Noncanonical poly(A) polymerase stabilizing HBV RNAs [2]
- TENT4B (PAPD7) - Noncanonical poly(A) polymerase stabilizing HBV RNAs [2]
- SLC10A1 (NTCP) - Cell surface receptor required for HBV entry [3]
- CDKN2C - Cell cycle regulator affecting HBV through G1 state modulation [4]



## HCV Host Factors (8 factors):

- EGFR - Epidermal Growth Factor Receptor involved in HCV entry
- CD81 - HCV entry coreceptor
- CLDN1 (Claudin-1) - HCV entry factor
- OCLN (Occludin) - HCV entry factor
- LDLR - LDL receptor for HCV entry
- SCARB1 (SR-B1) - HCV entry receptor
- PIK3CA - PI3K involved in HCV replication
- PIK3C3 (VPS34) - PI3K involved in HCV replication



## PPI (578 interactions)

- Unique interacting partners: 380

# Overlap and consistency

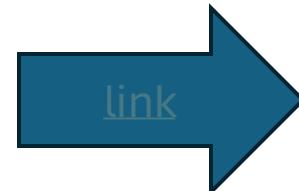
| Aspect                      | ChatGPT-CRISPR / BioGRID         | ChatGPT (Knowledge)                | Biomni-CRISPR / BioGRID                        |
|-----------------------------|----------------------------------|------------------------------------|--|
| Methodology                 | Directed functional genetics     | Mechanistic literature             | Coding agent integration of CRISPR and BioGRID |
| Focus                       | Cell-intrinsic host dependencies | Entry, immunity, genetics, disease | CRISPR and PPI                                 |
| Immune factors              | ✗                                | ✓                                  | ✗  |
| Entry receptors             | Partial                          | ✓                                  | ✓  |
| RNA stability / translation | Strong                           | Moderate                           | Strong   |
| Cell cycle / signaling      | Minimal                          | Moderate                           | ✓  |

Open access from Trail



<https://trailbiomed.app/>

Task-specific app to explore target  
identification and druggability using  
genomics or proteomics



# Druggability - 1



## **Target Validation and Biological Relevance:**

Confirm that the target plays a critical, disease-relevant role and is non-redundant within its biological pathway.

**Pathological Relevance:** Demonstrate association with disease progression and therapeutic benefit from modulation (e.g., inhibition, activation).

**Homology and Precedence:** Evaluate conservation across species and precedent for druggability in related protein families.

## **Structural and Sequence-Based Assessment:**

Assess presence of druggable domains, defined binding pockets, and available high-resolution structural data.

**Ligandability:** Identify known ligands, tool compounds, or fragments demonstrating binding feasibility.

**Chemical Tractability:** Evaluate feasibility of small-molecule or biologic targeting; assess structure-based design potential.

**Selectivity and Toxicity:** Evaluate on-target and off-target risks; determine therapeutic window and safety profile.

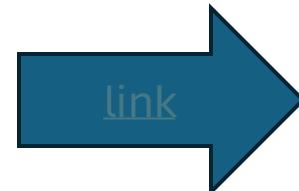
**Risk Assessment:** Continuously monitor for compensatory pathways, resistance mechanisms, and safety liabilities.

Open access from Trail



<https://trailbiomed.app/>

Task-specific app to explore target  
identification and druggability using  
genomics or proteomics



# Addressing hepatitis diagnostics and clinical practice



- Build/Identify your resource  
(=RAG, retrieval augmented generation)

A large, dark blue arrow-shaped button pointing to the right. The word "Test" is written in a white, sans-serif font, centered within the button.

Test

# Hepatitis Testing Support Agent

Interactive assistant for hepatitis testing based on:

- **OAML Guidelines (2010):** Test ordering and preparation
- **NIH Paper (Prasidhhrathsint & Stapleton, 2019):** Result interpretation

Ask questions about ordering tests, interpreting results, or understanding hepatitis serology.



Conversation



What tests should I order for chronic HCV?

[Order Preparation Assistant (OAML)]

## Summary

For chronic HCV, anti-HCV antibody is the appropriate screening test. Any patient with positive HCV antibody should be considered a chronic carrier and infectious until proven otherwise. HCV viral load testing is reserved for patients being considered for antiviral treatment or immunocompromised patients (OAML p4).

## Specific Test Orders

- Anti-HCV antibody - primary screening test for chronic HCV infection (OAML p4)
- HCV RNA (viral load) - only if:
  - Patient is being considered for antiviral treatment
  - Patient is immunocompromised (transplant, chemotherapy, corticosteroids, renal failure) (OAML p4)
- ALT, liver function tests, and abdominal ultrasound - recommended for specialist referral workup (OAML p4)

Requisition Details



# Summary



- There is real value in bringing AI solutions to **any research lab**
- **Understanding the offers** and uses are central to optimal implementation
- **Clinical and Diagnostic lab** implementations are also ready for testing/use