9. Supplementary section

9.1. Knowledge Graph seeds

Table S1
Table containing seeds used to build KG A.

Seed Name	**Seed ID**
DMD	HGNC:2928
DMD	MONDO:0010679

Table S2
Table containing seeds used to build KG B.

Seed Name	**Seed ID**
DMD	HGNC:2928
DMD	MONDO:0010679
Hypotonia	HP:0001252
Specific learning disability	HP:0001328
Arrhythmia	HP:0011675
Congestive heart failure	HP:0001635
Dilated cardiomyopathy	HP:0001644
Calf muscle hypertrophy	HP:0008981
Motor delay	HP:0001270
Muscular dystrophy	HP:0003560
Delayed speech and language development	HP:0000750
Hypoventilation	HP:0002791
Intellectual disability, mild	HP:0001256
Hyporeflexia	HP:0001265
Cognitive impairment	HP:0100543
Proximal muscle weakness	HP:0003701
Abnormal EKG	HP:0003115
Calf muscle pseudohypertrophy	HP:0003707
Cardiomyopathy	HP:0001638
Flexion contracture	HP:0001371
Elevated circulating creatine kinase concentration	HP:0003236
Global developmental delay	HP:0001263
Skeletal muscle atrophy	HP:0003202
Respiratory insufficiency	HP:0002093
Waddling gait	HP:0002515
Gowers sign	HP:0003391
Generalized hypotonia	HP:0001290
Progressive muscle weakness	HP:0003323
Scoliosis	HP:0002650
Hyperlordosis	HP:0003307

9.2. Number of edge types

Table S3
Number and percentage of edge types in KG A.

Edge Type	**Count**	**Percentage**
in 1 to 1 orthology relationship with	35650	37.96%
in orthology relationship with	25242	26.88%
has phenotype	15730	16.75%
interacts with	9824	10.46%
is part of	1465	1.56%
has affected feature	1101	1.17%
expressed in	1079	1.14%
enables	983	1.04%
pathogenic for condition	976	1.03%
targets	518	0.55%
involved in	432	0.46%
likely pathogenic for condition	182	0.19%
contributes to condition	171	0.18%
has role in modeling	134	0.14%
is allele of	96	0.10%
is substance that treats	86	0.09%
colocalizes with	84	0.09%
source	29	0.03%
is causal germline mutation in	16	0.02%
has genotype	7	0.01%
contributes to	5	0.01%
causes condition	3	0.003%
is marker for	1	0.001%
is causal germline mutation partially giving rise to	1	0.001%

Table S4
Number and percentage of edge types in the KG B.

Edge Type	Count	Percentage
has phenotype	836138	42.13%
in 1 to 1 orthology relationship with	520547	23.23%
in orthology relationship with	333288	16.79%
interacts with	226174	11.40%
expressed in	14589	0.74%
is part of	9427	0.47%
colocalizes with	8112	0.41%
involved in	7790	0.39%
enables	7053	0.36%
targets	5070	0.26%
has role in modeling	3449	0.17%
causes condition	2479	0.12%
contributes to condition	2203	0.11%
is allele of	1167	0.06%
has affected feature	1137	0.06%
pathogenic for condition	1024	0.05%
is causal germline mutation in	900	0.04%
is substance that treats	599	0.03%
contributes to	198	0.01%
likely pathogenic for condition	185	0.01%
is causal loss of function germline mutation of in	179	0.01%
is reference allele of	130	0.01%
is marker for	97	0.005%
has genotype	67	0.003%
is causal susceptibility factor for	42	0.002%
source	32	0.002%
is causal somatic mutation in	16	0.001%
is causal gain of function germline mutation of in	15	0.001%
is causal germline mutation partially giving rise to	12	0.001%

9.3. GNNExplainer algorithm

$GNN, NodeIdx1, NodeIdx2, G\ G_{s,m}$, Mask $Emb = GNN(G)$ // Obtain embeddings
$InitialPred = Emb[NodeIdx1] \cdot Emb[NodeIdx2]$ // Get initial prediction
$G_s = Subgraph(G, NodeIndex1, NodeIndex2)$ // Obtain subgraph
$Mask = InitializeMask(G_s)$ // Initialize Mask
for *Epoch in Epochs* **do**
    $G_{s,m} = ApplyMask(G_s, Mask)$ // Apply Mask to subgraph
    $NewEmb = GNN(G_{s,m})$ // Get new embeddings
    $NewPred = NewEmb[NodeIdx1] \cdot NewEmb[NodeIde2]$ // Get new prediction
    $Loss = GetLoss(InitialPred, NewPred)$ // Calculate loss
    $Mask = Backpropagate(Mask, Loss)$ // Backpropagate loss
end
return $G_{s,m}$, *Mask*

Algorithm 1: GNNExplainer Link Prediction Pseudocode. *GNN* stands for the trained GNN model. *G* stands for the Graph.

9.4. List of hyperparameters

Table S5
Table showing the different options of hyperparameters that were tested as well as their optimal values.

Process	**Hyperparameter**	**Options**	**Optimal Value**
edge2vec	Number of walks	2, 4, 6	2
	Walk Length	3, 5, 7	7
	Embedding Dimension	32, 64, 128	32
	Edge Direction	Undirected, Directed	Directed
	p	0.5, 0.7, 1	0.7
	q	0.5, 0.7, 1	1
	Epochs	5, 10	10
GNN	Hidden Dimension	64, 128, 256	256
	Output Dimension	64, 128, 256	64
	Layers	2, 4, 6	2
	Aggregation Function	mean, sum	mean
	Dropout	0, 0.1, 0.2	0.2
	Learning Rate	0.001 - 0.1	0.07
	Epochs	100, 150, 200	150

9.5. Visualization of explanations

To visualize the resulting explanations, a custom visualization function was developed to represent explanations as more human readable and semantic graphs and, thus, improving the one provided by Pytorch Geometric [143]. In the first place, the possibility of visualizing the edge types has been incorporated. Additionally, in this new formula several customizable parameters have been added. Now, it is possible to only visualize the active edges of the explanation, removing non-important edges. This will allow for clearer visualization of the subgraph. Figure S1 shows how an explanation is modified after applying this option. Finally, it is also possible to remove unconnected clusters from the explanations. This way, if an explanation is formed by several clusters, there is the possibility of just viewing the ones that contain the drug candidate and the targeted phenotype. Figure S2 shows how the explanation is modified after applying this filter.

