Figure S1: Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis of HF based on Swiss database. Top 20 signaling pathways of HF in (A) GO-BP pathway analysis, (B) GO-CC pathway analysis, and (C) GO-MF pathway analysis. (D) Top 20 signaling pathways of HF in KEGG enrichment pathway analysis.
Figure S2: Three dimensional schematic of the molecular docking of other conformations of HF onto PI3K and AKT1. (A), (B) Three-dimensional view of HF and PI3K docking scenario in two different conformations (LibDock score 121.363 and 118.8). (C), (D) Three-dimensional view of HF and AKT1 docking scenario in two different conformations (LibDock score 156.149 and 144.279).
Table S1: The top 20 of the gene ontology (GO) function enrichment analysis of potential targets from Pharma Mapper database

| Category | Term | Rich Factor % | P Value | Count |
|----------|------|---------------|---------|-------|
| GO-BP   | GO:0007165~signal transduction | 15.40697674 | 3.78E-08 | 53    |
| GO-BP   | GO:0045944~positive regulation of transcription from RNA polymerase II promoter | 12.20930233 | 6.79E-06 | 42    |
| GO-BP   | GO:0043066~negative regulation of apoptotic process | 10.75581395 | 2.13E-12 | 37    |
| GO-BP   | GO:0055114~oxidation-reduction process | 10.1744186 | 3.79E-08 | 35    |
| GO-BP   | GO:0006508~proteolysis | 9.30235581 | 2.80E-08 | 32    |
| GO-BP   | GO:0006468~protein phosphorylation | 8.430232558 | 1.65E-07 | 29    |
| GO-BP   | GO:0008284~positive regulation of cell proliferation | 8.430232558 | 2.57E-07 | 29    |
| GO-BP   | GO:0006367~transcription initiation from RNA polymerase II promoter | 8.139534884 | 3.17E-18 | 28    |
| GO-BP   | GO:0042493~response to drug | 7.848837209 | 5.38E-10 | 27    |
| GO-BP   | GO:0046777~protein autophosphorylation | 7.26744186 | 7.38E-14 | 25    |
| GO-BP   | GO:0045893~positive regulation of transcription, DNA-templated | 7.26744186 | 1.21E-04 | 25    |
| GO-BP   | GO:0043401~steroid hormone mediated signaling pathway | 6.686046512 | 4.09E-23 | 23    |
| GO-BP   | GO:0000122~negative regulation of transcription from RNA polymerase II promoter | 6.686046512 | 0.033573836 | 23 |
| GO-BP   | GO:0008283~cell proliferation | 6.395348837 | 1.69E-05 | 22    |
| GO-BP   | GO:0045087~innate immune response | 5.523255814 | 0.002769122 | 19 |
| GO-BP   | GO:0005829~cytosol | 52.03488372 | 2.34E-47 | 179   |
| GO-BP   | GO:0005737~cytoplasm | 43.60461516 | 8.03E-10 | 150   |
| GO-CC   | GO:0070062~extracellular exosome | 40.40697674 | 4.46E-30 | 139   |
| GO-CC   | GO:0005634~nucleus | 37.20930233 | 0.001059976 | 128 |
| GO-CC   | GO:0005886~plasma membrane | 27.90697674 | 0.01006021 | 96    |
| GO-CC   | GO:0005654~nucleoplasm | 27.61627907 | 1.95E-09 | 95    |
| GO-CC   | GO:0016020~membrane | 19.76744186 | 2.63E-05 | 68    |
| GO-CC   | GO:0005615~extracellular space | 18.89534884 | 2.20E-12 | 65    |
| GO-CC   | GO:0005576~extracellular region | 18.89534884 | 3.79E-09 | 65    |
| GO-CC   | GO:0005739~mitochondrion | 16.86046512 | 2.24E-09 | 58    |
| GO-CC   | GO:0048471~perinuclear region of | 6.686046512 | 0.002983913 | 23 |
| GO-CC     | GO:0005759~mitochondrial matrix | 6.395348837 | 8.79E-07 | 22 |
| GO-CC     | GO:0009896~cell surface          | 6.395348837 | 0.01253836 | 22 |
| GO-CC     | GO:0005925~focal adhesion        | 5.523255814 | 3.95E-04 | 19 |
| GO-CC     | GO:0031012~extracellular matrix  | 4.941860465 | 1.40E-04 | 17 |
| GO-CC     | GO:0045121~membrane raft         | 4.651162791 | 7.38E-06 | 16 |
| GO-CC     | GO:0043231~intracellular membrane-bounded organelle | 4.651162791 | 0.09701595 | 16 |
| GO-CC     | GO:0043234~protein complex       | 4.360465116 | 0.02211671 | 15 |
