

New approaches to hepatitis B and D using AI tools

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Discussion points



**CURRENT DIRECTIONS IN AI
RESEARCH AND DEVELOPMENT**



A CLOSER LOOK AT CO-SCIENTISTS



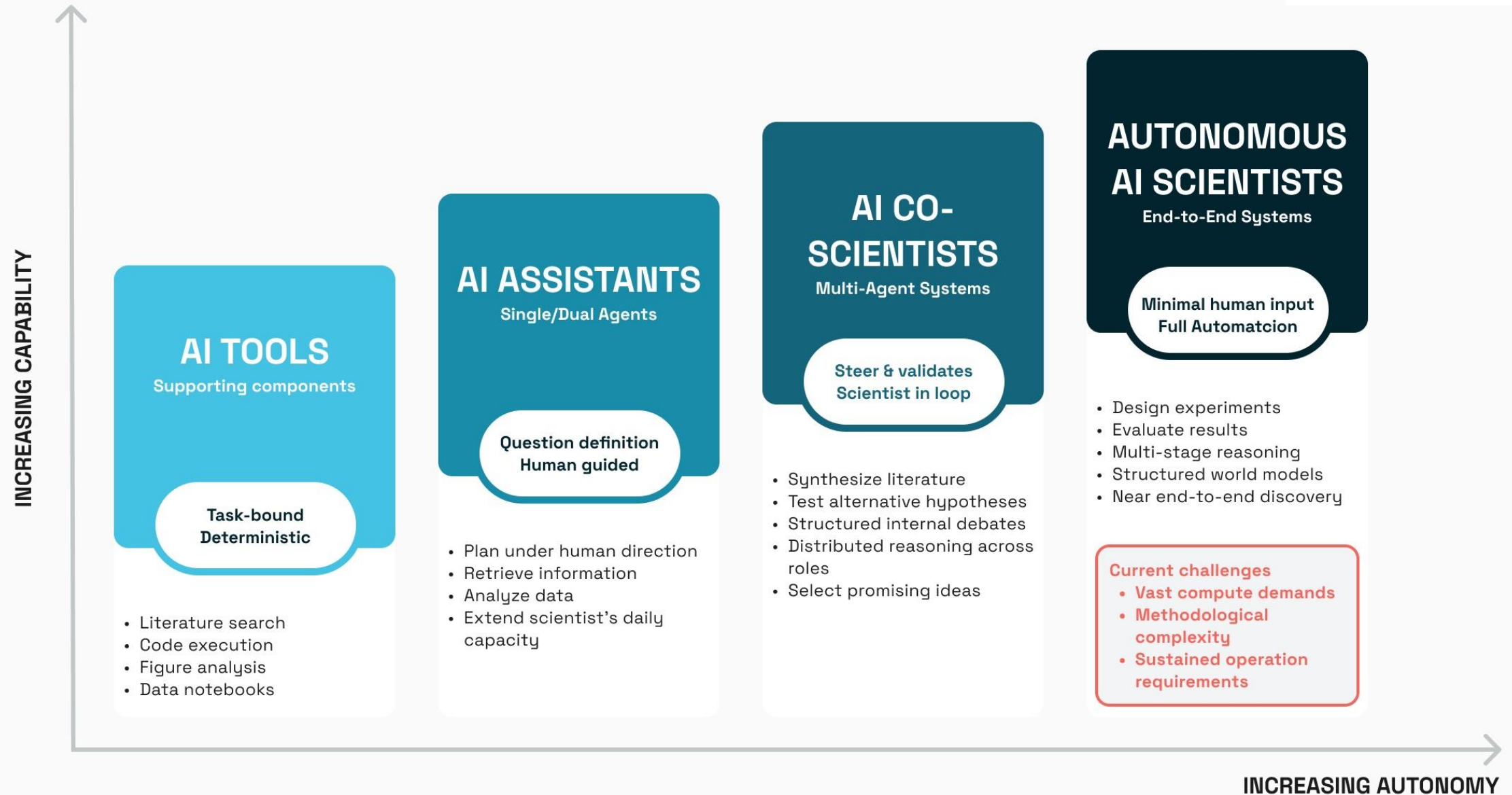
**ADDRESSING HEPATITIS RESEARCH
AND CLINICAL PRACTICE**

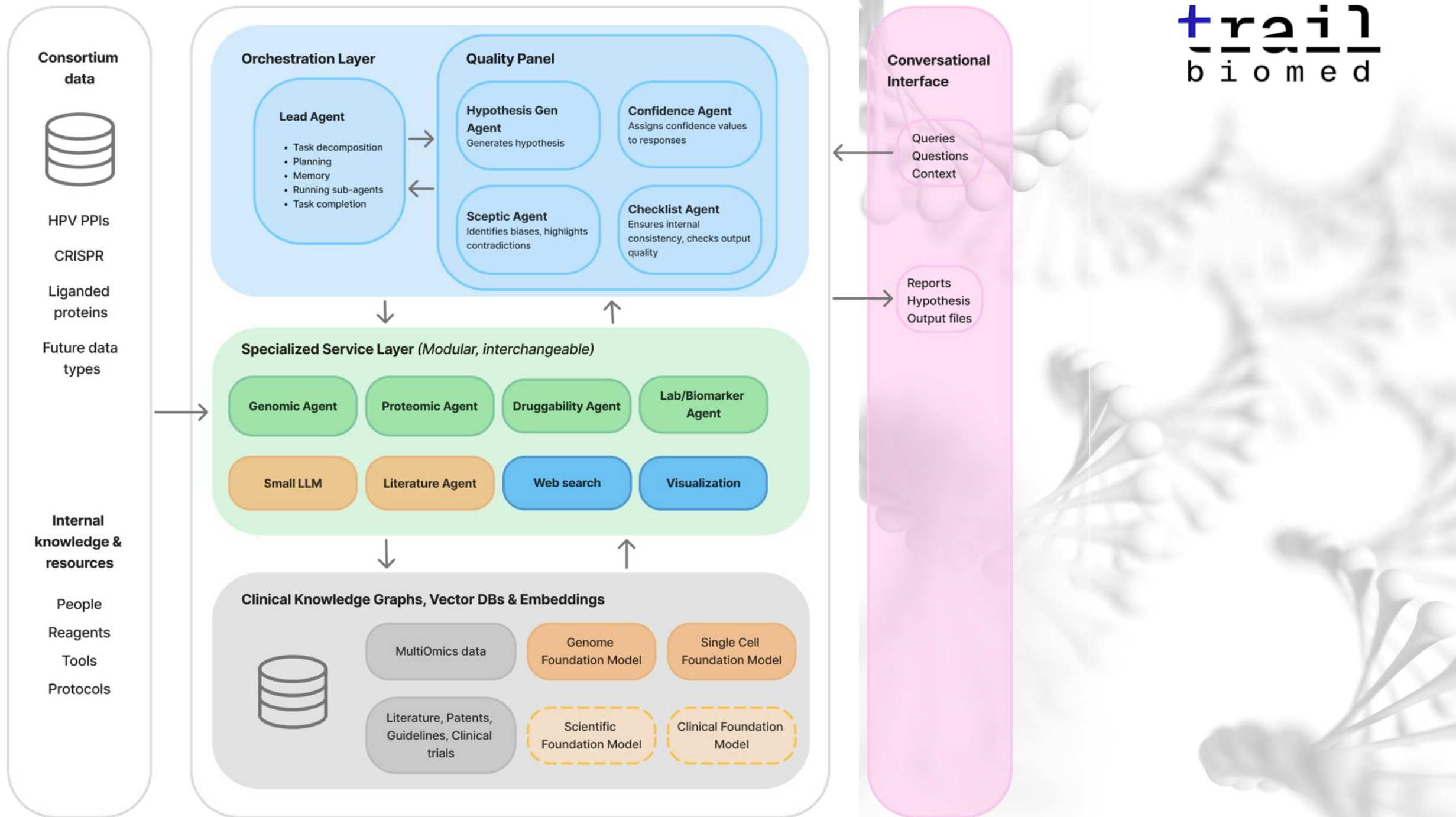
Current directions in AI research and development