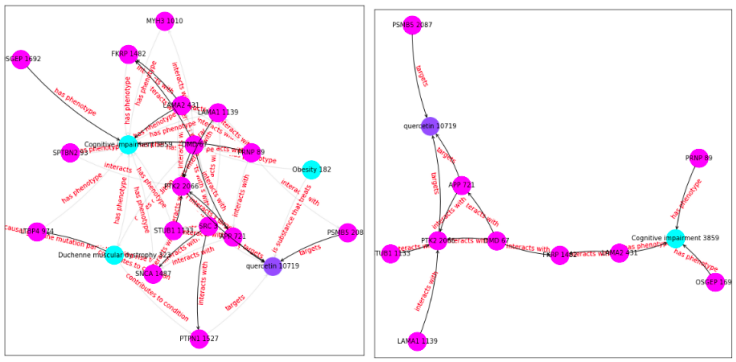

Fig. S1. Explanation after removing non-important edges. Left: Explanation keeping all the edges. Right: Explanation removing non-important edges.

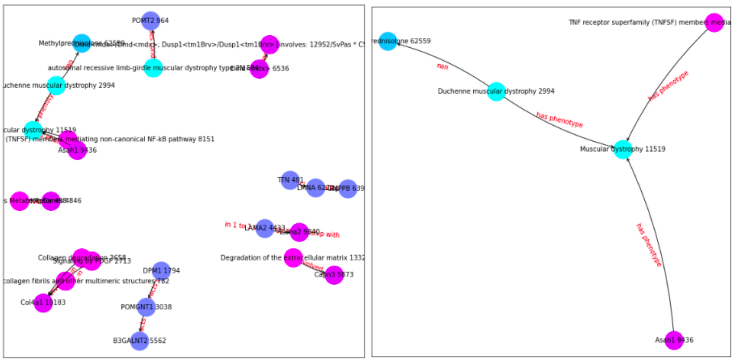

Fig. S2. Explanation after removing unconnected clusters. Left: Explanation keeping all the clusters. Right: Explanation removing additional clusters.

9.6. Complete/Incomplete explanation Example

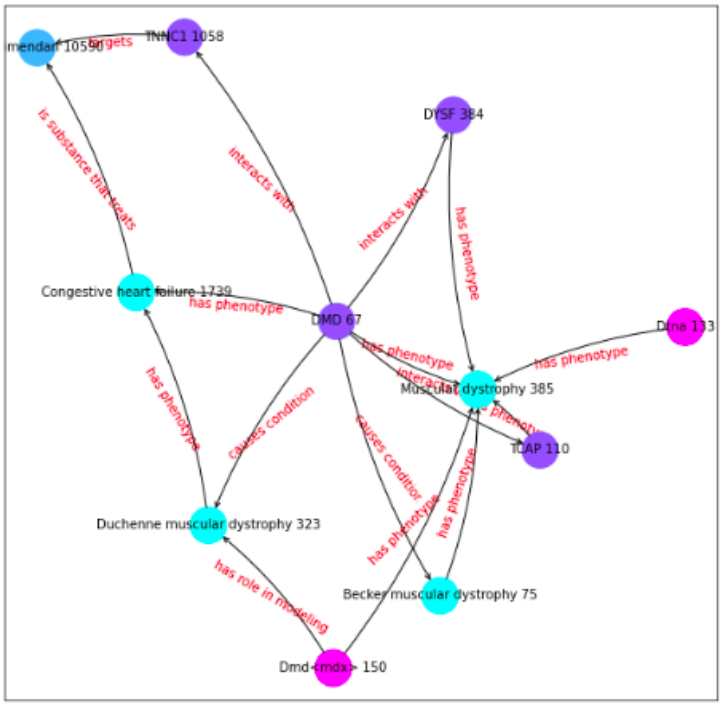

Fig. S3. Explanation of drug candidate Levosimendan as possible treatment for Muscular Dystrophy. Classified as complete explanation.

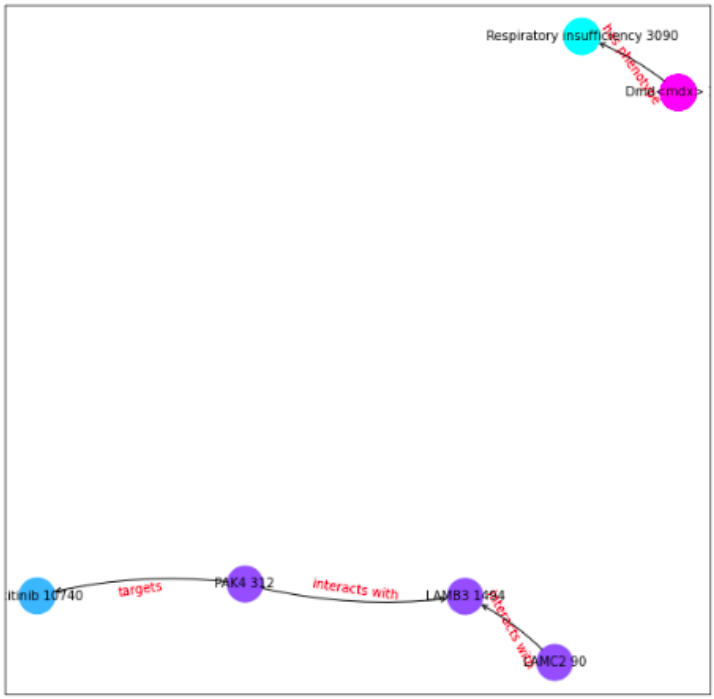

Fig. S4. Explanation of drug candidate Axitinib as possible treatment for Respiratory Insufficiency. Classified as incomplete explanation.