| GO-CC     | GO:0005764~lysosome              | 4.069767442 | 3.21E-04 | 14 |
| GO-CC     | GO:0043025~neuronal cell body    | 4.069767442 | 0.006241599 | 14 |
| GO-MT     | GO:0005515~protein binding       | 62.5        | 2.07E-05 | 215 |
| GO-MT     | GO:0005524~ATP binding           | 21.80232558 | 1.84E-13 | 75 |
| GO-MT     | GO:0008270~zinc ion binding      | 15.9837209  | 7.07E-09 | 55 |
| GO-MT     | GO:0042802~identical protein binding | 13.6627907 | 1.26E-11 | 47 |
| GO-MT     | GO:0019899~enzyme binding        | 9.302325581 | 1.21E-12 | 32 |
| GO-MT     | GO:0004672~protein kinase activity | 9.011627907 | 4.31E-11 | 31 |
| GO-MT     | GO:0003700~transcription factor activity, sequence-specific DNA binding | 7.848837209 | 0.076038974 | 27 |
| GO-MT     | GO:0003707~steroid hormone receptor activity | 7.558139535 | 4.75E-28 | 26 |
| GO-MT     | GO:0043565~sequence-specific DNA binding | 7.558139535 | 5.09E-05 | 26 |
| GO-MT     | GO:0004674~protein serine/threonine kinase activity | 7.26744186 | 6.63E-07 | 25 |
| GO-MT     | GO:0004713~protein tyrosine kinase activity | 6.686046512 | 2.31E-14 | 23 |
| GO-MT     | GO:0016301~kinase activity       | 6.686046512 | 3.63E-09 | 23 |
| GO-MT     | GO:0005102~receptor binding      | 6.686046512 | 2.88E-06 | 23 |
| GO-MT     | GO:0019901~protein kinase binding | 6.686046512 | 7.95E-06 | 23 |
| GO-MT     | GO:0004252~serine-type endopeptidase activity | 6.395348837 | 5.03E-08 | 22 |
| GO-MT     | GO:0008144~drug binding          | 5.523255814 | 7.82E-15 | 19 |
| GO-MT     | GO:0003824~catalytic activity    | 5.523255814 | 4.73E-08 | 19 |
| GO-MT     | GO:0016491~oxidoreductase activity | 4.941860465 | 2.94E-06 | 17 |
| GO-MT     | GO:0005525~GTP binding           | 4.941860465 | 0.00491645 | 17 |
Table S2: The top 20 of KEGG Pathway Enrichment Analyses of potential targets from Pharma Mapper database

| Category        | Term                                                      | Rich Factor % | P Value   | Count |
|-----------------|-----------------------------------------------------------|---------------|-----------|-------|
| KEGG-PATHWAY    | hsa01100:Metabolic pathways                              | 27.03488372   | 6.85E-10  | 93    |
| KEGG-PATHWAY    | hsa05200:Pathways in cancer                              | 13.6627907    | 6.10E-11  | 47    |
| KEGG-PATHWAY    | hsa04151:PI3K-Akt signaling pathway                      | 10.75581395   | 1.86E-07  | 37    |
| KEGG-PATHWAY    | hsa01130:Biosynthesis of antibiotics                     | 9.011627907   | 2.13E-09  | 31    |
| KEGG-PATHWAY    | hsa04014:Ras signaling pathway                           | 8.720930233   | 3.82E-08  | 30    |
| KEGG-PATHWAY    | hsa05205:Proteoglycans in cancer                         | 8.139534884   | 3.97E-08  | 28    |
| KEGG-PATHWAY    | hsa04015:Rap1 signaling pathway                          | 6.976744186   | 1.59E-05  | 24    |
| KEGG-PATHWAY    | hsa04068:FoxO signaling pathway                          | 6.686046512   | 2.17E-08  | 23    |
| KEGG-PATHWAY    | hsa04910:Insulin signaling pathway                       | 6.686046512   | 3.77E-08  | 23    |
| KEGG-PATHWAY    | hsa04510:Focal adhesion                                  | 6.395348837   | 1.08E-04  | 22    |
| KEGG-PATHWAY    | hsa00230:purine metabolism                              | 6.104651163   | 3.39E-05  | 21    |
| KEGG-PATHWAY    | hsa05152:Tuberculosis                                   | 6.104651163   | 3.68E-05  | 21    |
| KEGG-PATHWAY    | hsa04010:MAPK signaling pathway                          | 5.813953488   | 0.00821065| 20    |
| KEGG-PATHWAY    | hsa05215:Prostate cancer                                | 5.523255814   | 1.26E-08  | 19    |
