

Supplementary Materials for

“Predicting Human Microbe-Drug Associations via Graph Convolution Network with Conditional Random Field”

1 Supplementary Figures

In this paper, we compared our method with some diverse types of state-of-the-art computational methods developed for addressing other biomedical problems, such as microbe-disease prediction (i.e., KATZHMDA, NTSHMDA and WMGHMDA), miRNA-disease prediction (i.e., IMCMDA), miRNA-drug resistance prediction (i.e., GCMDR) and drug-target prediction (i.e., WNN-GIP and GCNMDA). We evaluated the performance for all methods using 2-fold CV, 5-fold CV and 10-fold CV in terms of AUC and AUPR scores. The results for AUC and AUPR have been shown in Table S1 and Table S2, respectively. In addition, for more intuitive comparison, Figure S1 and Figure S2 displayed corresponding ROC and PR curves, respectively.

Table S1. Performance comparison between baseline methods and our method in terms of AUC. The best results are marked in bold. * denotes the second best method.

Method	2-fold CV	5-fold CV	10-fold CV
KATZHMDA	0.7865±0.0254	0.8723±0.0032	0.8929±0.0265*
NTSHMDA	0.7766±0.0126	0.8302±0.0089	0.8547±0.0165
WMGHMDA	0.8519±0.0024	0.8654±0.0122	0.8729±0.0130
IMCMDA	0.7285±0.0065	0.7466±0.0102	0.7466±0.0221
GCMDR	0.8432±0.0016	0.8485±0.0062	0.8590±0.0241
BLMNII	0.8583±0.0239*	0.9231±0.0170*	0.8644±0.0227
WNNGIP	0.8256±0.0516	0.8721±0.0162	0.8711±0.0130
GCNMDA	0.9384±0.0028	0.9423±0.0105	0.9420±0.0078

Table S2. Performance comparison between baseline methods and our method in terms of AUPR. The best results are marked in bold. * denotes the second best method.

Method	2-fold CV	5-fold CV	10-fold CV
KATZHMDA	0.6559±0.0034	0.8081±0.0209	0.8403±0.0182
NTSHMDA	0.5674±0.0057	0.6735±0.0092	0.7118±0.0442
WMGHMDA	0.8201±0.0086	0.8381±0.0083	0.8452±0.0117
IMCMDA	0.7618±0.0038	0.7773±0.0113	0.7727±0.0136
GCMDR	0.8423±0.0025*	0.8509±0.0040	0.8634±0.0210
BLMNII	0.7805±0.0318	0.9263±0.0152*	0.8792±0.0221
WNNGIP	0.8299±0.0603	0.8922±0.0137	0.8863±0.0232*
GCNMDA	0.9316±0.0017	0.9376±0.0114	0.9359±0.0087

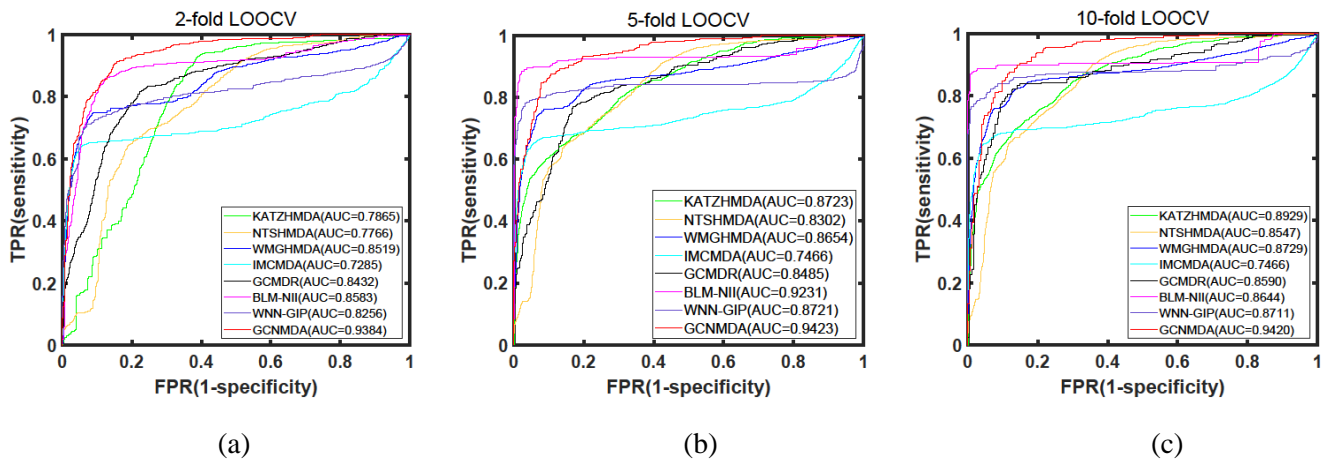


Figure. S1. Comparisons of prediction performance between our method and baseline methods based on MDAD under the frameworks of 2-fold CV, 5-fold CV and 10-fold CV in terms of AUC, respectively. (a) 2-fold CV; (b) 5-fold CV; (c) 10-fold CV.