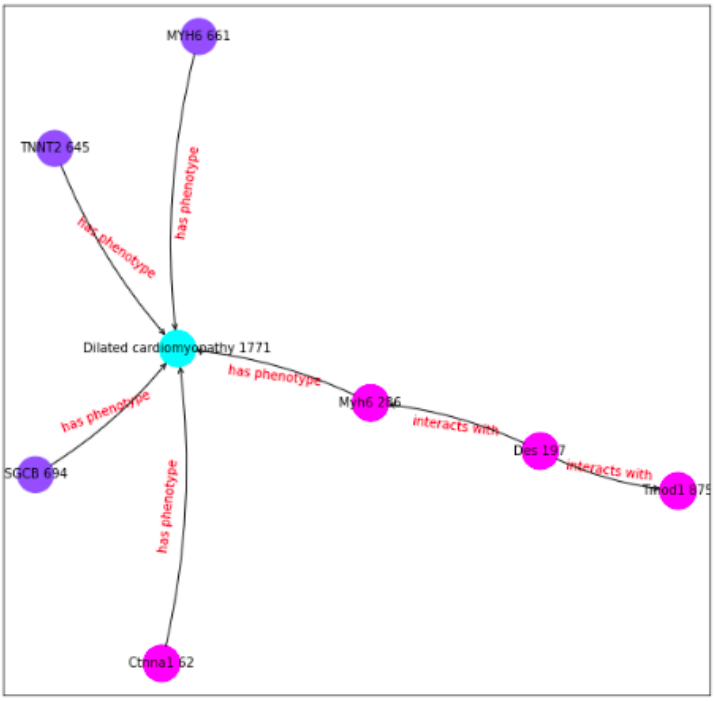

Fig. S5. Explanation of drug candidate Entrectinib as possible treatment for Dilated cardiomyopathy. Classified as incomplete explanation.

9.7. Evaluation of explanations

Table S6

Table showing the amount of times each drug appears as one of the top 3 drug candidates with highest score treat one of the 27 symptoms. It is also shown the amount of supporting evidence and contraindication evidence for each drug. This information was obtained using Graph A.

Drug	Appearances	Percentage	With Evidence	With Contraindications
Entrectinib	25	92.59 %	0	8
Axitinib	19	70.37 %	1	1
Nintedanib	12	44.44 %	2	0
Levosimendan	7	25.92 %	6	0
Disopyramide	6	22.22 %	2	0
Doxorubicin	2	7.40 %	0	2
Aprindine	2	7.40 %	2	0
Amiodarone	1	3.70 %	1	0
Acepromazine	1	3.70 %	0	0
Mezlocillin	1	3.70 %	0	0
Sunitinib	1	3.70 %	0	0
Fedratinib	1	3.70 %	0	0
Carvedilol	1	3.70 %	1	0
Queracetin	1	3.70 %	1	0

Table S7

Table showing the number and percentage of explanations with no evidence, with supporting evidence, and with contraindications for each type of explanation and each graph.

		With Evidence	Percentage With Evidence	With Contraindications	Percentage With Contraindications	No Evidence	Percentage No Evidence
KG A	*Complete Explanations*	9	60%	1	7%	5	33%
	Incomplete Explanations	0	0%	5	83%	1	17%
KG B (Large)	*Complete Explanations*	4	67%	2	33%	0	0%
	Incomplete Explanations	6	40%	2	13%	7	47%

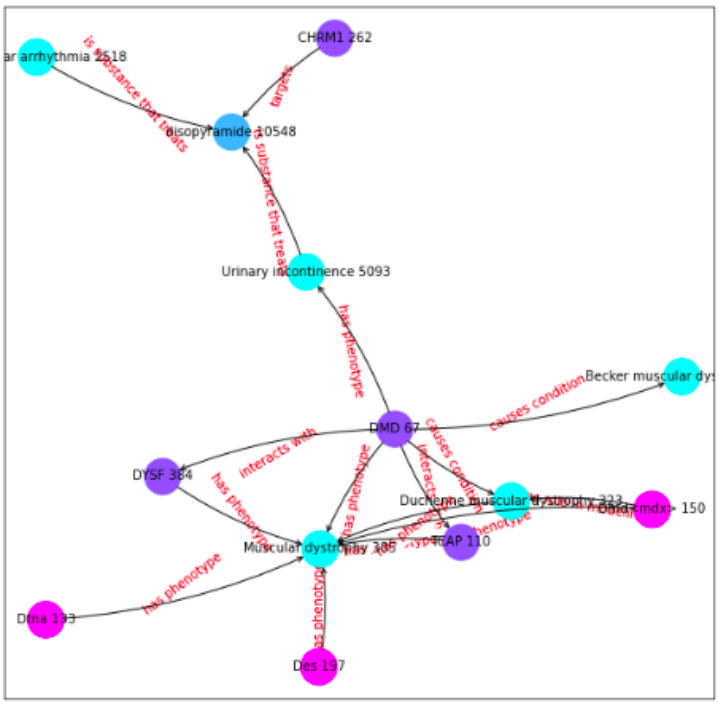

Fig. S6. Explanation of drug candidate Disopyramide as possible treatment for Muscular Dystrophy. Classified as complete explanation.

Table S8

Table showing the analysis of the explanation. The Good/Bad column shows the subjective evaluation. The Supporting Evidence Link shows if the Drug-Disease link contains supporting evidence. The Supporting Evidence Explanation shows if the explanation itself has supporting evidence.

