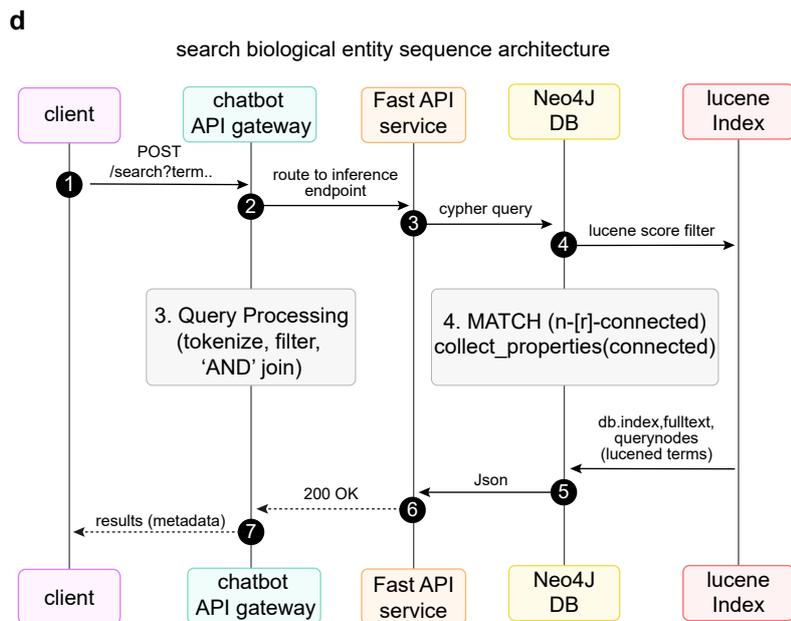**a** EvoAge backend architecture

b

c youden J cutoff by relation type

d search biological entity sequence architecture

e predict rank score sequence architecture
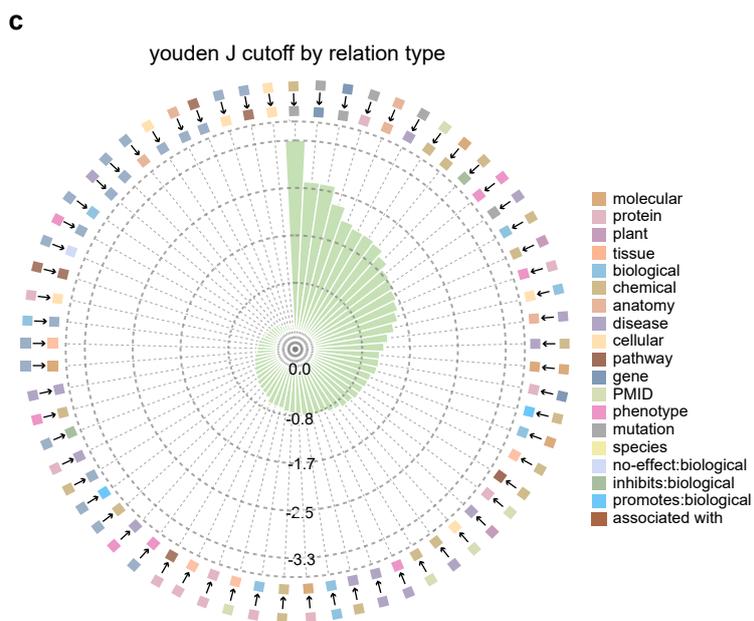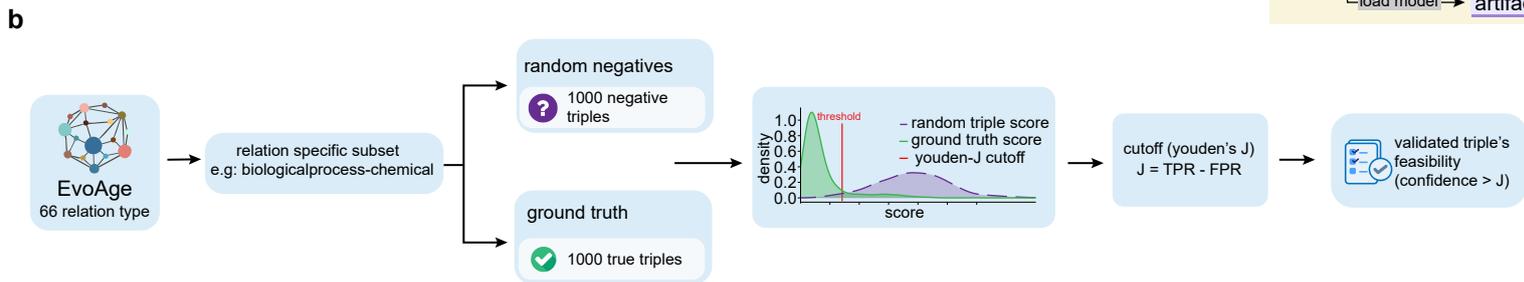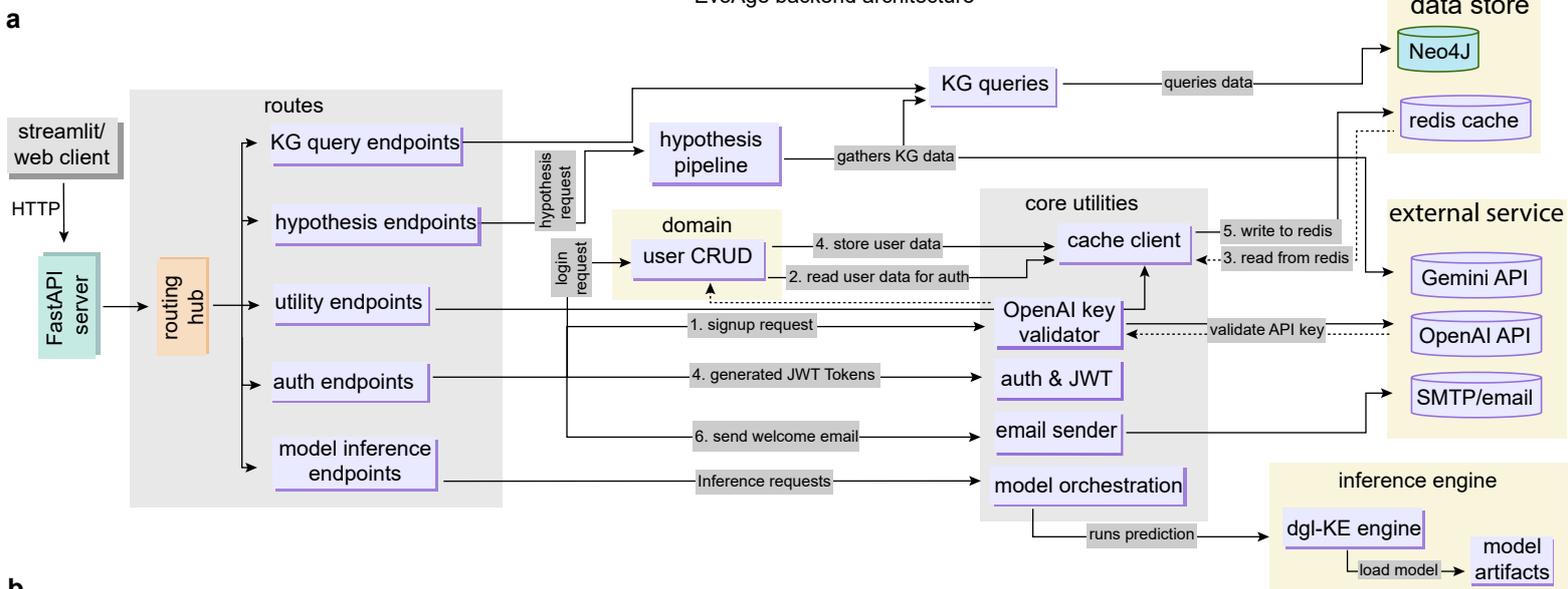
f EvoAge reponse