| KEGG-PATHWAY    | hsa05161:Hepatitis B                                     | 5.523255814   | 2.57E-05  | 19    |
| KEGG-PATHWAY    | hsa04915:Estrogen signaling pathway                     | 5.23255814    | 4.71E-07  | 18    |
| KEGG-PATHWAY    | hsa04931:Insulin resistance                              | 5.23255814    | 1.68E-06  | 18    |
| KEGG-PATHWAY    | hsa04919:Thyroid hormone signaling pathway              | 5.23255814    | 4.09E-06  | 18    |
| KEGG-PATHWAY    | hsa04722:Neurotrophin signaling pathway                 | 5.23255814    | 7.39E-06  | 18    |
| KEGG-PATHWAY    | hsa05203:Viral carcinogenesis                            | 5.23255814    | 0.00463360| 18    |
### Table S3: The top 20 of the gene ontology (GO) function enrichment analysis of potential targets from Swiss database

| Category | Term                                                                 | Rich Factor %   | P Value     | Count |
|----------|----------------------------------------------------------------------|-----------------|-------------|-------|
| GO-BP    | GO:0043066--negative regulation of apoptotic process                  | 17.47572816     | 1.96E-09    | 18    |
| GO-BP    | GO:0055114--oxidation-reduction process                               | 16.50485437     | 5.31E-07    | 17    |
| GO-BP    | GO:0006468--protein phosphorylation                                   | 15.53398058     | 1.03E-07    | 16    |
| GO-BP    | GO:0046777--protein autophosphorylation                               | 14.5631068      | 2.23E-12    | 15    |
| GO-BP    | GO:0007165--signal transduction                                       | 14.5631068      | 0.010386567 | 15    |
| GO-BP    | GO:0042493--response to drug                                          | 13.59223301     | 3.84E-08    | 14    |
| GO-BP    | GO:0008284--positive regulation of cell proliferation                 | 13.59223301     | 4.84E-06    | 14    |
| GO-BP    | GO:0008283--cell proliferation                                       | 11.65048544     | 1.37E-05    | 12    |
| GO-BP    | GO:0045944--positive regulation of transcription from RNA polymerase II promoter | 11.65048544   | 0.03569245  | 12    |
| GO-BP    | GO:0015701--bicarbonate transport                                     | 9.708737864     | 4.67E-12    | 10    |
| GO-BP    | GO:0008285--negative regulation of cell proliferation                 | 9.708737864     | 6.83E-04    | 10    |
| GO-BP    | GO:0007169--transmembrane receptor protein tyrosine kinase signaling pathway | 8.737864078   | 1.20E-07    | 9     |
| GO-BP    | GO:0018105--peptidyl-serine phosphorylation                            | 8.737864078     | 9.19E-07    | 9     |
| GO-BP    | GO:0030335--positive regulation of cell migration                      | 8.737864078     | 1.63E-05    | 9     |
| GO-BP    | GO:0006954--inflammatory response                                     | 8.737864078     | 0.002168912 | 9     |
| GO-BP    | GO:0006730--one-carbon metabolic process                               | 7.766990291     | 4.50E-10    | 8     |
| GO-BP    | GO:0018108--peptidyl-tyrosine phosphorylation                          | 7.766990291     | 4.07E-05    | 8     |
| GO-BP    | GO:0045893--positive regulation of transcription, DNA-templated       | 7.766990291     | 0.037381048 | 8     |
| GO-BP    | GO:0038083--peptidyl-tyrosine autophosphorylation                      | 7.766116505     | 1.41E-07    | 7     |
| GO-BP    | GO:0044267--cellular protein metabolic process                        | 6.796116505     | 8.24E-05    | 7     |
| GO-CC    | GO:0005886--plasma membrane                                           | 49.51456311     | 4.20E-09    | 51    |