Graph	Drug	Disease	Good/Bad	Supporting Evidence Link	Supporting Evidence Explanation
KG A	Levosimendan	*Muscular Dystrophy*	Good	Yes	-
	Disopyramide	*Muscular Dystrophy*	Bad	Yes	-
	Entrectinib	*Muscular Dystrophy*	Good	No	-
	Entrectinib	*Respiratory Insufficiency*	Good	No	-
	Doxorubicin	*Respiratory Insufficiency*	Good	Contraindication	Unclear: https://grantome.com/grant/NIH/R01-HL146443-01
	Levosimendan	*Arrhythmia*	Bad	Yes	-
	Amiodarone	*Arrhythmia*	Good	Yes	-
	Isradipine	*Arrhythmia*	Good	Yes	-
	Levosimendan	*Dilated Cardiomyopathy*	Bad	Yes	-
	Aprindine	*Congestive Heart Failure*	Bad	Yes	-
	Nintedanib	*Congestive Heart Failure*	Good	No	-
	Levosimendan	*Progressive Muscle Weakness*	Good	Yes	https://www.frontiersin.org/articles/10.3389/fphys.2021.786895/full
	Entrectinib	*Cognitive Impairment*	Good	Contraindication	-
	Axitinib	*Cognitive Impairment*	Good	Yes	-
	Quercetin	*Cognitive Impairment*	Good	Yes	-
KG B (Large)	Methylprednisolone	*Muscular Dystrophy*	Good	Yes	-
	Methylprednisolone	*Respiratory Insufficiency*	Good	Yes	-
	Sorafenib	*Respiratory Insufficiency*	Good	Contraindication	Unclear: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3961597/
	Methylprednisolone	*Progressive Muscle Weakness*	Good	Contraindication	-
	Resveratrol	*Progressive Muscle Weakness*	Good	Yes	-
	Sorafenib	*Cognitive Impairment*	Good	Contraindication	-

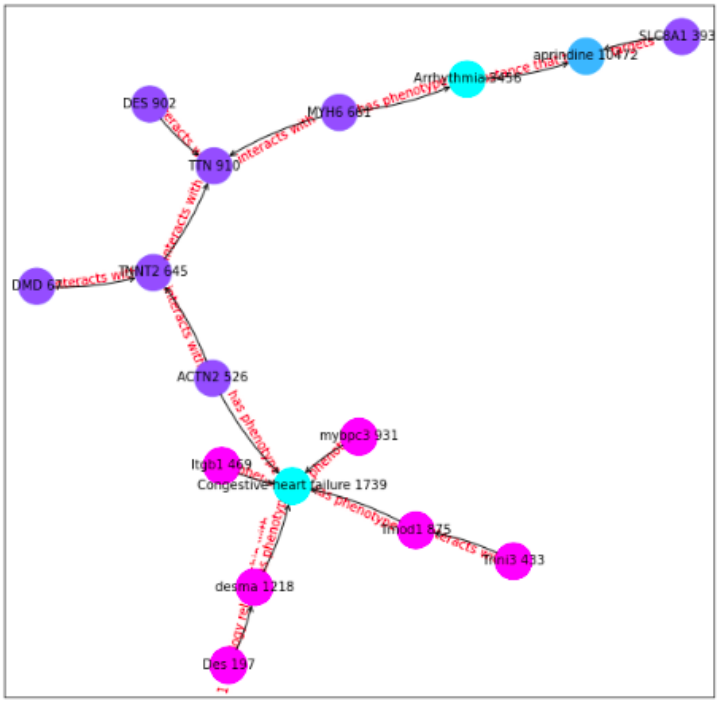

Fig. S7. Explanation of drug candidate Aprindine as possible treatment for Congestive heart failure. Classified as complete explanation.

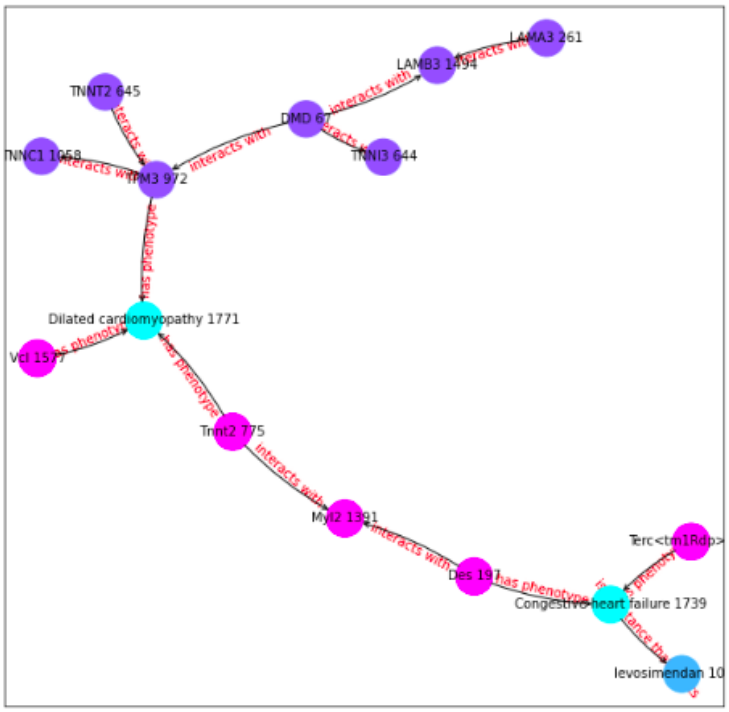

Fig. S8. Explanation of drug candidate Levosimendan as possible treatment for Dilated cardiomyopathy. Classified as complete explanation.

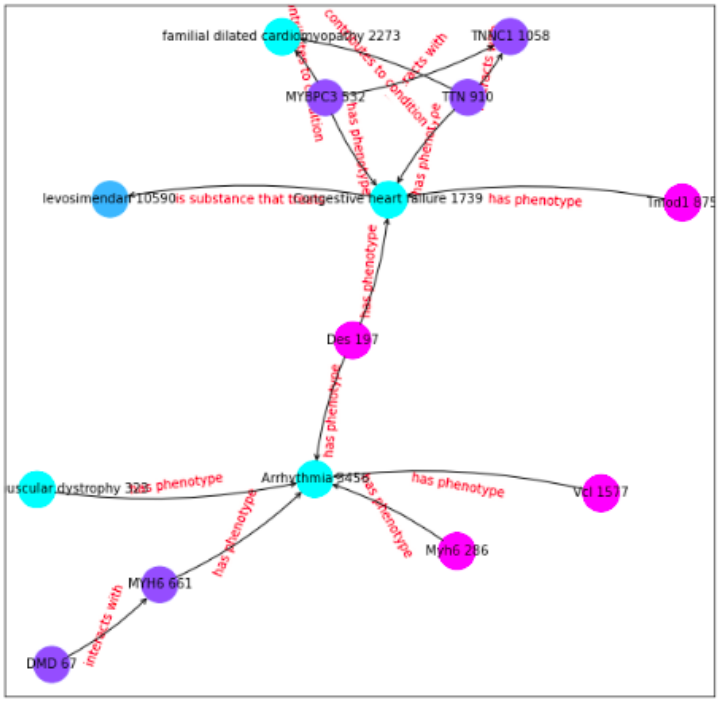

Fig. S9. Explanation of drug candidate Levosimendan as possible treatment for Arrhythmia. Classified as complete explanation.

