

Fig. S1. Overview of gene–disease association prediction.

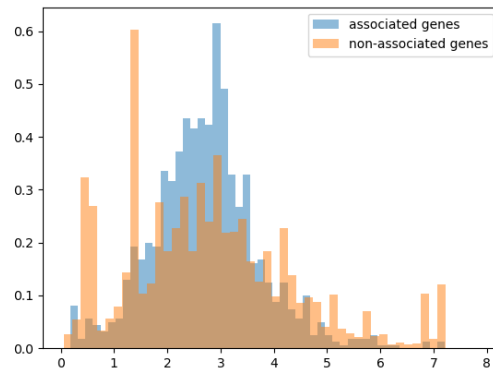


Fig. S2. Average information content difference between *Drosophila* gene phenotype annotations and *m* informative common human phenotype class in disease associated genes and non-disease associated genes.

Table S1. Evaluating the use of model organism phenotypes in the prediction of gene–disease associations using the Alliance dataset with all the available associations.

	Mouse	Fish	Fly	Yeast
Resnik's	0.753 ± 0.006	0.575 ± 0.011	0.601 ± 0.01	0.491 ± 0.041
OPA2Vec	0.519 ± 0.007	0.359 ± 0.010	0.312 ± 0.009	0.420 ± 0.040
DL2Vec	0.678 ± 0.007	0.464 ± 0.011	0.406 ± 0.010	0.477 ± 0.041
OWL2Vec*	0.610 ± 0.007	0.445 ± 0.011	0.419 ± 0.010	0.470 ± 0.041
genes with phenotypes	14210	6182	11061	4443
associated diseases (mapped to OMIM)	4022	2366	2681	406
disease-gene associations	18017	8811	9840	595

Table S2. Evaluating the use of model organism phenotypes in the prediction of gene–disease associations using the Alliance dataset, filtering out the automated assertions, and associations of genotype based on phenotypes and sequence alignment and similarity evidence.

	Mouse	Fish	Fly	Yeast
Resnik's	0.933 ± 0.009	0.691 ± 0.044	0.621 ± 0.043	0.458 ± 0.062
OPA2Vec	0.688 ± 0.017	0.262 ± 0.042	0.321 ± 0.04	0.465 ± 0.062
DL2Vec	0.876 ± 0.012	0.440 ± 0.047	0.397 ± 0.042	0.478 ± 0.062
OWL2Vec*	0.807 ± 0.014	0.385 ± 0.046	0.442 ± 0.045	0.492 ± 0.062
genes with phenotypes	14210	6182	11061	4443
associated diseases (mapped to OMIM)	1544	265	287	186
disease-gene associations	3057	445	498	256

Table S3. Comparison of performance in predicting gene–disease associations evaluated on diseases associated with genes which have orthologs with at least one phenotype: (a) in mouse and fish (2830 genes); (b) mouse and fly (4946 genes); (c) mouse and yeast (1227 genes), on the human evaluation data set

(a)	Combined	Fish	Mouse	#genes
Resnik's	0.488 ± 0.020	0.531 ± 0.019	0.793 ± 0.016	2830
OPA2Vec	0.720 ± 0.018	0.464 ± 0.019	0.691 ± 0.018	
OWL2Vec	0.762 ± 0.017	0.487 ± 0.019	0.721 ± 0.018	
DL2Vec	0.778 ± 0.017	0.519 ± 0.019	0.786 ± 0.016	
(b)	Combined	Fly	Mouse	#genes
Resnik's	0.470 ± 0.018	0.555 ± 0.019	0.767 ± 0.015	4946
OPA2Vec	0.671 ± 0.017	0.444 ± 0.018	0.656 ± 0.017	
OWL2Vec	0.726 ± 0.016	0.492 ± 0.018	0.693 ± 0.016	
DL2Vec	0.739 ± 0.015	0.454 ± 0.018	0.751 ± 0.015	
(c)	Combined	Yeast	Mouse	#genes
Resnik's	0.458 ± 0.037	0.458 ± 0.035	0.655 ± 0.035	1227
OPA2Vec	0.605 ± 0.036	0.536 ± 0.035	0.562 ± 0.037	
OWL2Vec	0.625 ± 0.036	0.534 ± 0.035	0.558 ± 0.037	
DL2Vec	0.669 ± 0.035	0.554 ± 0.035	0.641 ± 0.036	

