网络药理学 +Mandenol 与 piezo1 分子对接

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Contents

List of Figures

List of Tables

1 摘要

- 三七总皂苷 panax notoginseng saponins 中有效成分
  - 使用来源于文献 (PMID: 29673237)[1] 以及附件文档中表格的化合物 (Tab. 1)
- 结合疾病骨折愈合（软骨内骨化，血管生成）做网络药理学分析
  - 成分的靶点由 Super-Pred 预测 (Fig. 1) (SwissTarget 限制太多，速度慢，大分子无法预测，今后将以 Super-pred 替代)。
  - 先单独分析成分靶点 (Fig. 2)，后再与疾病交集过滤 (Fig. 4)。
  - 疾病相关基因来源见 (Fig. 3)
- 候选基因的功能通路富集分析
  - 结果见 6.2
- 分子对接，与 piezo1 (如果 Mandenol 与 piezo1)
  - 分子对接见 Fig. 10

2 前言

3 材料和方法

3.1 材料

3.2 方法

Mainly used method:

- R package `ClusterProfiler` used for gene enrichment analysis[2].
- Databses of `DisGeNet`, `GeneCards`, `PharmGKB` used for collating disease related targets[3–5].
- R package `PubChemR` used for querying compounds information.
- Web tool of `Super-PRED` used for drug-targets prediction[6].
- The `Transcription Factor Target Gene Database` (https://tfbsdb.systemsbiology.net/) was used for discovering relationship between transcription factors and genes.[7]
- `AutoDock vina` used for molecular docking[8].
- Other R packages (eg., `dplyr` and `ggplot2`) used for statistic analysis or data visualization.

4 分析结果

5 结论

6 附：分析流程

6.1 网络药理学

6.1.1 三七总皂苷 (panax notoginseng saponins, PNS) 成分

来源于文献 (PMID: 29673237)[1] 以及附件文档中表格的化合物。

Table 1 (下方表格) 为表格 PNS compounds 概览。

(对应文件为 Figure+Table/PNS-compounds.csv)

> 注：表格共有 18 行 3 列，以下预览的表格可能省略部分数据；表格含有 13 个唯一 'No.'。

Table 1: PNS compounds

No.	Name	Structure
PNS-1	Ginsenoside Rg1	
PNS-2	Ginsenoside Rg3	
PNS-3	Ginsenoside Rg5	
PNS-4	Ginsenoside Rb1	
PNS-5	Ginsenoside Rb3	
PNS-6	Ginsenoside Re	
PNS-7	Ginsenoside Rh1	
PNS-8	Ginsenoside Rh2	
PNS-9	Pseudoginsenoside-F11	
PNS-10	Ginsenoside Ro	
PNS-11	Ginsenoside K	
PNS-12	Notoginsenoside R1	
NA	Mandenol	NA
NA	DFV	NA
NA	Diop	NA
...	...	...

