

# #5 Explainable AI for DMD Drug-Repurposing

**Obtaining drug candidates that can treat symptoms observed in Duchenne muscular dystrophy disease**

\* Indicates required question

---

This questionnaire is part of a Leiden University master's thesis project performed by Rosa Zwart in collaboration with the LUMC BioSemantics group. This project aims to investigate whether the explainability of explainable AI algorithms can be improved by using Foundational Ontologies.

## Introduction

This questionnaire is meant for obtaining feedback from users with knowledge and experience in drug repurposing and/or the rare disease DMD.

A knowledge graph is created containing phenotypic and genetic information directly and indirectly associated with Duchenne muscular dystrophy (DMD). Subsequently, data have been incorporated into the graph that relate to drugs and their associated protein targets as well as information regarding the symptoms and diseases for which a drug is used during treatment. Using this knowledge graph, a deep learning model is trained which results in predictions of new links between drugs and phenotypes directly associated with DMD. Due to the black-box nature of deep learning algorithms, it is difficult for human decision-makers to assess the reliability of these predictions. To enable decision-makers to subject the predictions obtained by the model to their own reasoning, interpretable explanations are added to the link predictions of the trained graph neural network (GNN) model. By adding an explanation-generating method to the deep learning algorithm, we arrive at the field of explainable AI that already shows promising developments into the direction of applying trustworthy deep learning techniques to important medical decisions.

During this research project, we want to investigate whether the explanations generated for the predictions by the trained model can be improved. To attempt this, we tested two different approaches, and we are now running a blind assessment of the results. In this questionnaire, you got an explanation generated by one of the two approaches.

The explanations are subgraphs that explain the predicted existence of a certain link between a drug and DMD-related symptom node by showing the most impactful links that lead to this prediction.

## Background Information

In order to acquire an idea about the background of all participants, some questions will be asked regarding your research experience.

1. How many years of experience do you have in the field of drug repurposing and/or rare diseases research? \*

---

2. Do you conduct research on the rare disease Duchenne muscular dystrophy? \*

*Mark only one oval.*

☐ Yes

☐ No

## Explanation

To assess the explainability of the given explanation, Likert scaled scores need to be assigned for each explainability aspect.

A caption is added to the subgraph to show the meaning of the most relevant paths for explaining the prediction and to provide additional information about the instances found in the graphs.