Table S4. Prediction of gene–disease association for diseases mapped to *nervous system disease* (DOID:863) – Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.817 ± 0.024	0.593 ± 0.042	0.633 ± 0.042	0.483 ± 0.083
OPA2Vec	0.645 ± 0.030	0.347 ± 0.041	0.348 ± 0.039	0.495 ± 0.083
DL2Vec	0.767 ± 0.026	0.430 ± 0.042	0.410 ± 0.040	0.563 ± 0.083
OWL2Vec*	0.720 ± 0.028	0.446 ± 0.042	0.418 ± 0.041	0.542 ± 0.083

Table S5. Prediction of gene–disease association for diseases mapped to *nervous system disease* (DOID:863) – Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.955 ± 0.023	0.633 ± 0.077	0.670 ± 0.098	0.434 ± 0.159
OPA2Vec	0.755 ± 0.048	0.337 ± 0.076	0.352 ± 0.093	0.451 ± 0.159
DL2Vec	0.910 ± 0.032	0.422 ± 0.079	0.454 ± 0.097	0.487 ± 0.160
OWL2Vec*	0.835 ± 0.041	0.432 ± 0.079	0.455 ± 0.102	0.437 ± 0.159

Table S6. Prediction of gene–disease association for diseases mapped to *disease of metabolism* (DOID:0014667) – Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.719 ± 0.042	0.546 ± 0.083	0.514 ± 0.067	0.425 ± 0.074
OPA2Vec	0.647 ± 0.044	0.384 ± 0.081	0.389 ± 0.061	0.579 ± 0.074
DL2Vec	0.759 ± 0.040	0.473 ± 0.083	0.486 ± 0.063	0.579 ± 0.074
OWL2Vec*	0.714 ± 0.042	0.444 ± 0.083	0.497 ± 0.064	0.499 ± 0.075

Table S7. Prediction of gene–disease association for diseases mapped to *disease of metabolism* (DOID:0014667) – Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.924 ± 0.036	0.572 ± 0.112	0.478 ± 0.136	0.416 ± 0.154
OPA2Vec	0.677 ± 0.063	0.366 ± 0.109	0.380 ± 0.124	0.591 ± 0.154
DL2Vec	0.911 ± 0.039	0.446 ± 0.113	0.488 ± 0.128	0.528 ± 0.156
OWL2Vec*	0.814 ± 0.053	0.451 ± 0.113	0.555 ± 0.134	0.538 ± 0.156

Table S8. Prediction of gene–disease association for diseases mapped to *inherited metabolic disorder* (DOID:655) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.715 ± 0.042	0.545 ± 0.086	0.512 ± 0.067	0.425 ± 0.074
OPA2Vec	0.644 ± 0.045	0.387 ± 0.084	0.394 ± 0.062	0.579 ± 0.074
DL2Vec	0.756 ± 0.040	0.472 ± 0.086	0.488 ± 0.063	0.579 ± 0.074
OWL2Vec*	0.712 ± 0.043	0.445 ± 0.086	0.497 ± 0.064	0.499 ± 0.075

Table S9. Prediction of gene–disease association for diseases mapped to *inherited metabolic disorder* (DOID:655) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.918 ± 0.040	0.570 ± 0.125	0.472 ± 0.138	0.404 ± 0.155
OPA2Vec	0.690 ± 0.068	0.372 ± 0.122	0.386 ± 0.128	0.604 ± 0.155
DL2Vec	0.909 ± 0.042	0.449 ± 0.125	0.502 ± 0.131	0.538 ± 0.158
OWL2Vec*	0.838 ± 0.054	0.454 ± 0.125	0.562 ± 0.135	0.548 ± 0.157

Table S10. Prediction of gene–disease association for diseases mapped to *central nervous system disease* (DOID:331) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.775 ± 0.039	0.632 ± 0.064	0.644 ± 0.059	0.468 ± 0.105
OPA2Vec	0.599 ± 0.045	0.340 ± 0.062	0.388 ± 0.057	0.504 ± 0.105
DL2Vec	0.709 ± 0.042	0.434 ± 0.065	0.428 ± 0.058	0.603 ± 0.103
OWL2Vec*	0.675 ± 0.043	0.426 ± 0.065	0.440 ± 0.060	0.570 ± 0.104