6.1.2 成分靶点

使用 Super-Pred 预测化合物靶点。

Figure 1 (下方图) 为图 SuperPred results 概览。

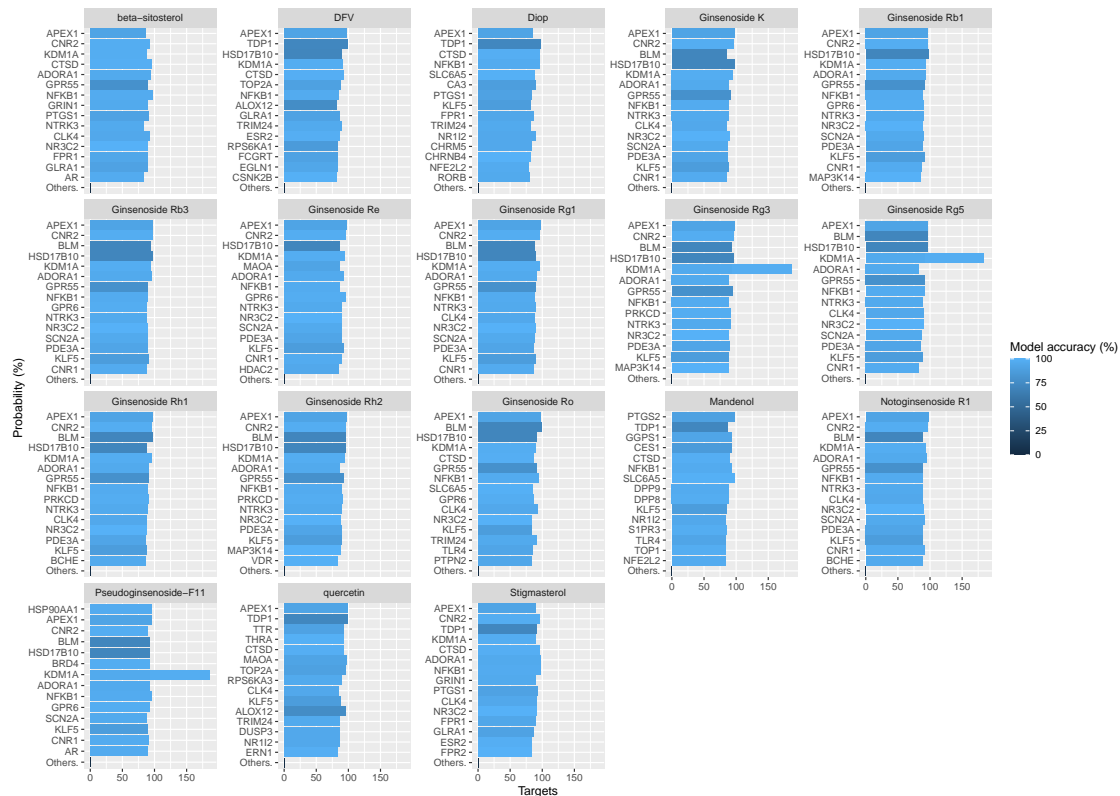**(对应文件为 Figure+Table/SuperPred-results.pdf)**

Figure 1: SuperPred results

Figure 2 (下方图) 为图 Network pharmacology visualization 概览。

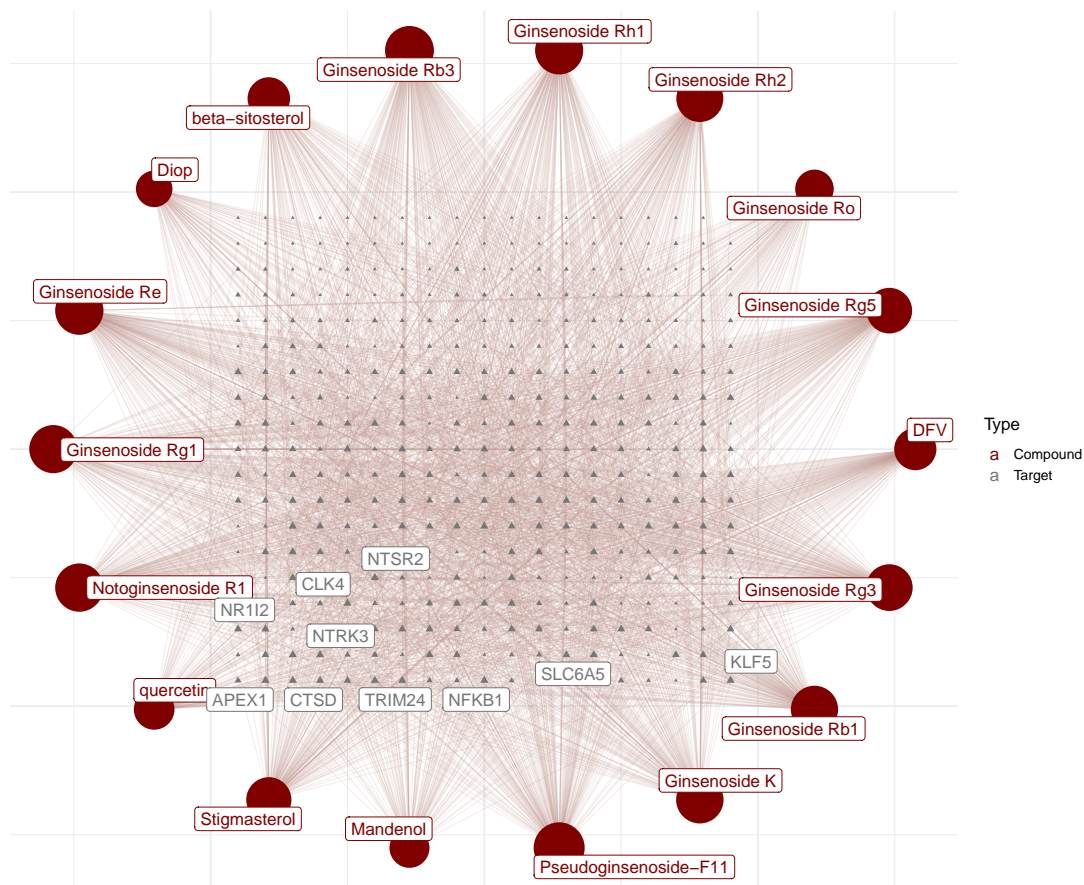**(对应文件为 Figure+Table/Network-pharmacology-visualization.pdf)**

