

Supplementary file: Prediction of Protein–Protein Interaction based on Interaction-Specific Learning and Hierarchical Information

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1 Case study on post-translational modification (ptm)

HI-PPI successfully identifies 9 ptm-mediated PPIs in the SHS27K dataset, while other state-of-the-art methods failed to do so. The details of these protein pairs are presented in Table S1.

Among the identified protein pairs, the frequently occurring protein ENSP00000215832 corresponds to GAPDH (Glyceraldehyde-3-Phosphate Dehydrogenase), a multifunctional protein involved in glycolysis, apoptosis, DNA repair, and transcriptional regulation. The prediction results further validate its central role in cellular signaling and stress responses. Other proteins in the predicted pairs, such as ENSP00000250971 (Epidermal Growth Factor Receptor, EGFR) and ENSP00000005257 (Breast Cancer Type 1 Susceptibility Protein, BRCA1), are well-known for their implications in diseases, including cancer, neurodegenerative disorders, and metabolic syndromes. These predictions have the potential to uncover novel therapeutic targets or biomarkers for these conditions.

Furthermore, ptm-mediated interactions are often dysregulated in diseases, making them highly attractive targets for drug development. The prediction results from HI-PPI can significantly contribute to the identification of novel drug targets or mechanisms of action, thereby advancing therapeutic strategies.

Table S1: The protein pairs related to ptm PPIs that only identified by HI-PPI

ENSP00000215832	ENSP00000262134
ENSP00000215832	ENSP00000261254
ENSP00000215832	ENSP00000262160
ENSP00000215832	ENSP00000225538
ENSP00000212015	ENSP00000215832
ENSP00000184956	ENSP00000215832
ENSP00000250971	ENSP00000262269
ENSP00000005257	ENSP00000216911
ENSP00000228307	ENSP00000250971
ENSP00000225577	ENSP00000257749

2 Groups of proteins in hyperbolic space

Table S2: The group of subgraph in SHS27K dataset

Group 1			
ENSP00000261890	ENSP00000245479	ENSP00000229135	ENSP00000231449
ENSP00000244050	ENSP00000256474	ENSP00000261349	ENSP00000262320
ENSP00000220764	ENSP00000242104	ENSP00000257627	ENSP00000230990
ENSP00000258930	ENSP00000261047	ENSP00000261609	ENSP00000262103
ENSP00000262300	ENSP00000257497	ENSP00000250160	ENSP00000258743
ENSP00000262160	ENSP00000259915	ENSP00000262056	ENSP00000258080
ENSP00000262269	ENSP00000252723	ENSP00000231454	ENSP00000227163
ENSP00000232014	ENSP00000259988	ENSP00000240123	ENSP00000257566
ENSP00000225538	ENSP00000245222	ENSP00000262134	ENSP00000257749
ENSP00000256104	ENSP00000256720	ENSP00000261439	
Group 2			
ENSP00000257290	ENSP00000256458	ENSP00000256797	ENSP00000233057
ENSP00000215574	ENSP00000238994	ENSP00000248600	ENSP00000240100
ENSP00000254301			
Group 3			
ENSP00000261845	ENSP00000241453	ENSP00000253055	ENSP00000241463
ENSP00000245304	ENSP00000248706	ENSP00000250559	ENSP00000078445
ENSP00000223364	ENSP00000223167	ENSP00000237500	ENSP00000239223
ENSP00000226004	ENSP00000228862	ENSP00000232375	ENSP00000259806
Group 4			
ENSP00000229812	ENSP00000251849	ENSP00000216911	ENSP00000246792
ENSP00000216127	ENSP00000216101	ENSP00000201979	ENSP00000230419
ENSP00000175756	ENSP00000245960	ENSP00000257904	ENSP00000246069
ENSP00000171887	ENSP00000202788		
Group 5			
ENSP00000005340	ENSP00000078429	ENSP00000228307	ENSP00000206249
ENSP00000261991	ENSP00000251630	ENSP00000259089	ENSP00000256078
ENSP00000220507	ENSP00000256953	ENSP00000244741	ENSP00000254654
ENSP00000179259			
Group 6			
ENSP00000000233	ENSP00000250971	ENSP00000212015	ENSP00000220062
ENSP00000207437	ENSP00000217652	ENSP00000228841	ENSP00000216160
ENSP00000260967	ENSP00000261211	ENSP00000162391	
Group 7			
ENSP00000222305	ENSP00000219070	ENSP00000232975	ENSP00000222390
ENSP00000230361	ENSP00000226193	ENSP00000252818	ENSP00000261254
ENSP00000228682	ENSP00000184956	ENSP00000221166	ENSP00000248071

Group 8			
ENSP00000054666	ENSP00000262211	ENSP00000261799	ENSP00000259808
ENSP00000261937	ENSP00000261233	ENSP00000240652	ENSP00000222157
ENSP00000219334	ENSP00000239938	ENSP00000245908	
Group 9			
ENSP00000253339	ENSP00000256196	ENSP00000229002	ENSP00000225688
ENSP00000234040	ENSP00000257430	ENSP00000056233	ENSP00000226247
Group 10			
ENSP00000229264	ENSP00000232461	ENSP00000232564	ENSP00000248996
ENSP00000251337	ENSP00000238738	ENSP00000248553	ENSP00000249071
ENSP00000220931	ENSP00000216200	ENSP00000216144	ENSP00000244007
ENSP00000053469	ENSP00000234310	ENSP00000230771	ENSP00000248594
ENSP00000254667	ENSP00000226574	ENSP00000216797	ENSP00000261207
ENSP00000222329	ENSP00000228741	ENSP00000199389	ENSP00000261302
ENSP00000250896	ENSP00000254066		
Group 11			
ENSP00000256682	ENSP00000262039	ENSP00000261636	ENSP00000262187
ENSP00000247161	ENSP00000256261	ENSP00000243924	ENSP00000243440
ENSP00000245919			
Group 12			
ENSP00000012443	ENSP00000211287	ENSP00000178640	ENSP00000215659
ENSP00000215832	ENSP00000219476	ENSP00000221138	ENSP00000229794
ENSP00000240139	ENSP00000217244	ENSP00000229328	ENSP00000254101
ENSP00000222330	ENSP00000222254	ENSP00000225577	ENSP00000005257
ENSP00000166244	ENSP00000075503	ENSP00000217188	ENSP00000216274
ENSP00000217185	ENSP00000220003	ENSP00000220751	ENSP00000155926
ENSP00000217233	ENSP00000233607	ENSP00000224337	