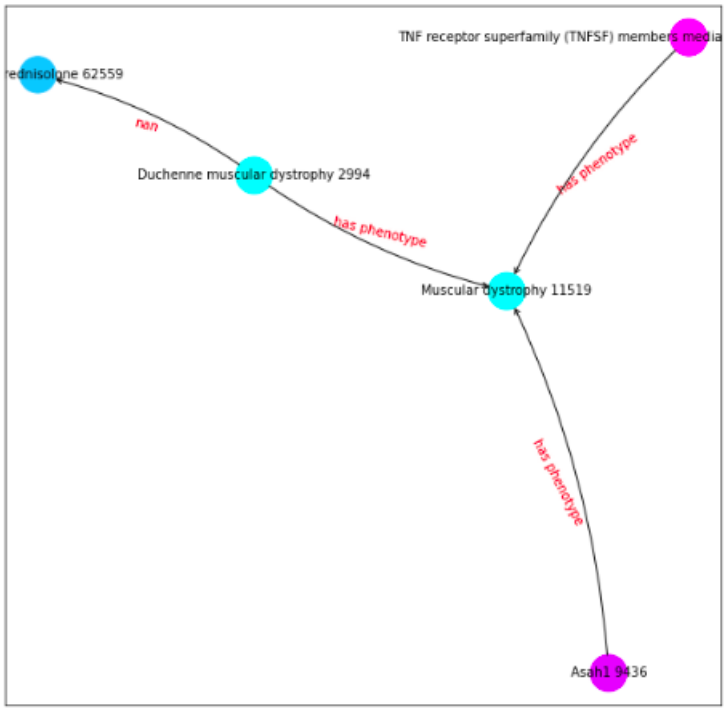

Fig. S10. Explanation of drug candidate Methylprednisolone as possible treatment for Muscular dystrophy. Classified as complete explanation.

9.8. Drug Candidates on KG A

Table S9: Table showing the drug candidates with the highest scores for each symptom/phenotype obtained in Graph A. Any evidence that supports the prediction will be shown in the *Supporting Evidence* column. If the drug is contraindicated for the given symptom/phenotype it will also be shown in this column.

Symptom	**ID**	**Drug Candidate**	**Score**	**Supporting Evidence**
Muscular dystrophy	HP:0003560	Levosimendan	0.849	https://pubmed.ncbi.nlm.nih.gov/30796500/
		Disopyramide	0.848	https://pubmed.ncbi.nlm.nih.gov/7045292/
		Entrectinib	0.845	None
Respiratory insufficiency	HP:0002093	Entrectinib	0.954	None
		Axitinib	0.925	None
		Doxorubicin	0.915	May produce respiratory dysfunction: https://grantome.com/grant/NIH/R01-HL146443-01
Gowers sign	HP:0003391	Entrectinib	0.963	None
		Axitinib	0.945	None
		Nintedanib	0.932	None
Global developmental delay	HP:0001263	Entrectinib	0.985	Can produce developmental delay: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8341080/
		Axitinib	0.974	None
		Nintedanib	0.968	None
Hyporeflexia	HP:0001265	Entrectinib	0.923	None
		Axitinib	0.905	None
		Nintedanib	0.872	None
Proximal muscle weakness	HP:0003701	Entrectinib	0.961	Can produce muscle weakness: https://www.drugs.com/sfx/entrectinib-side-effects.html
		Axitinib	0.944	None
		Nintedanib	0.925	https://pubmed.ncbi.nlm.nih.gov/29991677/
Intellectual disability	HP:0001256	Entrectinib	0.947	None
		Axitinib	0.921	None
		Doxorubicin	0.884	Can produce cognitive impairment: https://pubmed.ncbi.nlm.nih.gov/34055643
Calf muscle pseudohypertrophy	HP:0003707	Disopyramide	0.813	None
		Entrectinib	0.784	None
		Axitinib	0.776	None
Elevated serum creatine kinase	HP:0003236	Entrectinib	0.929	Can increase more: https://www.oncolink.org/cancer-treatment/oncolink-rx/entrectinib-rozlytrek
		Levosimendan	0.920	None
		Disopyramide	0.915	None

Abnormal EKG	HP:0003115	Levosimendan	0.777	https://pubmed.ncbi.nlm.nih.gov/20814559/
		Aprindine	0.747	https://pubmed.ncbi.nlm.nih.gov/10068848/
		Disopyramide	0.713	https://pubmed.ncbi.nlm.nih.gov/9141608/
Arrhythmia	HP:0011675	Levosimendan	0.890	https://ccforum.biomedcentral.com/articles/10.1186/cc1595#:$\sim$:text=Effects%20of%20levosimendan%20on%20cardiac%20arrhythmia%20in%20patients%20with%20severe%20heart%20failure,-J%20Lilleberg%20%26&text=Levosimendan%20(LS)%20is%20a%20novel,oxygen%20consumption%2C%20and%20induces%20vasodilation.
		Amiodarone	0.792	https://www.aafp.org/pubs/afp/issues/2003/1201/p2189.html#:$\sim$:text=Amiodarone%20is%20a%20potent%20antiarrhythmic,deaths%20in%20high%2Drisk%20patients.
		Isradipine	0.953	https://pubmed.ncbi.nlm.nih.gov/8480504/
Waddling gait	HP:0002515	Entrectinib	0.976	None
		Axitinib	0.964	None
		Nintedanib	0.947	None
Dilated cardiomyopathy	HP:0001644	Entrectinib	0.967	Can produce heart disease: https://www.drugs.com/cons/entrectinib.html
		Levosimendan	0.950	https://pubmed.ncbi.nlm.nih.gov/25863426/#:$\sim$:text=Conclusions%3A%20Levosimendan%20seems%20to%20improve,support%20while%20awaiting%20heart%20transplantation.
		Nintedanib	0.933	None
Flexion contracture	HP:0001371	Entrectinib	0.980	None
		Axitinib	0.975	None
		Nintedanib	0.958	None
Specific learning disability	HP:0001328	Entrectinib	0.871	None
		Axitinib	0.862	None
		Acepromazine	0.830	None
Skeletal muscle atrophy	HP:0003202	Entrectinib	0.962	None
		Axitinib	0.946	None