Table S11. Prediction of gene–disease association for diseases mapped to *central nervous system disease* (DOID:331) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.936 ± 0.044	0.700 ± 0.115	0.751 ± 0.118	0.427 ± 0.206
OPA2Vec	0.698 ± 0.082	0.310 ± 0.116	0.379 ± 0.128	0.473 ± 0.208
DL2Vec	0.889 ± 0.056	0.386 ± 0.122	0.516 ± 0.132	0.439 ± 0.207
OWL2Vec*	0.827 ± 0.067	0.447 ± 0.124	0.498 ± 0.143	0.397 ± 0.204

Table S12. Prediction of gene–disease association for diseases mapped to *musculoskeletal system disease* (DOID:17) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.854 ± 0.032	0.620 ± 0.053	0.593 ± 0.063	0.533 ± 0.140
OPA2Vec	0.683 ± 0.042	0.353 ± 0.052	0.329 ± 0.057	0.444 ± 0.139
DL2Vec	0.836 ± 0.033	0.482 ± 0.054	0.390 ± 0.059	0.555 ± 0.139
OWL2Vec*	0.789 ± 0.037	0.450 ± 0.054	0.447 ± 0.061	0.427 ± 0.139

Table S13. Prediction of gene–disease association for diseases mapped to *musculoskeletal system disease* (DOID:17) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.964 ± 0.026	0.609 ± 0.09	0.560 ± 0.163	0.589 ± 0.246
OPA2Vec	0.750 ± 0.061	0.321 ± 0.086	0.308 ± 0.128	0.524 ± 0.250
DL2Vec	0.934 ± 0.035	0.484 ± 0.092	0.353 ± 0.133	0.437 ± 0.248
OWL2Vec*	0.872 ± 0.047	0.389 ± 0.090	0.488 ± 0.141	0.564 ± 0.248

Table S14. Prediction of gene–disease association for diseases mapped to *sensory system disease* (DOID:0050155) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.870 ± 0.035	0.555 ± 0.067	0.601 ± 0.076	0.601 ± 0.188
OPA2Vec	0.700 ± 0.047	0.358 ± 0.065	0.301 ± 0.066	0.404 ± 0.189
DL2Vec	0.825 ± 0.039	0.437 ± 0.067	0.404 ± 0.070	0.439 ± 0.191
OWL2Vec*	0.763 ± 0.044	0.443 ± 0.067	0.364 ± 0.070	0.523 ± 0.192

Table S15. Prediction of gene–disease association for diseases mapped to *sensory system disease* (DOID:0050155) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.972 ± 0.028	0.585 ± 0.125	0.481 ± 0.208	0.532 ± 0.333
OPA2Vec	0.805 ± 0.066	0.375 ± 0.123	0.316 ± 0.170	0.313 ± 0.309
DL2Vec	0.922 ± 0.045	0.470 ± 0.127	0.366 ± 0.176	0.516 ± 0.333
OWL2Vec*	0.851 ± 0.0600	0.394 ± 0.124	0.359 ± 0.178	0.452 ± 0.332

Table S16. Prediction of gene–disease association for diseases mapped to *brain disease* (DOID:936) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.788 ± 0.047	0.615 ± 0.083	0.627 ± 0.077	0.427 ± 0.139
OPA2Vec	0.593 ± 0.056	0.344 ± 0.081	0.386 ± 0.073	0.546 ± 0.139
DL2Vec	0.703 ± 0.052	0.471 ± 0.085	0.418 ± 0.074	0.615 ± 0.136
OWL2Vec*	0.668 ± 0.054	0.433 ± 0.084	0.464 ± 0.076	0.564 ± 0.139

Table S17. Prediction of gene–disease association for diseases mapped to *brain disease* (DOID:936) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.934 ± 0.057	0.697 ± 0.158	0.696 ± 0.180	0.545 ± 0.332
OPA2Vec	0.716 ± 0.104	0.351 ± 0.164	0.417 ± 0.186	0.346 ± 0.317
DL2Vec	0.876 ± 0.076	0.402 ± 0.168	0.492 ± 0.189	0.347 ± 0.317
OWL2Vec*	0.858 ± 0.081	0.521 ± 0.171	0.524 ± 0.196	0.471 ± 0.333

Table S18. Prediction of gene–disease association for diseases mapped to *eye disease* (DOID:5614) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.880 ± 0.040	0.567 ± 0.078	0.584 ± 0.094	0.542 ± 0.257
OPA2Vec	0.725 ± 0.055	0.357 ± 0.076	0.283 ± 0.079	0.437 ± 0.256
DL2Vec	0.857 ± 0.043	0.440 ± 0.078	0.407 ± 0.086	0.364 ± 0.248
OWL2Vec*	0.773 ± 0.052	0.454 ± 0.078	0.391 ± 0.087	0.483 ± 0.258