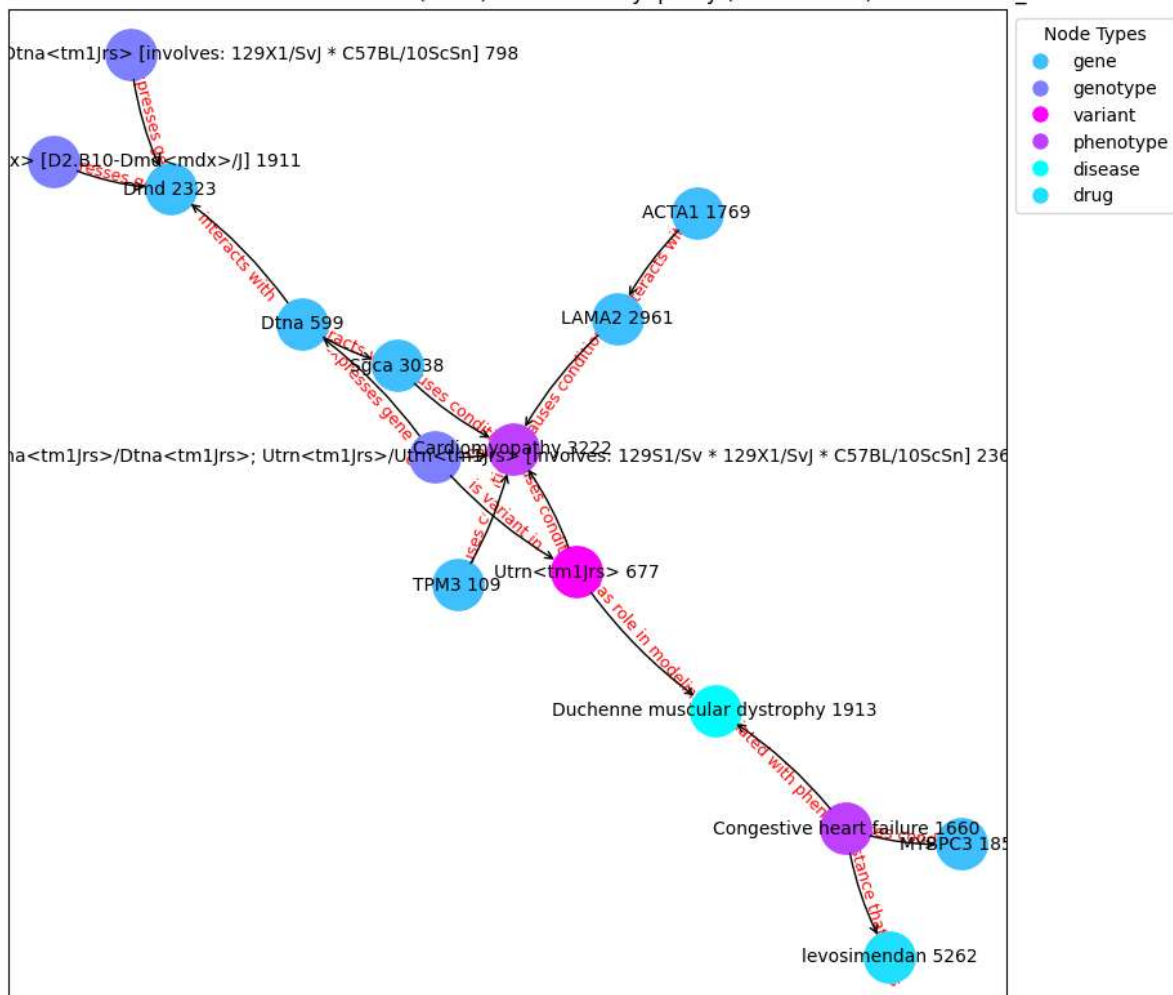
## Prediction

It has been predicted that levosimendan treats [cardiomyopathy](#).

## Explanation (Check the graph before reading the text below)

Levosimendan is a substance that treats [congestive heart failure](#). This phenotype is associated with Duchenne muscular dystrophy. The variant Utrn<tm1Jrs> with identifier MGI:2148539 has a role in modeling [Duchenne muscular dystrophy](#). Utrn<tm1Jrs> is a variant found in genotype Dmd<mdx>; Dtna<tm1Jrs>/Dtna<tm1Jrs>; Utrn<tm1Jrs>/Utrn<tm1Jrs> [involves: 129S1/Sv \* 129X1/SvJ \* C57BL/10ScSn] with identifier MGI:2176891. In this genotype the gene [Dtna](#) is expressed. This gene interacts with [Sgca](#). Changes in Sgca can cause the condition cardiomyopathy as well as the previously mentioned variant Utrn<tm1Jrs>.

Explanation for link between levosimendan (1576) and Cardiomyopathy (HP:0001638) from run run\_004



3. **Clarity** \*

I believe that the explanation is unambiguous regarding the use of concepts and relations.

*Mark only one oval.*

1   2   3   4   5

Stro ☐ ☐ ☐ ☐ ☐ Strongly applies

4. **Parsimony** \*

I believe that the explanation is presented in a way that is not too complex.

*Mark only one oval.*

1   2   3   4   5

Stro ☐ ☐ ☐ ☐ ☐ Strongly applies

5. **Completeness** \*

I believe that the explanation provides sufficient information to explain a new drug candidate.

*Mark only one oval.*

1   2   3   4   5

Stro ☐ ☐ ☐ ☐ ☐ Strongly applies

6. **Soundness** \*

I believe that the information paths shown in the explanation are useful for finding potential drug candidates.

*Mark only one oval.*

1   2   3   4   5

Stro ☐ ☐ ☐ ☐ ☐ Strongly applies

7. Do you have any specific comments about this explanation? If so, please enter these comments below:

---

---

---

---

---

---

This content is neither created nor endorsed by Google.

Google Forms