Figure 2: Network pharmacology visualization

6.1.3 Disease

Figure 3 (下方图) 为图 All diseases Overall targets number of datasets 概览。

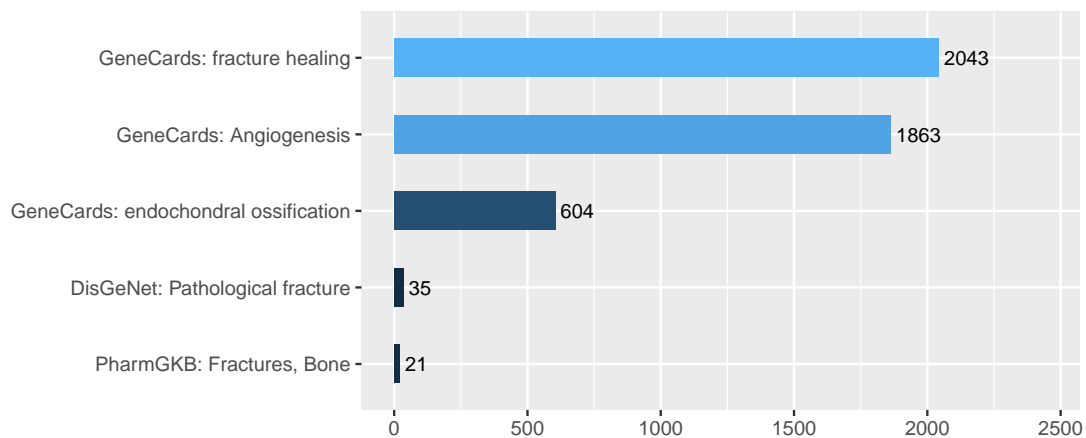**(对应文件为 Figure+Table/All-diseases-Overall-targets-number-of-datasets.pdf)**

Figure 3: All diseases Overall targets number of datasets

6.1.4 成分-靶点-疾病

Figure 4 (下方图) 为图 Targets intersect with targets of diseases 概览。

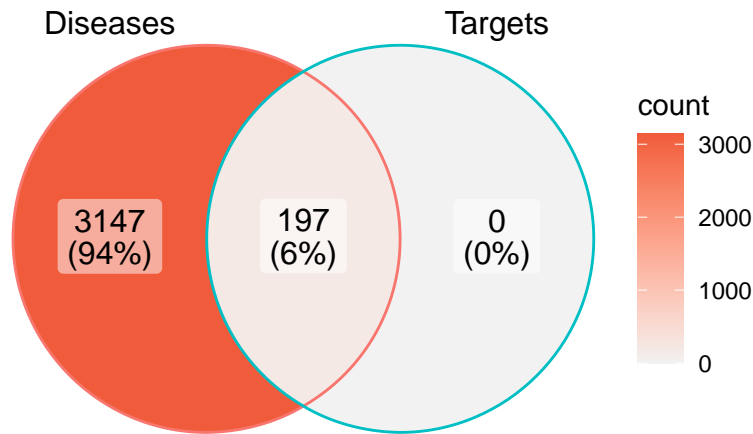**(对应文件为 `Figure+Table/Targets-intersect-with-targets-of-diseases.pdf`)**

Figure 4: Targets intersect with targets of diseases

> **Intersection :**
>
> ABCB1, FLT3, MAP4K4, VDR, STAT3, ESR1, TGFBR2, F13A1, NTRK1, MMP2, SER-PINE1, TLR4, MMP1, HIF1A, CTSK, GBA1, ENPP1, CXCR4, ITGB1, SCN9A, IDH1, PDGFRB, TTR, PTGS2, NOS2, PIK3CA, NOS3, NFKB1, ESR2, PTPN11, MMP7, TERT, P2RX7, MMP8, TGM2, PDGFRA, CREBBP, HDAC4, KDR, ALOX5, AR, MTOR, STAT1, F2R, PIK3CG...