Table S19. Prediction of gene–disease association for diseases mapped to *eye disease* (DOID:5614) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.971 ± 0.033	0.590 ± 0.142	0.389 ± 0.244	0.525 ± 0.378
OPA2Vec	0.839 ± 0.071	0.371 ± 0.139	0.306 ± 0.201	0.315 ± 0.351
DL2Vec	0.940 ± 0.046	0.455 ± 0.144	0.327 ± 0.205	0.429 ± 0.374
OWL2Vec*	0.856 ± 0.068	0.411 ± 0.142	0.355 ± 0.209	0.505 ± 0.378

Table S20. Prediction of gene–disease association for diseases mapped to *connective tissue disease* (DOID:65) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.888 ± 0.04	0.623 ± 0.077	0.618 ± 0.090	0.610 ± 0.271
OPA2Vec	0.662 ± 0.06	0.366 ± 0.077	0.256 ± 0.077	0.433 ± 0.275
DL2Vec	0.861 ± 0.044	0.505 ± 0.08	0.388 ± 0.085	0.665 ± 0.262
OWL2Vec*	0.800 ± 0.050	0.421 ± 0.079	0.405 ± 0.088	0.523 ± 0.277

Table S21. Prediction of gene–disease association for diseases mapped to *connective tissue disease* (DOID:65) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.963 ± 0.034	0.599 ± 0.115	0.542 ± 0.257	0.726 ± 0.282
OPA2Vec	0.716 ± 0.081	0.363 ± 0.113	0.305 ± 0.181	0.457 ± 0.315
DL2Vec	0.925 ± 0.047	0.488 ± 0.117	0.341 ± 0.186	0.366 ± 0.305
OWL2Vec*	0.873 ± 0.060	0.379 ± 0.114	0.487 ± 0.196	0.565 ± 0.314

Table S22. Prediction of gene–disease association for diseases mapped to *bone disease* (DOID:0080001) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.888 ± 0.043	0.623 ± 0.082	0.606 ± 0.098	0.661 ± 0.285
OPA2Vec	0.656 ± 0.065	0.369 ± 0.081	0.230 ± 0.081	0.426 ± 0.298
DL2Vec	0.854 ± 0.048	0.496 ± 0.084	0.381 ± 0.093	0.629 ± 0.291
OWL2Vec*	0.799 ± 0.055	0.428 ± 0.083	0.391 ± 0.095	0.500 ± 0.302

Table S23. Prediction of gene–disease association for diseases mapped to *bone disease* (DOID:0080001) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.969 ± 0.033	0.604 ± 0.121	0.544 ± 0.276	0.687 ± 0.351
OPA2Vec	0.719 ± 0.087	0.370 ± 0.120	0.248 ± 0.176	0.513 ± 0.378
DL2Vec	0.932 ± 0.049	0.513 ± 0.124	0.335 ± 0.193	0.390 ± 0.369
OWL2Vec*	0.867 ± 0.065	0.376 ± 0.120	0.497 ± 0.204	0.624 ± 0.366

Table S24. Prediction of gene–disease association for diseases mapped to *neurodegenerative disease* (DOID:1289) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.753 ± 0.063	0.665 ± 0.100	0.656 ± 0.088	0.549 ± 0.154
OPA2Vec	0.604 ± 0.072	0.367 ± 0.102	0.382 ± 0.086	0.454 ± 0.154
DL2Vec	0.721 ± 0.066	0.384 ± 0.103	0.486 ± 0.089	0.585 ± 0.152
OWL2Vec*	0.680 ± 0.069	0.434 ± 0.104	0.394 ± 0.089	0.627 ± 0.149

Table S25. Prediction of gene–disease association for diseases mapped to *neurodegenerative disease* (DOID:1289) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.942 ± 0.063	0.733 ± 0.167	0.802 ± 0.159	0.342 ± 0.254
OPA2Vec	0.677 ± 0.126	0.288 ± 0.171	0.424 ± 0.190	0.568 ± 0.265
DL2Vec	0.905 ± 0.079	0.382 ± 0.184	0.586 ± 0.190	0.455 ± 0.266
OWL2Vec*	0.802 ± 0.108	0.381 ± 0.184	0.498 ± 0.213	0.414 ± 0.263

