Phenotype-driven COVID-19 Knowledge Graph from Biomedical Literature Facilitates Hypothesis Generation

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Introduction

The Problem

- Starting December 2019, the COVID-19 pandemic has triggered a research ***“literature explosion”*** (Chahrour et al., 2020)
- Academics are struggling to ***differentiate*** knowns from unknowns and ***connect*** existing findings

Our Solution

- ***Knowledge graphs*** (KG) map unstructured information onto a network of nodes and edges (Figure A)
- KGs ***support multiple downstream tasks***, such as embedding, link prediction, and graph completion, that facilitate novel knowledge syntheses
- Past researchers have utilized KGs to display existing COVID-19 information but not for ***knowledge discovery***
- Our approach employs natural-language processing (NLP) and machine learning to construct, embed, and leverage a KG to ***predict potential COVID-19 treatments, risk factors, and symptoms***

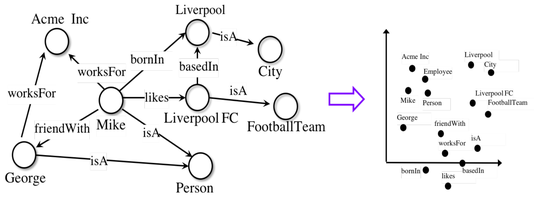


Figure A (above): An example knowledge graph depicts ideas as circular nodes and relationships as connecting lines. Algorithmically, components of this network can be mapped into a vector space, a process known as embedding (Accenture, 2020).

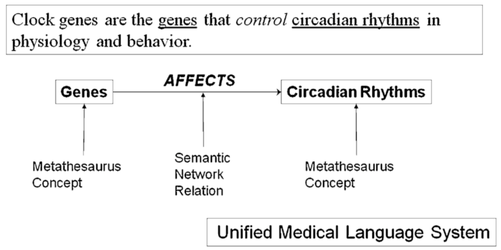
Materials & Methods

Step 1: Data Sourcing

- Sourced data from the ***COVID-19 Open Research Dataset*** (CORD-19) v22, a collection of 200,000+ scholarly texts related to COVID-19

Step 2: Triple Extraction

- ***SemRep:*** program by the National Institutes of Health that ***extracts triples from biomedical texts*** (subject-relation-object); see example (Rindflesch et al., 2011)



- Applied SemRep to corpus generated from CORD-19 to isolate triples involving ***genes, drugs, and symptoms***
- Included more entities and relations relevant to COVID-19 from an earlier list by Rashed et al. (2020)

Step 3: Knowledge Graph Creation & Embedding

- Imported triples into ***Neo4J***, a graph database system, along with paper authorship information to create and visualize the KG
- *KG Embedding:*
  - With the Trans-D approach from the OpenKE-Tensorflow1.0 package, ***triples embedded into a continuous vector space***
  - Evaluated embedding performance by feeding model “corrupted” triples with missing components and scoring its triple-completion predictions
  - Further trained model to process incomplete triples and ***rank predictions*** in descending order of likelihood and relevance

Results

Treatment Predictions	*Symptom Predictions*	*Risk Factor Predictions*
Chloroquine	**COVID-19**	**COVID-19**
Pharmaceutical Preparations	Cessation of Life	Diabetes
Antiviral Agents	**SARS**	Diabetes Mellitus
Iopinavir/Ritonavir	Complication	Cardiovascular Disease
Ribavirin	Disease	Chronic Disease
Hydroxychloroquine	Acute Kidney Failure	**SARS**
Azithromycin	Inflammatory Response	Angiotensin-Converting Enzyme Inhibitors
Nucleoside Analogs	Pneumonia	**Influenza**
Lead compound	Inflammation	Opportunistic Infections
Investigational new drugs	**Infection**	**CD69 Protein, Human**
Iopinavir	Vertical Disease Transmission	**ACE2 Gene**
Hydroxychloroquine Sulfate	Disorder of circulatory system	**Disease**

* bolded terms do not already exist in the KG

Figure B (left): At BFS depth of 1, the embedding model effectively predicts treatments, symptoms, and risk factors associated with COVID-19. Many of these new predictions are confirmed by promising literature, validating our methodology.

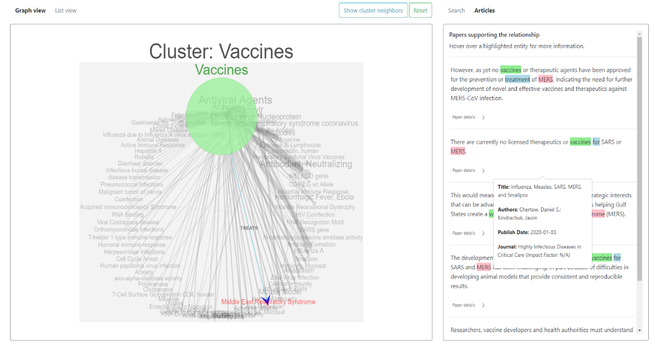


Figure C (above): Searching “vaccine” on our online interface returns the relevant cluster of nodes, paper excerpts, and authorship data.

Discussion

Conclusions

- Promising results reinforce KGs as effective tools to ***display*** and ***explore*** knowledge, especially for COVID-19
- In the context of COVID-19, our workflow uniquely provides a ***link-prediction mechanism*** and an online, ***user-friendly interface***

Future Directions

- Weight triples during KG creation based on their frequency to enhance and fine-tune link prediction
- Incorporate clinical phenotype notes to adapt KG for diagnostic purposes

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