| GO-CC    | GO:0005829--cytosol                                                   | 47.57281553     | 2.19E-11    | 49    |
| GO-CC    | GO:0005737--cytoplasm                                                 | 41.74757282     | 0.004411007 | 43    |
| GO-CC    | GO:0005634--nucleus                                                  | 40.77669903     | 0.015066776 | 42    |
| GO-CC    | GO:0070062--extracellular exosome                                     | 28.15533981     | 0.001290672 | 29    |
| GO-CC    | GO:0016020--membrane                                                 | 26.21359223     | 1.47E-04    | 27    |
| GO-CC    | GO:0005654--nucleoplasm                                              | 23.30097807     | 0.032765441 | 24    |
| GO-CC    | GO:0005615--extracellular space                                       | 19.41747573     | 1.54E-04    | 20    |
| GO-CC    | GO:0005887--integral component of plasma membrane                     | 14.5631068      | 0.025949188 | 15    |
| GO-CC    | GO:0005576--extracellular region                                      | 14.5631068      | 0.064629709 | 15    |
| GO-CC    | GO:0048471--perinuclear region of cytoplasm                           | 13.59223301     | 4.26E-05    | 14    |
| Term                                      | ID             | Adjusted p-value | FDR   | Rank |
|-------------------------------------------|----------------|------------------|-------|------|
| GO-CC protein complex                      | GO:0043234     | 8.737864078      | 0.002197903 | 9    |
| GO-CC postsynaptic density                 | GO:0014069     | 7.766990291      | 7.86E-05 | 8    |
| GO-CC cell surface                         | GO:0009986     | 7.766990291      | 0.032498798 | 8    |
| GO-CC basolateral plasma membrane          | GO:0016323     | 6.796116505      | 5.25E-04 | 7    |
| GO-CC membrane raft                        | GO:0045121     | 6.796116505      | 0.001061451 | 7    |
| GO-CC endosome                             | GO:0005768     | 5.825242718      | 0.008679528 | 6    |
| GO-CC apical plasma membrane               | GO:0016324     | 5.825242718      | 0.02386082 | 6    |
| GO-CC neuronal cell body                   | GO:0043025     | 5.825242718      | 0.032029473 | 6    |
| GO-CC centrosome                           | GO:0005813     | 5.825242718      | 0.00964998 | 6    |
| GO-MT protein binding                      | GO:0005515     | 72.81553398      | 1.77E-05 | 75   |
| GO-MT ATP binding                          | GO:0005524     | 31.06796117      | 4.70E-10 | 32   |
| GO-MT zinc ion binding                     | GO:0008270     | 19.41747573      | 6.47E-05 | 20   |
| GO-MT protein kinase activity              | GO:0019901     | 12.62135922      | 2.79E-06 | 13   |
| GO-MT protein kinase activity              | GO:00055524    | 11.65048544      | 1.68E-05 | 12   |
| GO-MT identical protein binding            | GO:0042802     | 11.65048544      | 0.005527812 | 12    |
| GO-MT protein homodimerization activity    | GO:0042803     | 14.5631068       | 3.29E-08 | 15   |
| GO-MT enzyme binding                       | GO:0019899     | 13.59223301      | 1.05E-07 | 14   |
| GO-MT protein kinase binding               | GO:0019901     | 12.62135922      | 2.79E-06 | 13   |
| GO-MT kinase activity                      | GO:0016301     | 11.65048544      | 2.27E-07 | 12   |
| GO-MT protein serine/threonine kinase      | GO:0004672     | 11.65048544      | 1.68E-05 | 12   |
| GO-MT identical protein binding            | GO:0042802     | 11.65048544      | 0.005527812 | 12    |
| GO-MT protein kinase activity              | GO:0004693     | 9.708737864      | 0.002012056 | 10   |
| GO-MT carbonate dehydratase activity       | GO:0004089     | 8.737864078      | 3.90E-15 | 9    |