Table S26. Prediction of gene–disease association for diseases mapped to *immune system disease* (DOID:2914) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.884 ± 0.049	0.513 ± 0.126	0.621 ± 0.125	0.486 ± 0.316
OPA2Vec	0.702 ± 0.070	0.366 ± 0.121	0.228 ± 0.104	0.501 ± 0.316
DL2Vec	0.850 ± 0.054	0.499 ± 0.126	0.437 ± 0.123	0.476 ± 0.316
OWL2Vec*	0.749 ± 0.066	0.395 ± 0.123	0.417 ± 0.131	0.474 ± 0.316

Table S27. Prediction of gene–disease association for diseases mapped to *immune system disease* (DOID:2914) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.927 ± 0.064	0.622 ± 0.177	0.523 ± 0.378	0.609 ± 0.399
OPA2Vec	0.643 ± 0.118	0.393 ± 0.178	0.236 ± 0.300	0.508 ± 0.408
DL2Vec	0.852 ± 0.087	0.464 ± 0.182	0.394 ± 0.346	0.488 ± 0.408
OWL2Vec*	0.798 ± 0.099	0.481 ± 0.182	0.589 ± 0.348	0.647 ± 0.390

Table S28. Prediction of gene–disease association for diseases mapped to *retinal disease* (DOID:5679) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.880 ± 0.054	0.546 ± 0.112	0.560 ± 0.130	0.508 ± 0.316
OPA2Vec	0.772 ± 0.070	0.412 ± 0.111	0.336 ± 0.113	0.524 ± 0.316
DL2Vec	0.867 ± 0.057	0.487 ± 0.112	0.419 ± 0.118	0.395 ± 0.309
OWL2Vec*	0.815 ± 0.065	0.406 ± 0.111	0.413 ± 0.120	0.590 ± 0.311

Table S29. Prediction of gene–disease association for diseases mapped to *retinal disease* (DOID:5679) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.984 ± 0.033	0.506 ± 0.208	0.373 ± 0.306	0.438 ± 0.573
OPA2Vec	0.877 ± 0.085	0.411 ± 0.205	0.324 ± 0.250	0.539 ± 0.576
DL2Vec	0.954 ± 0.054	0.470 ± 0.208	0.362 ± 0.257	0.519 ± 0.577
OWL2Vec*	0.912 ± 0.073	0.358 ± 0.200	0.415 ± 0.263	0.689 ± 0.534

Table S30. Prediction of gene–disease association for diseases mapped to *bone development disease* (DOID:0080006) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.880 ± 0.053	0.624 ± 0.093	0.597 ± 0.109	0.625 ± 0.323
OPA2Vec	0.653 ± 0.077	0.378 ± 0.093	0.234 ± 0.090	0.468 ± 0.333
DL2Vec	0.857 ± 0.057	0.487 ± 0.096	0.389 ± 0.104	0.723 ± 0.299
OWL2Vec*	0.804 ± 0.064	0.445 ± 0.096	0.376 ± 0.106	0.583 ± 0.329

Table S31. Prediction of gene–disease association for diseases mapped to *bone development disease* (DOID:0080006) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.966 ± 0.042	0.642 ± 0.14	0.512 ± 0.289	0.694 ± 0.376
OPA2Vec	0.743 ± 0.101	0.359 ± 0.140	0.214 ± 0.188	0.491 ± 0.408
DL2Vec	0.944 ± 0.053	0.535 ± 0.146	0.308 ± 0.212	0.298 ± 0.373
OWL2Vec*	0.877 ± 0.076	0.339 ± 0.138	0.442 ± 0.228	0.572 ± 0.404

Table S32. Prediction of gene–disease association for diseases mapped to *hematopoietic system disease* (DOID:74) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.838 ± 0.057	0.573 ± 0.094	0.733 ± 0.098	0.451 ± 0.141
OPA2Vec	0.701 ± 0.071	0.368 ± 0.092	0.264 ± 0.092	0.536 ± 0.141
DL2Vec	0.855 ± 0.055	0.625 ± 0.092	0.462 ± 0.104	0.542 ± 0.141
OWL2Vec*	0.764 ± 0.066	0.428 ± 0.094	0.379 ± 0.103	0.480 ± 0.141

