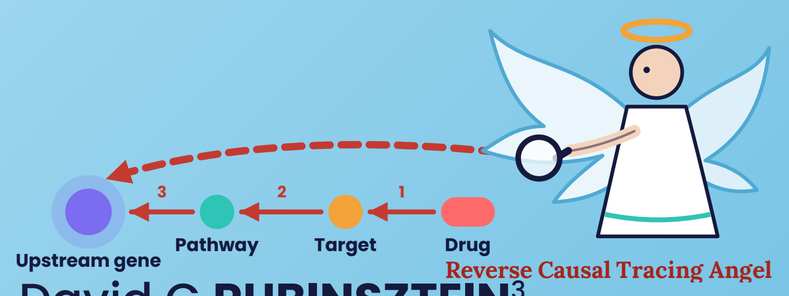
Entropy-Guided Reverse-Causal AI to Identify Upstream Bottleneck Genes for Alzheimer's Drug Discovery



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Commercialisation Advisor: Bart **DECREM** · Firefox launch lead, Mozilla · Founder & CEO, Tapulous · SVP, Disney Mobile Games · *Fast Company* "Most Creative People in Business" (2009)

Our Key Novelty and Niche: **Using entropy-guided, reverse-causal AI, we find the most upstream causal bottleneck genes that start Alzheimer's disease, as targets for both approved and new drugs, so treatment can begin before cognition and independence are lost.**

How We Differ

Others design molecules for a known target. **We find the right target first.**

Cause, Not Damage
Upstream genes that start AD, not late hallmarks.

Reverse Tracing
Drug → target → pathway → gene

Entropy = Certainty
Every causal link carries a confidence score.

Explainable Paths
Each pick is a readable gene-to-drug path.

Approved and New Drugs
Approved drugs reach trials sooner; new molecules follow.

1 The Challenge

Anti-amyloid antibodies show Alzheimer's disease (AD) can be modified, but safety and clinical benefit remain limited. Two gaps hold the field back.

Gap 1 · No Rigorous Way to Find Upstream Causes

Most drugs still aim at late, downstream hallmarks:

amyloid-β · tau · neuroinflammation · neuronal loss

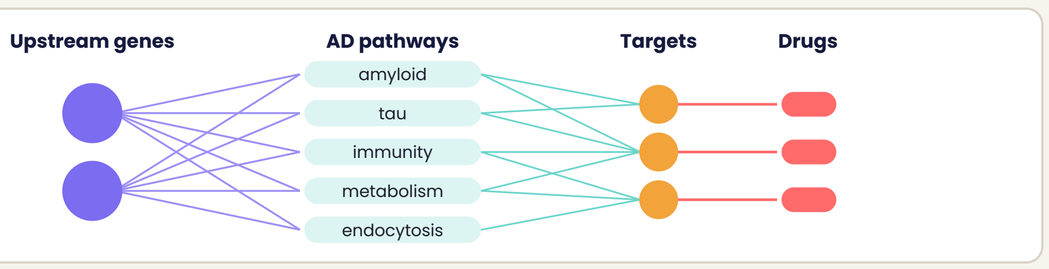
Gap 2 · Fragmented, Static Discovery

Biomedical knowledge graphs rarely update with new evidence or trace from genes to drugs and back again.



2 Our Aim

1. **Identify the most upstream bottleneck genes** that drive AD.
2. **Link them to drugs and drug combinations** through a dynamic, bidirectional gene–pathway–drug graph.



Causal
Drives disease, not just linked to it.

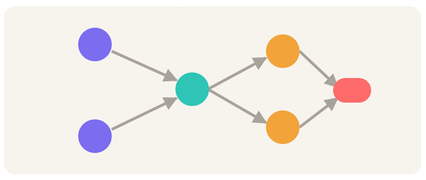
Upstream
Acts before amyloid and tau build up.

Bottleneck
Where many AD pathways meet.

3 A Five-Step, Entropy-Guided Reverse-Causal AI Platform

STEP 1

Build an AD-Specific Knowledge Graph



LLMs propose gene–pathway–drug links. STRING, KEGG, Reactome, Gene Ontology and our experts verify them.

$G_t = (V_t, E_t, W_t)$ *updates as evidence arrives*

STEP 2 · KEY NOVELTY

Reverse Pass: Drugs Back to Genes

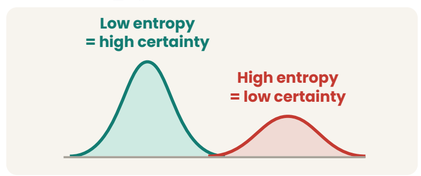


Finds causes. Drugs → targets → pathways → genes. B(g) weighs upstreamness U, disease-driving support D, pathway control P and drug reachability R.

$B(g) = f(U, D, P, R)$

STEP 3 · KEY NOVELTY

Measure Causal Certainty with Entropy



When a gene's evidence agrees, entropy is low: we are more certain it **drives** AD.