Supplementary Figure 6
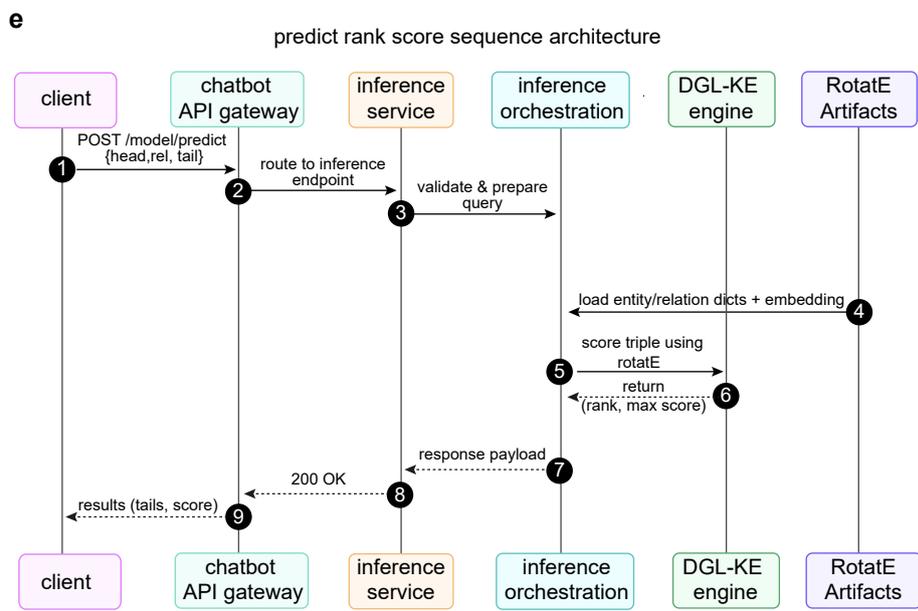
Supplementary Figure 6. EvoAge Platform Architecture Enables Robust Hypothesis Validation

(a) Detailed technical blueprint of the EvoAge backend. A FastAPI server routes client requests to five main "tool" endpoints (e.g., auth, KG query, model inference), orchestrating a core logic pipeline that uses Neo4j for KG queries, DGL-KE for model scoring, and external APIs (Gemini) for interpretation. **(b)** Workflow for determining optimal hypothesis testing cutoffs. Scores for 1,000 'Ground Truth' (purple) and 1,000 'Random Negative' (green) triples are plotted. The Youden's J statistic is applied to find the optimal relation-specific threshold (red line) for validating new triples. **(c)** Circular plot of the optimal Youden's J cutoff scores for all 66 relation types. The score for each relation (green bars) shows that optimal thresholds vary significantly across different biological contexts. **(d)** Sequence diagram for the 'Search Biological Entity' function, showing the API request flow from the client to the FastAPI service, which executes a Cypher query against the Neo4j DB using a Lucene Index. **(e)** Sequence diagram for the 'KGE Scoring' service, detailing the workflow for validating a triple and using the DGL-KE engine (with RotatE artifacts) to return a quantitative score. **(f)** Example of a 'Link Prediction' response for a FOXO3-'Disease' query, showing the ranked list of predictions, scores, and model identifiers as presented in the chat interface.