Table S33. Prediction of gene–disease association for diseases mapped to *hematopoietic system disease* (DOID:74) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.932 ± 0.057	0.582 ± 0.150	0.644 ± 0.220	0.745 ± 0.436
OPA2Vec	0.706 ± 0.104	0.369 ± 0.147	0.241 ± 0.187	0.124 ± 0.329
DL2Vec	0.916 ± 0.063	0.528 ± 0.152	0.397 ± 0.214	0.365 ± 0.481
OWL2Vec*	0.790 ± 0.093	0.401 ± 0.149	0.409 ± 0.226	0.242 ± 0.428

Table S34. Prediction of gene–disease association for diseases mapped to *primary immunodeficiency disease* (DOID:612) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.884 ± 0.051	0.481 ± 0.134	0.598 ± 0.137	0.486 ± 0.316
OPA2Vec	0.706 ± 0.073	0.357 ± 0.128	0.247 ± 0.115	0.501 ± 0.316
DL2Vec	0.851 ± 0.057	0.486 ± 0.134	0.428 ± 0.132	0.476 ± 0.316
OWL2Vec*	0.741 ± 0.070	0.383 ± 0.130	0.400 ± 0.141	0.474 ± 0.316

Table S35. Prediction of gene–disease association for diseases mapped to *primary immunodeficiency disease* (DOID:612) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.923 ± 0.069	0.601 ± 0.188	0.523 ± 0.378	0.609 ± 0.399
OPA2Vec	0.627 ± 0.126	0.371 ± 0.186	0.236 ± 0.300	0.508 ± 0.408
DL2Vec	0.847 ± 0.094	0.447 ± 0.191	0.394 ± 0.346	0.488 ± 0.408
OWL2Vec*	0.787 ± 0.107	0.453 ± 0.192	0.589 ± 0.348	0.647 ± 0.390

Table S36. Prediction of gene–disease association for diseases mapped to *disease of mental health* (DOID:150) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.732 ± 0.078	0.564 ± 0.110	0.550 ± 0.104	0.620 ± 0.235
OPA2Vec	0.537 ± 0.087	0.443 ± 0.110	0.315 ± 0.092	0.487 ± 0.242
DL2Vec	0.625 ± 0.085	0.477 ± 0.111	0.379 ± 0.096	0.530 ± 0.242
OWL2Vec*	0.618 ± 0.085	0.548 ± 0.111	0.454 ± 0.101	0.482 ± 0.242

Table S37. Prediction of gene–disease association for diseases mapped to *disease of mental health* (DOID:150) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.863 ± 0.082	0.575 ± 0.165	0.727 ± 0.190	0.587 ± 0.372
OPA2Vec	0.583 ± 0.118	0.446 ± 0.166	0.411 ± 0.201	0.293 ± 0.344
DL2Vec	0.677 ± 0.112	0.363 ± 0.160	0.333 ± 0.192	0.509 ± 0.378
OWL2Vec*	0.656 ± 0.114	0.513 ± 0.167	0.494 ± 0.213	0.452 ± 0.376

Table S38. Prediction of gene–disease association for diseases mapped to *mitochondrial metabolism disease* (DOID:700) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.510 ± 0.099	0.576 ± 0.233	0.528 ± 0.135	0.423 ± 0.114
OPA2Vec	0.612 ± 0.097	0.498 ± 0.236	0.461 ± 0.119	0.551 ± 0.115
DL2Vec	0.659 ± 0.094	0.478 ± 0.235	0.514 ± 0.119	0.596 ± 0.113
OWL2Vec*	0.666 ± 0.094	0.478 ± 0.235	0.523 ± 0.125	0.493 ± 0.115

Table S39. Prediction of gene–disease association for diseases mapped to *mitochondrial metabolism disease* (DOID:700) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.832 ± 0.207	0.418 ± 0.493	0.540 ± 0.377	0.248 ± 0.288
OPA2Vec	0.729 ± 0.247	0.355 ± 0.479	0.443 ± 0.351	0.713 ± 0.302
DL2Vec	0.905 ± 0.163	0.099 ± 0.299	0.400 ± 0.346	0.641 ± 0.320
OWL2Vec*	0.891 ± 0.173	0.610 ± 0.488	0.832 ± 0.374	0.417 ± 0.329

Table S40. Prediction of gene–disease association for diseases mapped to *muscular disease* (DOID:0080000) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.810 ± 0.065	0.645 ± 0.085	0.544 ± 0.111	0.569 ± 0.202
OPA2Vec	0.711 ± 0.075	0.362 ± 0.085	0.377 ± 0.105	0.398 ± 0.200
DL2Vec	0.805 ± 0.066	0.495 ± 0.089	0.403 ± 0.106	0.511 ± 0.204
OWL2Vec*	0.793 ± 0.067	0.466 ± 0.089	0.463 ± 0.110	0.374 ± 0.198