		Nintedanib	0.925	https://pubmed.ncbi.nlm.nih.gov/29991677/
Hypoventilation	HP:0002791	Axitinib	0.781	None
		Entrectinib	0.769	None
		Mezlocillin	0.759	None
Calf muscle hypertrophy	HP:0008981	Entrectinib	0.978	None
		Axitinib	0.977	None
		Disopyramide	0.976	None
Motor delay	HP:0001270	Entrectinib	0.991	None
		Sunitinib	0.985	None
		Fedratinib	0.978	None
Generalized hypotonia	HP:0001290	Entrectinib	0.995	None
		Axitinib	0.988	None
		Nintedanib	0.983	None
Cardiomyopathy	HP:0001638	Levosimendan	0.899	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6588712/
		Entrectinib	0.848	Can produce myocarditis: https://pubmed.ncbi.nlm.nih.gov/34315748/
		Carvedilol	0.837	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4055878/#:$\sim$:text=Pathways%20through%20which%20carvedilol%20exert,for%20beneficial%20effects%20in%20cardiomyopathy.
Hyperlordosis	HP:0003307	Entrectinib	0.970	None
		Axitinib	0.959	None
		Disopyramide	0.932	None
Congestive heart failure	HP:0001635	Entrectinib	0.863	Can produce heart failure: https://www.rozlytrek.com/ntrk/how-rozlytrek-may-help/possible-side-effects.html
		Aprindine	0.857	https://pubmed.ncbi.nlm.nih.gov/6871919/
		Nintedanib	0.835	None
Delayed speech and language development	HP:0000750	Entrectinib	0.986	None
		Axitinib	0.977	None
		Nintedanib	0.969	None
Scoliosis	HP:0002650	Entrectinib	0.994	None
		Axitinib	0.989	None
		Nintedanib	0.981	None
Progressive muscle weakness	HP:0003323	Levosimendan	0.864	https://www.frontiersin.org/articles/10.3389/fphys.2021.786895/full
		Entrectinib	0.985	Can cause weakness: https://www.drugs.com/sfx/entrectinib-side-effects.html

		Axitinib	0.960	Can cause weakness: https://www.mayoclinic.org/drugs-supplements/axitinib-oral-route/side-effects/drg-20075455?p=1#:$\sim$:text=This%20medicine%20may%20cause%20serious,trouble%20talking%2C%20or%20vision%20changes.
Cognitive impairment	HP:0100543	Entrectinib	0.952	Can induce cognitive disorders: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8149347/#:$\sim$:text=Cognitive%20disorders%20included%20events%20reported,(0.2%25)%20%5B20%5D.
		Axitinib	0.931	https://www.neuro-central.com/reversing-alzheimers-symptoms-in-mice-with-axitinib-treatment/
		Quercetin	0.991	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3736941/#:$\sim$:text=In%20vitro%20research%20also%20suggests,similar%20to%20that%20of%20caffeine.

9.9. Drug Candidates on KG B

Table S10: Table showing the drug candidates with the highest scores for each symptom/phenotype obtained with Graph B. Any evidence that supports the prediction will be shown in the *Supporting Evidence* column. If the drug is contraindicated for the given symptom/phenotype it will also be shown in this column.

Symptom	**ID**	**Drug Candidate**	**Score**	**Reference**
Muscular dystrophy	HP:0003560	Methylprednisolone	0.993	https://pubmed.ncbi.nlm.nih.gov/17541998/
		Resveratrol	0.963	https://www.nature.com/articles/s41598-020-77197-6
		Tofisopam	0.919	https://extrapharmacy.ru/grandaxin-tofisopam-50mg-60tabs
Respiratory insufficiency	HP:0002093	Methylprednisolone	0.984	https://jintensivecare.biomedcentral.com/articles/10.1186/s40560-018-0321-9
		Fedratinib	0.981	None
		Sorafenib	0.975	Can cause pneumonia: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3961597/
Gowers sign	HP:0003391	Fedratinib	0.994	None
		Bosutinib	0.991	None
		Nintedanib	0.990	None
Global developmental delay	HP:0001263	Fedratinib	0.995	None
		Sorafenib	0.994	None
		Bosutinib	0.994	None
Hyporeflexia	HP:0001265	Fedratinib	0.996	None
		Sunitinib	0.994	None
		Bosutinib	0.994	None
Proximal muscle weakness	HP:0003701	Fedratinib	0.997	Can produce muscle weakness: https://medlineplus.gov/druginfo/meds/a619058.html
		Bosutinib	0.995	None
		Methylprednisolone	0.995	Can produce weakness: https://erj.ersjournals.com/content/21/2/377.2#:$\sim$:text=Methylprednisolone%20is%20often%20given%20in,weakness%20following%20high%2Ddose%20steroids.
Intellectual disability	HP:0001256	Fedratinib	0.996	None
		Sorafenib	0.995	None
		Bosutinib	0.995	None
Calf muscle pseudohypertrophy	HP:0003707	Methylprednisolone	0.970	https://www.britannica.com/science/pseudohypertrophy
		Ruxolitinib	0.967	https://www.sciencedirect.com/science/article/pii/S147148921630100X