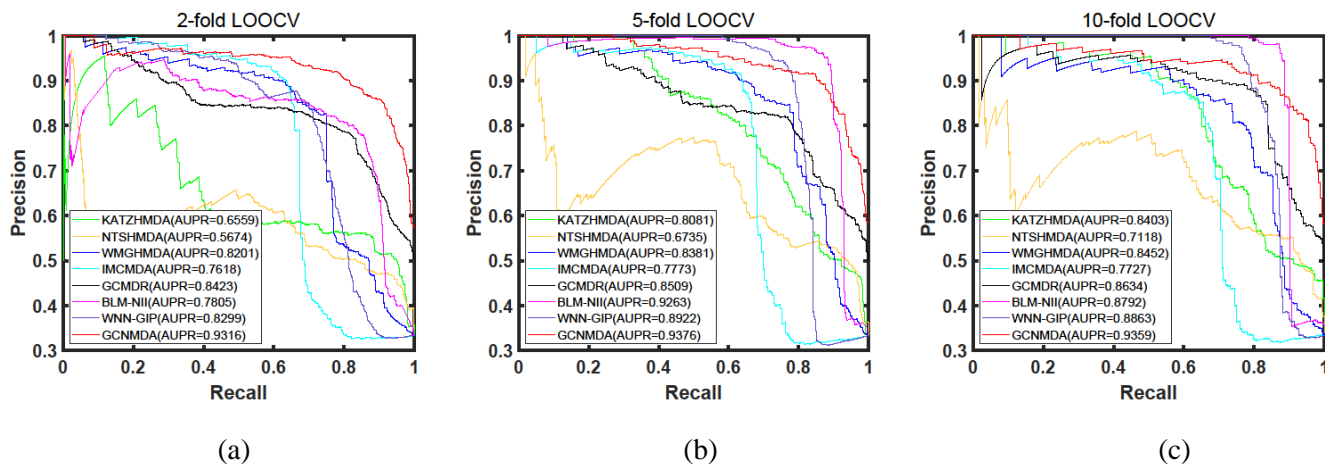


Figure. S2. Comparisons of prediction performance between our method and baseline methods based on MDAD under the frameworks of 2-fold CV, 5-fold CV and 10-fold CV in terms of AUPR, respectively. (a) 2-fold CV; (b) 5-fold CV; (c) 10-fold CV.

2 Supplementary Tables

For further verify the effectiveness of our method, we adopted two popular antimicrobial agents (i.e., Ciprofloxacin and Moxifloxacin) for case study. We validated the predicted candidate microbes using previous reports. The top 50 predicted candidate microbes have been listed in Table S1 and Table S2 for Ciprofloxacin and Moxifloxacin, respectively.

Table S3. Prediction results of the top 50 Ciprofloxacin-associated microbes. The first column records top 1-25 associated microbes. The third column records top 26-50 associated microbes.