(上述信息框内容已保存至 `Figure+Table/Targets-intersect-with-targets-of-diseases-content`)

Figure 5 (下方图) 为图 Network pharmacology with disease 概览。
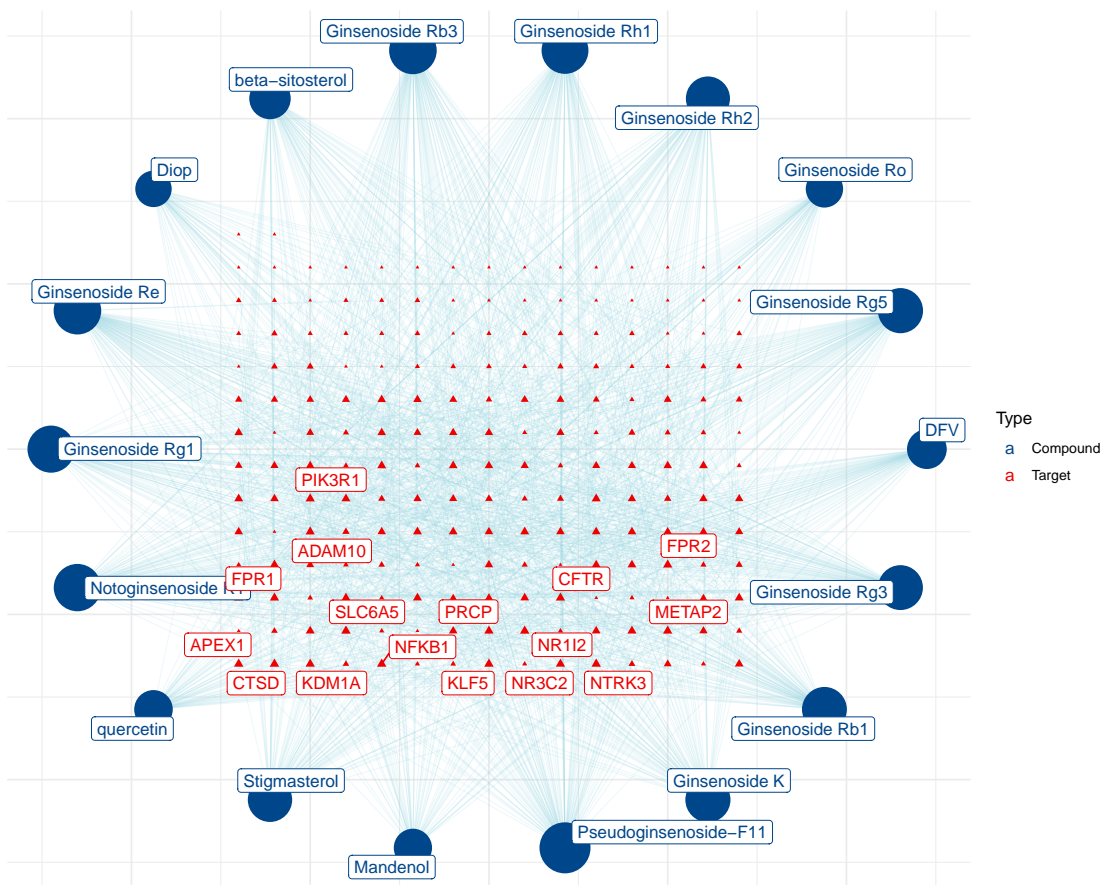
(对应文件为 `Figure+Table/Network-pharmacology-with-disease.pdf`)

Figure 5: Network pharmacology with disease

6.1.5 PIEZO1 的转录因子分析

The `Transcription Factor Target Gene Database` (https://tfbsdb.systemsbiology.net/) was used for discovering relationship between transcription factors and genes.