Table S41. Prediction of gene–disease association for diseases mapped to *muscular disease* (DOID:0080000) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.970 ± 0.050	0.668 ± 0.175	0.480 ± 0.301	0.456 ± 0.704
OPA2Vec	0.797 ± 0.119	0.263 ± 0.163	0.335 ± 0.262	0.476 ± 0.706
DL2Vec	0.934 ± 0.073	0.536 ± 0.185	0.384 ± 0.270	0.429 ± 0.700
OWL2Vec*	0.887 ± 0.093	0.343 ± 0.176	0.526 ± 0.301	0.317 ± 0.658

Table S42. Prediction of gene–disease association for diseases mapped to *integumentary system disease* (DOID:16) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.840 ± 0.061	0.595 ± 0.130	0.617 ± 0.116	0.548 ± 0.182
OPA2Vec	0.712 ± 0.076	0.483 ± 0.132	0.279 ± 0.102	0.495 ± 0.183
DL2Vec	0.849 ± 0.060	0.550 ± 0.132	0.356 ± 0.108	0.557 ± 0.181
OWL2Vec*	0.728 ± 0.074	0.525 ± 0.132	0.389 ± 0.110	0.420 ± 0.180

Table S43. Prediction of gene–disease association for diseases mapped to *integumentary system disease* (DOID:16) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.963 ± 0.054	0.638 ± 0.240	0.573 ± 0.330	0.537 ± 0.499
OPA2Vec	0.797 ± 0.115	0.593 ± 0.246	0.351 ± 0.288	0.578 ± 0.494
DL2Vec	0.935 ± 0.070	0.550 ± 0.249	0.388 ± 0.294	0.517 ± 0.500
OWL2Vec*	0.857 ± 0.100	0.674 ± 0.234	0.374 ± 0.292	0.383 ± 0.486

Table S44. Prediction of gene–disease association for diseases mapped to *cardiovascular system disease* (DOID:1287) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.891 ± 0.050	0.664 ± 0.092	0.617 ± 0.101	0.510 ± 0.447
OPA2Vec	0.696 ± 0.074	0.329 ± 0.143	0.267 ± 0.088	0.362 ± 0.430
DL2Vec	0.861 ± 0.056	0.329 ± 0.091	0.408 ± 0.098	0.391 ± 0.436
OWL2Vec*	0.751 ± 0.070	0.413 ± 0.096	0.422 ± 0.101	0.702 ± 0.409

Table S45. Prediction of gene–disease association for diseases mapped to *cardiovascular system disease* (DOID:1287) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.949 ± 0.051	0.690 ± 0.141	0.693 ± 0.224	0.776 ± 0.295
OPA2Vec	0.761 ± 0.099	0.329 ± 0.143	0.310 ± 0.218	0.293 ± 0.322
DL2Vec	0.927 ± 0.060	0.347 ± 0.145	0.305 ± 0.217	0.255 ± 0.308
OWL2Vec*	0.852 ± 0.083	0.465 ± 0.152	0.272 ± 0.216	0.501 ± 0.354

Table S46. Prediction of gene–disease association for diseases mapped to *muscle tissue disease* (DOID:66) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.820 ± 0.065	0.653 ± 0.086	0.540 ± 0.114	0.556 ± 0.207
OPA2Vec	0.724 ± 0.076	0.369 ± 0.087	0.387 ± 0.108	0.393 ± 0.204
DL2Vec	0.822 ± 0.065	0.491 ± 0.091	0.401 ± 0.109	0.530 ± 0.208
OWL2Vec*	0.810 ± 0.067	0.471 ± 0.090	0.469 ± 0.113	0.374 ± 0.202

Table S47. Prediction of gene–disease association for diseases mapped to *muscle tissue disease* (DOID:66) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.971 ± 0.050	0.682 ± 0.179	0.480 ± 0.301	0.456 ± 0.704
OPA2Vec	0.814 ± 0.116	0.275 ± 0.172	0.335 ± 0.262	0.476 ± 0.706
DL2Vec	0.949 ± 0.065	0.515 ± 0.192	0.384 ± 0.270	0.429 ± 0.700
OWL2Vec*	0.890 ± 0.093	0.352 ± 0.184	0.526 ± 0.301	0.317 ± 0.658