- 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

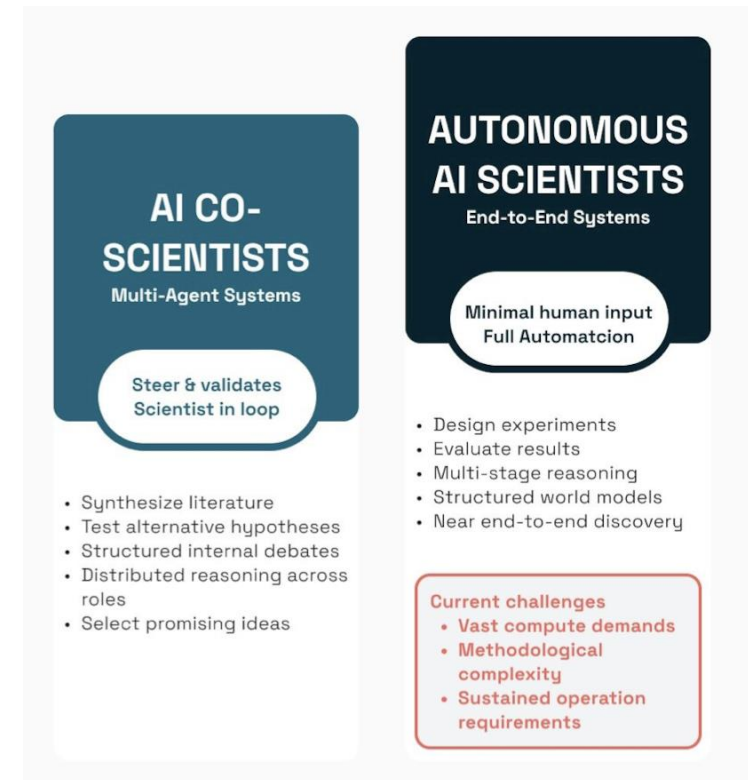
- **Protein foundation models** (ESM family, AlphaFold-class models)

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>)