		Fedratinib	0.948	None
Elevated serum creatine kinase	HP:0003236	Methylprednisolone	0.994	Can increase creatinine: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4275145/
		Fedratinib	0.989	Can increase more: https://jamanetwork.com/journals/jamaoncology/fullarticle/2330618
		Bosutinib	0.982	Can increase more: https://www.sciencedirect.com/science/article/pii/S2152265017305840
Abnormal EKG	HP:0003115	Methylprednisolone	0.982	Can affect EKG: https://pubmed.ncbi.nlm.nih.gov/29668335/
		Patisiran	0.879	None
		Silodosin	0.878	None
Arrhythmia	HP:0011675	Methylprednisolone	0.989	Can produce arrhythmia: http://www.ijps.ir/article_2090.html#:$\sim$:text=Cardiac%20dysrhythmias%20have%20been%20reported,turn%2C%20may%20initiate%20cardiac%20dysrhythmias.
		Fedratinib	0.980	None
		Sorafenib	0.979	None
Waddling gait	HP:0002515	Fedratinib	0.991	Can produce gait: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/212327Orig1s000MultidisciplineR.pdf
		Sorafenib	0.990	Can produce gait: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4094497/
		Midostaurin	0.990	None
Dilated cardiomyopathy	HP:0001644	Methylprednisolone	0.993	https://pubmed.ncbi.nlm.nih.gov/25614863/
		Adefovir dipivoxil	0.980	None
		Milrinone	0.966	https://pubmed.ncbi.nlm.nih.gov/10488574/#:$\sim$:text=Conclusion%3A%20Milrinone%20lactate%20is%20an,and%20IV%20of%20heart%20failure.
Flexion contracture	HP:0001371	Fedratinib	0.997	None
		Sorafenib	0.996	https://pubmed.ncbi.nlm.nih.gov/35274715/
		Bosutinib	0.995	None
Specific learning disability	HP:0001328	Fedratinib	0.984	None
		Sorafenib	0.978	None
		Sunitinib	0.977	https://pubmed.ncbi.nlm.nih.gov/27046396/
Skeletal muscle atrophy	HP:0003202	Fedratinib	0.995	None
		Ruxolitinib	0.994	None

		Sunitinib	0.993	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4413636/
Hypoventilation	HP:0002791	Methylprednisolone	0.990	https://jintensivecare.biomedcentral.com/articles/10.1186/s40560-018-0321-9
		Resveratrol	0.966	None
		Fedratinib	0.993	None
Calf muscle hypertrophy	HP:0008981	Methylprednisolone	0.978	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2879072/
		Fedratinib	0.977	None
		Resveratrol	0.976	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0083518
Motor delay	HP:0001270	Fedratinib	0.995	None
		Sunitinib	0.994	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6586148/
		Vincristine	0.993	None
Generalized hypotonia	HP:0001290	Fedratinib	0.982	None
		Sorafenib	0.980	None
		Primidone	0.980	None
Cardiomyopathy	HP:0001638	Methylprednisolone	0.995	https://pubmed.ncbi.nlm.nih.gov/7971647/
		Resveratrol	0.974	https://onlinelibrary.wiley.com/doi/full/10.1002/fsn3.92
		Adefovir dipivoxil	0.971	None
Hyperlordosis	HP:0003307	Methylprednisolone	0.986	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4897302/
		Fedratinib	0.982	None
		Sorafenib	0.980	None
Congestive heart failure	HP:0001635	Methylprednisolone	0.979	https://www.sciencedirect.com/science/article/pii/S1071916414005843#:$\sim$:text=Methylprednisolone%20improved%20HF%20outcomes.,of%20patients%20from%20the%20study.
		Daunorubicinol	0.957	Can produce cardiotoxicity: https://www.sciencedirect.com/topics/medicine-and-dentistry/daunorubicinol
		Adefovir dipivoxil	0.946	None
Delayed speech and language development	HP:0000750	Fedratinib	0.994	None
		Midostaurin	0.993	None
		Sunitinib	0.993	None
Scoliosis	HP:0002650	Sorafenib	0.995	None
		Fedratinib	0.995	None
		Midostaurin	0.994	None
Progressive muscle weakness	HP:0003323	Methylprednisolone	0.999	Can cause weakness: https://pubmed.ncbi.nlm.nih.gov/14629908/

		Resveratrol	0.985	https://pubmed.ncbi.nlm.nih.gov/33239684/
		Patisiran	0.960	None
Cognitive impairment	HP:0100543	Sunitinib	0.997	None
		Ruxolitinib	0.997	Can produce cognitive impairment: https://pubmed.ncbi.nlm.nih.gov/24661373/
		Bosutinib	0.997	https://pubmed.ncbi.nlm.nih.gov/34484904/

9.10. Drug Candidates AD

Table S11: Table showing the drug candidates with the highest scores for each symptom/phenotype obtained in the AD KG. Any evidence that supports the prediction will be shown in the *Supporting Evidence* column. If the drug is contraindicated for the given symptom/phenotype it will also be shown in this column.

Symptom	Symptom ID	Candidate	Score	Evidence?
Personality changes	HP:0000751	flortaucipir F 18	0.986	https://www.sciencedirect.com/science/article/abs/pii/S0006322321015663
		fedratinib	0.979	May cause: https://medlineplus.gov/druginfo/meds/a619058.html
		lansoprazole	0.978	None
Dysphagia	HP:0002015	fedratinib	0.998	None
		midostaurin	0.998	Causes no dysphagia ? https://www.ons.org/cjon/23/6/midostaurin-nursing-perspectives-managing-treatment-and-adverse-events-patients-flt3
		nintedanib	0.997	None
Alzheimer disease	HP:0002511	Resveratrol	0.983	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5664214/
		pexidartinib	0.980	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8101105/
		memantine	0.980	https://pubmed.ncbi.nlm.nih.gov/16906789/
Cerebral cortical atrophy	HP:0002120	midostaurin	0.998	None
		fedratinib	0.998	None
		sunitinib	0.998	treats Brain Cancer: https://clinicaltrials.gov/ct2/show/NCT00923117
Abnormality of extrapyramidal motor function	HP:0002071	midostaurin	0.991	None
		fedratinib	0.990	None
		bosutinib	0.989	None
Dementia	HP:0000726	midostaurin	0.995	https://www.sciencedirect.com/topics/chemistry/midostaurin
		fedratinib	0.995	None
		pazopanib	0.994	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5757517/
Babinski sign	HP:0003487	midostaurin	0.998	None
		fedratinib	0.997	None
		sunitinib	0.997	None
Lower limb hyperreflexia	HP:0002395	flortaucipir F 18	0.964	None
		Donepezil	0.956	None
		Clioquinol	0.956	None
Dysarthria	HP:0001260	midostaurin	0.999	None
		fedratinib	0.999	None