Table S48. Prediction of gene–disease association for diseases mapped to *peripheral nervous system disease* (DOID:574) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.799 ± 0.068	0.566 ± 0.112	0.655 ± 0.111	0.404 ± 0.205
OPA2Vec	0.663 ± 0.080	0.308 ± 0.105	0.346 ± 0.103	0.569 ± 0.207
DL2Vec	0.802 ± 0.067	0.401 ± 0.111	0.369 ± 0.104	0.543 ± 0.208
OWL2Vec*	0.746 ± 0.074	0.500 ± 0.113	0.456 ± 0.110	0.448 ± 0.207

Table S49. Prediction of gene–disease association for diseases mapped to *peripheral nervous system disease* (DOID:574) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.799 ± 0.068	0.566 ± 0.112	0.655 ± 0.111	0.404 ± 0.205
OPA2Vec	0.663 ± 0.080	0.308 ± 0.105	0.346 ± 0.103	0.569 ± 0.207
DL2Vec	0.802 ± 0.067	0.401 ± 0.111	0.369 ± 0.104	0.543 ± 0.208
OWL2Vec*	0.746 ± 0.074	0.500 ± 0.113	0.456 ± 0.110	0.448 ± 0.207

Table S50. Prediction of gene–disease association for diseases mapped to *developmental disorder of mental health* (DOID:0060037) - Human dataset

Method	mouse	fish	fly	yeast
Resnik's	0.719 ± 0.087	0.563 ± 0.121	0.537 ± 0.111	0.665 ± 0.252
OPA2Vec	0.528 ± 0.097	0.451 ± 0.122	0.293 ± 0.096	0.476 ± 0.267
DL2Vec	0.606 ± 0.095	0.501 ± 0.122	0.380 ± 0.102	0.557 ± 0.266
OWL2Vec*	0.627 ± 0.094	0.561 ± 0.121	0.451 ± 0.107	0.508 ± 0.267

Table S51. Prediction of gene–disease association for diseases mapped to *developmental disorder of mental health* (DOID:0060037) - Mouse dataset

Method	mouse	fish	fly	yeast
Resnik's	0.827 ± 0.178	0.645 ± 0.428	0.561 ± 0.444	0.532 ± 0.499
OPA2Vec	0.576 ± 0.233	0.286 ± 0.404	0.166 ± 0.333	0.199 ± 0.399
DL2Vec	0.689 ± 0.218	0.247 ± 0.386	0.291 ± 0.406	0.567 ± 0.496
OWL2Vec*	0.682 ± 0.220	0.467 ± 0.446	0.383 ± 0.435	0.534 ± 0.499

Supplementary Materials and Methods

In order to test the hypothesis that *Drosophila* phenotype (DP) classes are not well connected with specific human phenotype classes, we define MIS-HP. MIS-HP is the most informative superclass from human phenotypes to a certain class. Let C be a *Drosophila* phenotype class, we define MIS-HP for this class as shown in equation 1. Then we calculate the absolute difference between the information content of DP and its MIS-HP, we will use ($sum\Delta_G$) to refer to some of this difference for all the annotations of a gene. Let G_i be the i^{th} annotation for a gene, we calculate $sum\Delta_G$ as shown in equation 2.

$$MIS - HP(C) = \max_{P \in Superclasses(C) \cap HP} IC(P) \quad (1)$$

$$sum\Delta_G = \sum_i \left| IC(G_i) - IC(MIS - HP(G_i)) \right| \quad (2)$$

$$avg\Delta_G = \frac{\sum_i \left| IC(G_i) - IC(MIS - HP(G_i)) \right|}{n} \quad (3)$$

To visualize the difference between the associated genes and the non-associated genes, we calculate $avg\Delta_G$ as the average of the absolute difference between DP and its $MIS - HP$. Let n be the number of annotations a gene have, equation 3 shows how we calculate $avg\Delta_G$. Figure S2 shows the density histogram for the $avg\Delta_G$ for disease-associated genes and non-disease associated genes.

We compare the list of $sum\Delta_G$ for the disease-associated genes and the non-disease-associated genes. This comparison is done using a t-test and the result shows that $sum\Delta_G$ for the disease-association genes is significantly higher than the non-disease-associations p-value ($p = 4 \times 10^{-61}$), and mean 44.5 for disease-associated genes and mean 13.9 for non-disease-associated genes.