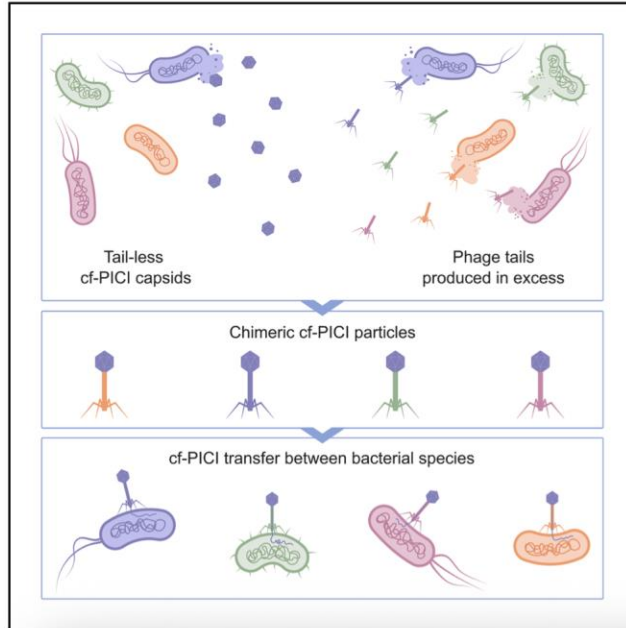
Deeper loops

Cell

Article

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

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In brief

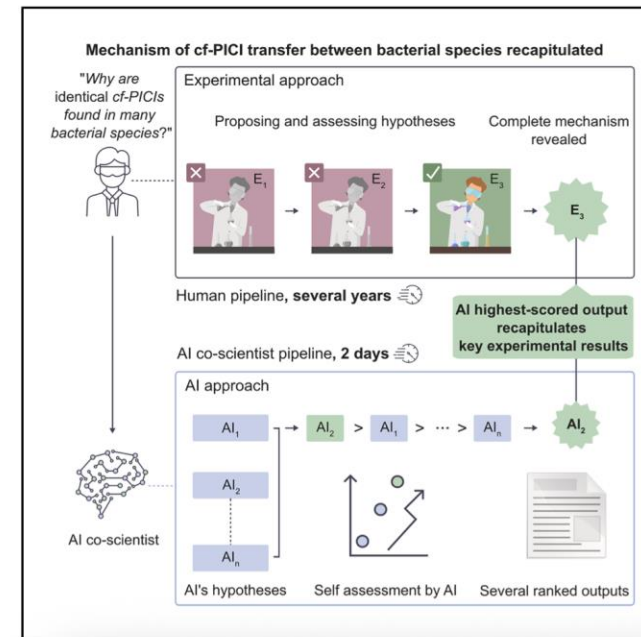
Capsid-forming PICs (cf-PICs) produce their own capsids and exploit phage tails from unrelated species to transfer their DNA across bacterial hosts. This tail piracy enables broad dissemination and reveals a new mechanism of horizontal gene transfer with major implications for bacterial evolution and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

Cell

Theory

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

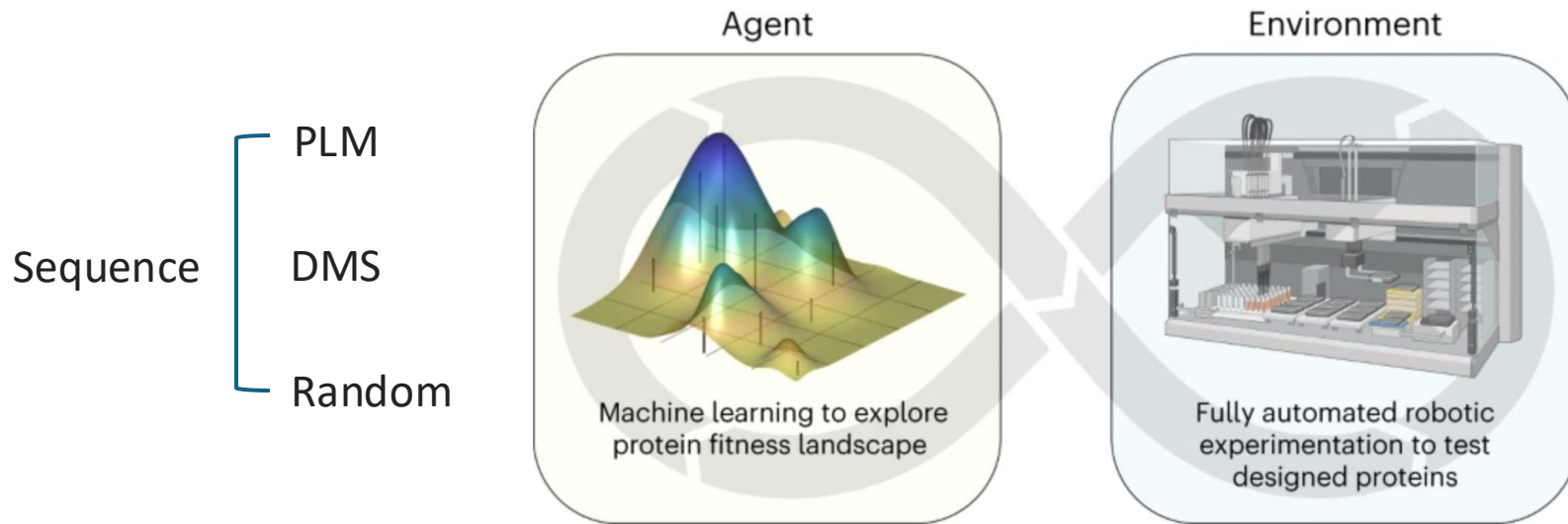
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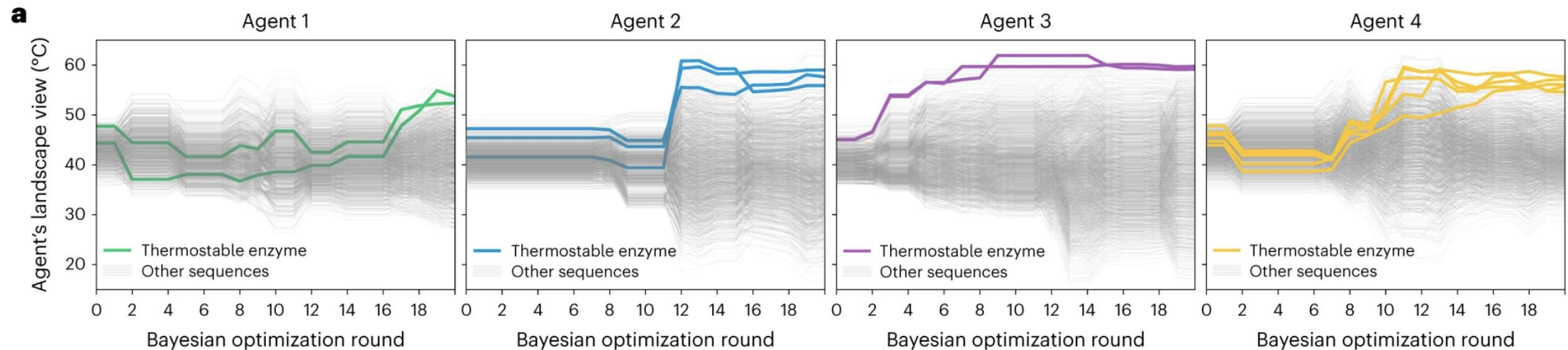
In brief