Microbe	Evidence	Microbe	Evidence
<i>Candida albicans</i>	PMID:31471074	<i>Vibrio anguillarum</i>	PMID:19146525
<i>Streptococcus mutans</i>	PMID:30468214	<i>Proteus mirabilis</i>	PMID:26953206
<i>Staphylococcus epidermis</i>	PMID:10632381	<i>Eikenella corrodens</i>	PMID:16875802
<i>Staphylococcus epidermidis</i>	PMID:28481197	<i>Micrococcus luteus</i>	PMID:26954218
<i>Enterococcus faecalis</i>	PMID:27790716	<i>Bacillus cereus</i>	PMID:26358183
<i>Vibrio harveyi</i>	PMID:27247095	<i>Plasmodium falciparum</i>	PMID:17214980
<i>Salmonella enterica</i>	PMID:26933017	<i>Human immunodeficiency virus</i>	PMID:26195465
<i>Human immunodeficiency virus 1</i>	PMID:9566552	<i>Porphyromonas gingivalis</i>	PMID: 15231772
<i>Actinomyces oris</i>	Unconfirmed	<i>Enterococcus faecium</i>	PMID:28193670
<i>Streptococcus sanguis</i>	PMID: 11347679	<i>Streptococcus gordonii</i>	PMID:22887906
<i>Enteric bacteria and other eubacteria</i>	PMID:27436461	<i>Campylobacter jejuni</i>	PMID:27900889
<i>Listeria monocytogenes</i>	PMID:28355096	<i>Vibrio campbellii</i>	Unconfirmed
<i>Burkholderia cenocepacia</i>	PMID:27799222	<i>Klebsiella planticola</i>	PMID:25465871
<i>Streptococcus pneumoniae</i>	PMID:26100702	<i>Human herpesvirus 1</i>	Unconfirmed
<i>Burkholderia pseudomallei</i>	PMID:24502667	<i>Pichia anomala</i>	Unconfirmed
<i>Burkholderia multivorans</i>	PMID: 19633000	<i>Candida tropicalis</i>	Unconfirmed
<i>Clostridium perfringens</i>	PMID:29978055	<i>Candida glabrata</i>	Unconfirmed
<i>Serratia marcescens</i>	PMID:23751969	<i>Cryptococcus neoformans</i>	Unconfirmed
<i>Streptococcus epidermidis</i>	Unconfirmed	<i>Aeromonas hydrophila</i>	PMID:23084650
<i>Klebsiella pneumoniae</i>	PMID:27257956	<i>Streptococcus pneumoniae serotype 4</i>	PMID: 12543698
<i>Vibrio cholerae</i>	PMID:28270803	<i>Influenza A virus</i>	Unconfirmed
<i>Acinetobacter baumannii</i>	PMID:29998878	<i>Aeromonas sobria</i>	PMID:28484157
<i>Vibrio vulnificus</i>	PMID:28971862	<i>Hafnia alvei</i>	PMID:28537065
<i>Propionibacterium acnes</i>	PMID:27801379	<i>Enterococcus gallinarum</i>	PMID:29030312
<i>Streptococcus sanguinis</i>	PMID:21507381	<i>Mycobacterium avium</i>	PMID:30012773

Table S4. Prediction results of the top 50 Moxifloxacin-associated microbes. The first column records top 1-25 associated microbes. The third column records top 26-50 associated microbes.

Microbe	Evidence	Microbe	Evidence
<i>Pseudomonas aeruginosa</i>	PMID:31691651	<i>Mycobacterium tuberculosis</i>	PMID:31713607
<i>Staphylococcus aureus</i>	PMID:31689174	<i>Vibrio vulnificus</i>	PMID: 12384368
<i>Escherichia coli</i>	PMID:31542319	<i>Propionibacterium acnes</i>	PMID:31538294
<i>Streptococcus mutans</i>	PMID:29160117	<i>Streptococcus sanguinis</i>	Unconfirmed
<i>Staphylococcus epidermis</i>	PMID: 11249827	<i>Vibrio anguillarum</i>	Unconfirmed
<i>Staphylococcus epidermidis</i>	PMID:31516359	<i>Proteus mirabilis</i>	PMID:27351708
<i>Enterococcus faecalis</i>	PMID:31763048	<i>Eikenella corrodens</i>	PMID:14614671
<i>Bacillus subtilis</i>	PMID:30036828	<i>Micrococcus luteus</i>	PMID:24231380
<i>Vibrio harveyi</i>	Unconfirmed	<i>Bacillus cereus</i>	PMID:21834669
<i>Salmonella enterica</i>	PMID:22151215	<i>Plasmodium falciparum</i>	PMID:15125930
<i>Human immunodeficiency virus 1</i>	Unconfirmed	<i>Human immunodeficiency virus</i>	PMID:31388545
<i>Actinomyces oris</i>	PMID: 26538502	<i>Porphyromonas gingivalis</i>	PMID:30048853
<i>Streptococcus sanguis</i>	PMID:10629010	<i>Enterococcus faecium</i>	PMID:23524466
<i>Enteric bacteria and other eubacteria</i>	Unconfirmed	<i>Streptococcus gordonii</i>	PMID:29160117
<i>Listeria monocytogenes</i>	PMID:28739228	<i>Campylobacter jejuni</i>	PMID:16027651
<i>Burkholderia cenocepacia</i>	Unconfirmed	<i>Vibrio campbellii</i>	Unconfirmed

Streptococcus pneumoniae	PMID:31542319	Klebsiella planticola	Unconfirmed
Burkholderia pseudomallei	PMID:15731198	Proteus vulgaris	PMID: 19692210
Burkholderia multivorans	Unconfirmed	Human herpesvirus 1	Unconfirmed
Clostridium perfringens	PMID:29486533	Pichia anomala	Unconfirmed
Serratia marcescens	PMID:17592324	Candida tropicalis	PMID:20455400
Streptococcus epidermidis	Unconfirmed	Candida glabrata	PMID:20455400
Klebsiella pneumoniae	PMID:30058553	Cryptococcus neoformans	Unconfirmed
Vibrio cholerae	PMID:16341343	Aeromonas hydrophila	PMID:12821471
Acinetobacter baumannii	PMID:31261589	Streptococcus pneumoniae serotype	Unconfirmed
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