		sunitinib	0.998	None
Memory impairment	HP:0002354	flortaucipir F 18	0.982	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8175307/
		pexidartinib	0.977	https://www.alzdiscovery.org/uploads/cognitive_vitality_media/Pexidartinib-Cognitive-Vitality-For-Researchers.pdf
		sorafenib	0.974	None
Dystonia	HP:0001332	fedratinib	0.997	None
		midostaurin	0.997	None
		bosutinib	0.995	None
Optic ataxia	HP:0031868	Clioquinol	0.986	None
		Donepezil	0.986	None
		Memantine	0.970	Optic nerve atrophy: https://pubmed.ncbi.nlm.nih.gov/26666888/
Myoclonus	HP:0001336	fedratinib	0.996	None
		midostaurin	0.996	None
		bosutinib	0.996	None
Apraxia	HP:0002186	midostaurin	0.989	None
		fedratinib	0.988	None
		nintedanib	0.988	None
Seizure	HP:0001250	fedratinib	0.999	Can cause: https://www.mskcc.org/cancer-care/patient-education/medications/fedratinib
		midostaurin	0.999	None
		bosutinib	0.998	Can cause: https://www.ema.europa.eu/en/documents/product-information/bosulif-epar-product-information_en.pdf
Gait disturbance	HP:0001288	fedratinib	0.986	None
		bosutinib	0.977	None
		midostaurin	0.973	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8301989/
Neurofibrillary tangles	0.973	flortaucipir F 18	0.974	https://pubchem.ncbi.nlm.nih.gov/compound/70957463
		cycloserine	0.962	https://pubmed.ncbi.nlm.nih.gov/36159454/
		lansoprazole	0.961	https://pubmed.ncbi.nlm.nih.gov/24900410/
Spastic tetraparesis	HP:0001285	duloxetine	0.959	None
		flortaucipir F 18	0.952	None
		metformin	0.951	None
Agnosia	HP:0010524	Donepezil	0.980	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3504981/
		Clioquinol	0.980	None
		Memantine	0.967	https://pubmed.ncbi.nlm.nih.gov/19898670/

9.11. Drug Candidates ALS

Table S12: Table showing the drug candidates with the highest scores for each symptom/phenotype obtained in the ALS KG. Any evidence that supports the prediction will be shown in the *Supporting Evidence* column. If the drug is contraindicated for the given symptom/phenotype it will also be shown in this column.

Symptom	Symptom ID	Candidate	Score	Evidence?
Sleep apnea	HP:0010535	Riluzole	0.808	https://pubmed.ncbi.nlm.nih.gov/11732759/
		Gabapentin	0.767	Can cause: https://pubmed.ncbi.nlm.nih.gov/28116804/
		Vitamin E	0.756	https://pubmed.ncbi.nlm.nih.gov/23389837/
Degeneration of anterior horn cells	HP:0002398	Riluzole	0.821	Spinal muscular atrophy: https://pubmed.ncbi.nlm.nih.gov/14623733/
		tacrolimus	0.785	Not significant: https://www.nature.com/articles/sc2015172
		brilliant Blue G	0.768	Can help ELA: https://peerj.com/articles/3064/
Dysarthria	HP:0001260	hexachlorophene	0.976	None
		dabrafenib	0.972	None
		dichlorophen	0.954	None
Skeletal muscle atrophy	HP:0003202	hexachlorophene	0.953	None
		dabrafenib	0.935	Can cause: https://pubmed.ncbi.nlm.nih.gov/32898388/
		quercetin	0.907	https://pubmed.ncbi.nlm.nih.gov/25614714/#:$\sim$:text=Together%2C%20these%20findings%20suggest%20that,induced%20muscle%20inflammation%20and%20sarcopenia.
Muscle weakness	HP:0001324	hexachlorophene	0.951	None
		dabrafenib	0.944	None
		quercetin	0.989	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6356612/#:$\sim$:text=Taken%20together%2C%20the%20findings%20from,sarcolemmal%20action%20potential%20propagation%20impairment.
Muscle spasm	HP:0003394	hexachlorophene	0.975	None
		dabrafenib	0.958	Can cause: https://www.macmillan.org.uk/cancer-information-and-support/treatments-and-drugs/dabrafenib-and-trametinib
		dichlorophen	0.945	None
Amyotrophic lateral sclerosis	HP:0007354	hexachlorophene	0.911	https://pubmed.ncbi.nlm.nih.gov/25987361/

		oleic acid	0.884	https://pubmed.ncbi.nlm.nih.gov/29760648/
		dabrafenib	0.881	None
Dysphagia	HP:0002015	hexachlorophene	0.987	None
		dabrafenib	0.980	None
		dichlorophen	0.968	None
Fasciculations	HP:0002380	hexachlorophene	0.920	None
		oleic acid	0.891	Can increase: https://www.sciencedirect.com/science/article/pii/S0006899314005861?via%3Dihub
		dabrafenib	0.998	None
Degeneration of the lateral corticospinal tracts	HP:0002314	hexachlorophene	0.829	None
		dabrafenib	0.787	None
		celecoxib	0.787	None
Pseudobulbar paralysis	HP:0007024	Riluzole	0.788	https://www.nejm.org/doi/full/10.1056/NEJM199403033300901
		Gabapentin	0.727	None
		celecoxib	0.720	None
Hyperreflexia	HP:0001347	hexachlorophene	0.983	Can cause: https://pubchem.ncbi.nlm.nih.gov/compound/Hexachlorophene#section=Human-Toxicity-Excerpts
		dabrafenib	0.977	None
		dichlorophen	0.963	None
Spasticity	HP:0001257	hexachlorophene	0.989	None
		dabrafenib	0.986	None
		sotorasib	0.970	None