$H(g) = -\Sigma_i\, p_i(g)\, log\, p_i(g)$
$Score(g) = \alpha B(g) - \beta H(g)$

STEP 4 · FORWARD PASS

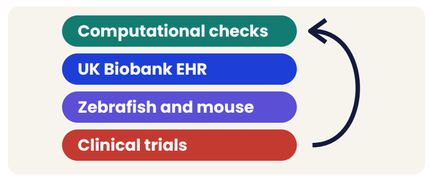
Forward Pass: Genes On to Drugs



Ranks treatments. Updated gene scores re-rank pathways, drugs and combinations that cover several bottlenecks with low safety risk, until rankings converge.

STEP 5

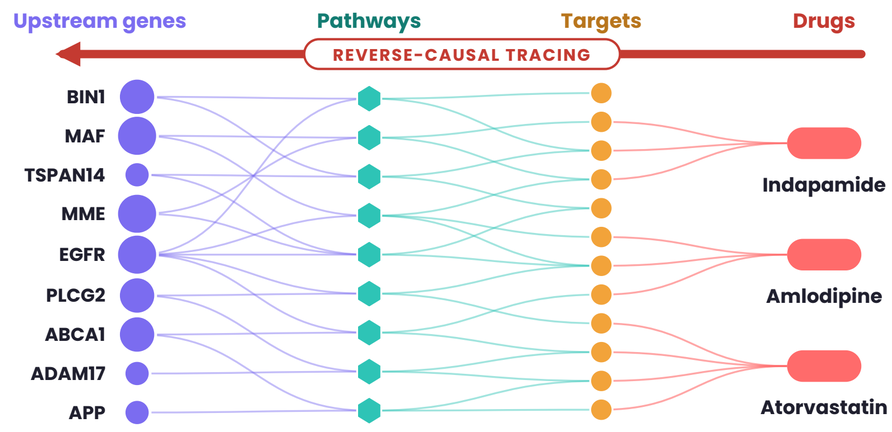
Validate in Stages and Feed Back



Positive results strengthen links in the graph. Negative results trigger re-ranking, so the platform learns from every study.

4 Reverse-Causal Tracing in Action

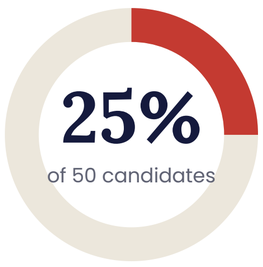
ILLUSTRATIVE



Illustrative example, not yet confirmed: from three drugs with real-world associations, the platform traces back to genes such as EGFR, BIN1, PLCG2 and ABCA1.

Why APOE (incl. the ε4 risk variant) is excluded: its dominant signal would mask other upstream genes, it has been studied for 30 years, and it is hard to drug.

5 Evidence by Rubinsztein Lab, Cambridge



25% of 50 DeepDrug2 candidates were validated in tauopathy animal models at the Cambridge Institute for Medical Research (CIMR).

Led by **Prof. David C Rubinsztein** FRS FMedSci, Deputy Director of CIMR and Group Leader, UK Dementia Research Institute. Results feed back into the graph.

Zebrafish
Tauopathy models, CIMR

→

Mouse
Tauopathy models, CIMR

→

Clinical Trials
Next: CROs with Prof. Rowe (Cambridge) and Prof. Chan (HKU)

6 Impact Built on Four HLCA Rounds

2021
Network backbone
Graph AI for AD drug repurposing
DeepDrug (*Sci. Reports*); 1 US patent

2022
Causal layer
Causal AI for upstream genetic biomarkers
Reverse-Gene-Finder, AAAI-25; 1 US patent

2023
Multimodal data
Multimodal platform for AD prediction
LMP-TX; HKU Seed Fund

2024
Phenotype layer
LLM-driven speech-based AD prediction
3 papers; 2 US patents; CUHK grant

10+
papers in Nature portfolio, AAAI, EMNLP

4
US patents pending

US$995K+
follow-on funding, incl. US$575K angel

1
HKU spin-off; Geneva Gold Medal 2025

7 Why It Matters for Healthy Longevity

Treat root causes, earlier
Target the genes that start the cascade, before decline.

Safer combinations of approved drugs
Hit several bottlenecks at once, with known safety.

Low-cost reach worldwide
A smartphone speech readout where PET, MRI and CSF tests are out of reach.

Next (2026–27): human validation in Hong Kong and Cambridge, new molecules for validated targets, multimorbidity and a cloud hub.

Why ElohaX for the Grand Prize: **of 700+ projects funded by NAM Healthy Longevity, we won four consecutive Catalyst Awards and built them into one platform, validated in human records and animal models and heading to clinical trials: the healthspan breakthrough the Grand Prize rewards.**

ElohaX.ai
An HKU spin-off translating AI-driven Alzheimer's drug discovery. Scan for our platform and team.

▶ Watch This Poster as a Video
Scan for a short video walkthrough of our work.

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