| GO-MT protein tyrosine kinase activity     | GO:0004713     | 8.737864078      | 1.42E-06 | 9    |
| GO-MT chromatin binding                    | GO:0003682     | 7.766990291      | 0.009535505 | 8    |
| GO-MT transmembrane receptor protein kinase activity | GO:0004714  | 6.796116505      | 9.90E-08 | 7    |
| GO-MT heme binding                         | GO:0020037     | 6.796116505      | 1.82E-04 | 7    |
| GO-MT serine-type endopeptidase activity   | GO:0004252     | 6.796116505      | 0.004509241 | 7    |
| GO-MT receptor binding                     | GO:0005102     | 6.796116505      | 0.020182276 | 7    |
| GO-MT cyclin-dependent protein kinase       | GO:0004693     | 5.825242718      | 1.77E-06 | 6    |
| GO-MT iron ion binding                     | GO:0005506     | 5.825242718      | 0.002356184 | 6    |
| Category       | Term                                                                 | Rich Factor % | P Value      | Count |
|----------------|----------------------------------------------------------------------|---------------|--------------|-------|
| KEGG-PATHWAY   | hsa05200:Pathways in cancer                                          | 15.5398058    | 1.18E-04     | 16    |
| KEGG-PATHWAY   | hsa04151:PI3K-Akt signaling pathway                                   | 13.5923301    | 3.99E-04     | 14    |
| KEGG-PATHWAY   | hsa04068:FoxO signaling pathway                                       | 9.708737864   | 4.80E-05     | 10    |
| KEGG-PATHWAY   | hsa05205:Proteoglycans in cancer                                      | 9.708737864   | 9.72E-04     | 10    |
| KEGG-PATHWAY   | hsa04080:Neuroactive ligand-receptor interaction                      | 9.708737864   | 0.008612731  | 10    |
| KEGG-PATHWAY   | hsa05206:MicroRNAs in cancer                                          | 9.708737864   | 0.010504379  | 10    |
| KEGG-PATHWAY   | hsa00910:Nitrogen metabolism                                          | 8.737864078   | 1.15E-11     | 9     |
| KEGG-PATHWAY   | hsa04915:Estrogen signaling pathway                                   | 8.737864078   | 3.45E-05     | 9     |
| KEGG-PATHWAY   | hsa04510:Focal adhesion                                               | 8.737864078   | 0.004656157  | 9     |
| KEGG-PATHWAY   | hsa04015:Rap1 signaling pathway                                       | 8.737864078   | 0.005224474  | 9     |
| KEGG-PATHWAY   | hsa04014:Ras signaling pathway                                        | 8.737864078   | 0.008046198  | 9     |
| KEGG-PATHWAY   | hsa04913:Ovarian steroidogenesis                                      | 7.766990291   | 2.45E-06     | 8     |
| KEGG-PATHWAY   | hsa04914:Progesterone-mediated oocyte maturation                      | 7.766990291   | 1.12E-04     | 8     |
| KEGG-PATHWAY   | hsa05222:Small cell lung cancer                                       | 6.796116505   | 7.19E-04     | 7     |
| KEGG-PATHWAY   | hsa05215:Prostate cancer                                              | 6.796116505   | 8.64E-04     | 7     |
| KEGG-PATHWAY   | hsa04066:HIF-1 signaling pathway                                      | 6.796116505   | 0.001362326  | 7     |
| KEGG-PATHWAY   | hsa04110:Cell cycle                                                  | 6.796116505   | 0.004938346  | 7     |
| KEGG-PATHWAY   | hsa04062:Chemokine signaling pathway                                  | 6.796116505   | 0.03139023   | 7     |
| KEGG-PATHWAY   | hsa04810:Regulation of actin cytoskeleton                             | 6.796116505   | 0.051641747  | 7     |
| KEGG-PATHWAY   | hsa05221:Acute myeloid leukemia                                       | 5.825242718   | 6.99E-04     | 6     |