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.

Lab-in-the-loop



Rapp, J.T., Bremer, B.J. & Romero, P.A. *Nat Chem Eng* (2024).



Addressing hepatitis research and clinical practice



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

Addressing hepatitis research

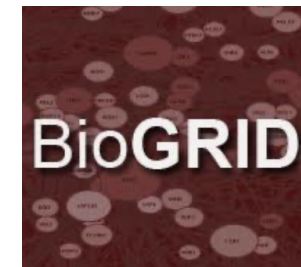
ChatGPT:
"Identify
hepatitis host
factors"



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



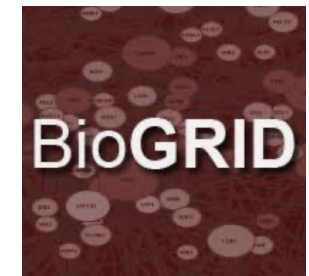
Biomni:
"Identify
hepatitis host
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ChatGPT 5.2 ("Identify hepatitis host factors in CRISPR screens in BioGrid")



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



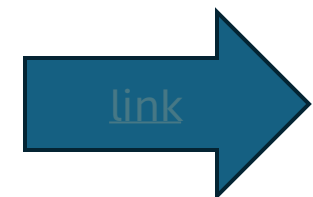
Overlap and consistency

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.

Druggability - 2

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.

Druggability - 3

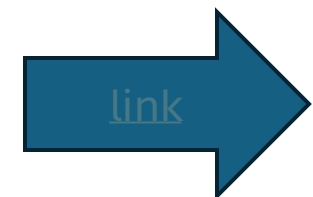
Selectivity and Toxicity: Evaluate on-target and off-target risks; determine therapeutic window and safety profile.

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



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

A blue arrow-shaped button pointing to the right, containing the word "Test" in a light blue, lowercase sans-serif font.

Test

Hepatitis Testing Support Agent

Interactive assistant for hepatitis testing based on:

- **OAML Guidelines (2010):** Test ordering and preparation
- **NIH Paper (Prasidhrathsint & 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