Table 2 (下方表格) 为表格 Transcription Factor binding sites 概览。

(对应文件为 `Figure+Table/Transcription-Factor-binding-sites.csv`)

> 注: 表格共有 238 行 10 列, 以下预览的表格可能省略部分数据; 表格含有 1 个唯一 'target'。

> 1. Start: 起始点

Table 2: Transcription Factor binding sites

target	TF_symbol	Motif	Source	Strand	Start	Stop	PValue	MatchS...	Overla...
PIEZO1	HOXD12	HOXD12...	SELEX	+	88856337	88856345	6.0E-06	GTGATAAAA	9
PIEZO1	HSF2	HSF2_H...	SELEX	-	88856344	88856356	2.0E-06	TTCCAG...	13

target	TF_symbol	Motif	Source	Strand	Start	Stop	PValue	MatchS...	Overla...
PIEZO1	SOX21	SOX21_...	SELEX	+	88856312	88856326	2.0E-06	AACAGT...	15
PIEZO1	FOXA2	Foxa2_...	JASPAR	-	88847053	88847064	9.0E-06	TGTTTA...	12
PIEZO1	NF-KAPPAB	NF-kap...	JASPAR	+	88851187	88851196	1.0E-06	GGGAAT...	10
PIEZO1	TBX1	TBX1_T...	SELEX	+	88848269	88848288	6.0E-06	GTGACA...	20
PIEZO1	SOX4	SOX4_H...	SELEX	+	88856311	88856326	2.0E-06	TAACAG...	16
PIEZO1	RXRB	Rxrb_n...	SELEX	+	88846744	88846757	1.0E-06	GAGCTC...	14
PIEZO1	ESRRA	ESRRA_...	SELEX	+	88846750	88846768	8.0E-06	AAAGGT...	19
PIEZO1	CREB3L2	Creb3l...	SELEX	+	88848344	88848355	7.0E-06	TGCCAC...	12
PIEZO1	IRF7	IRF7_I...	SELEX	+	88850912	88850925	3.0E-06	CCGAAA...	14
PIEZO1	IRF7	IRF7_I...	SELEX	-	88851996	88852009	3.0E-06	AGCAAA...	14
PIEZO1	IRF7	IRF7_I...	SELEX	-	88856323	88856336	1.0E-05	CCCAAA...	14
PIEZO1	target	SRY_HM...	SELEX	-	88856312	88856326	7.0E-06	AACTCT...	15
PIEZO1	SOX2	SOX2_H...	SELEX	+	88847416	88847432	9.0E-06	GAAGAC...	17
...	...	...	...	...	...	...	...	...	...

Figure 6 (下方图) 为图 Intersection of TFs with queried Candidates 概览。

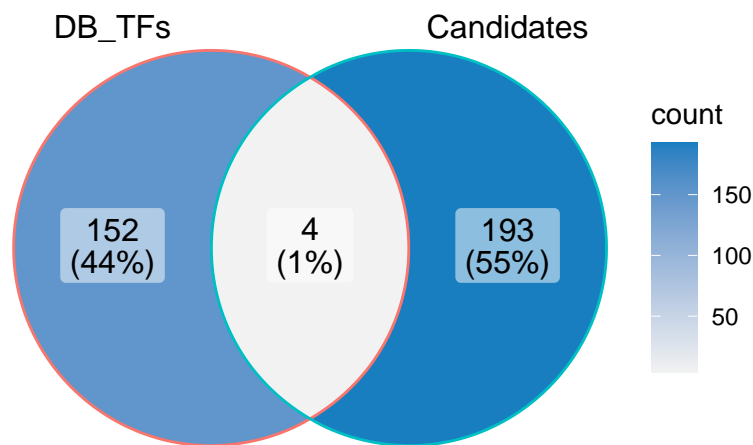**(对应文件为 `Figure+Table/Intersection-of-TFs-with-queried-Candidates.pdf`)**

Figure 6: Intersection of TFs with queried Candidates

> **Intersection :**
>
> NFKB1, RXRA, NFE2L2, PPARA

(上述信息框内容已保存至 `Figure+Table/Intersection-of-TFs-with-queried-Candidates-content`)

Figure 7 (下方图) 为图 The genes and related TFs 概览。

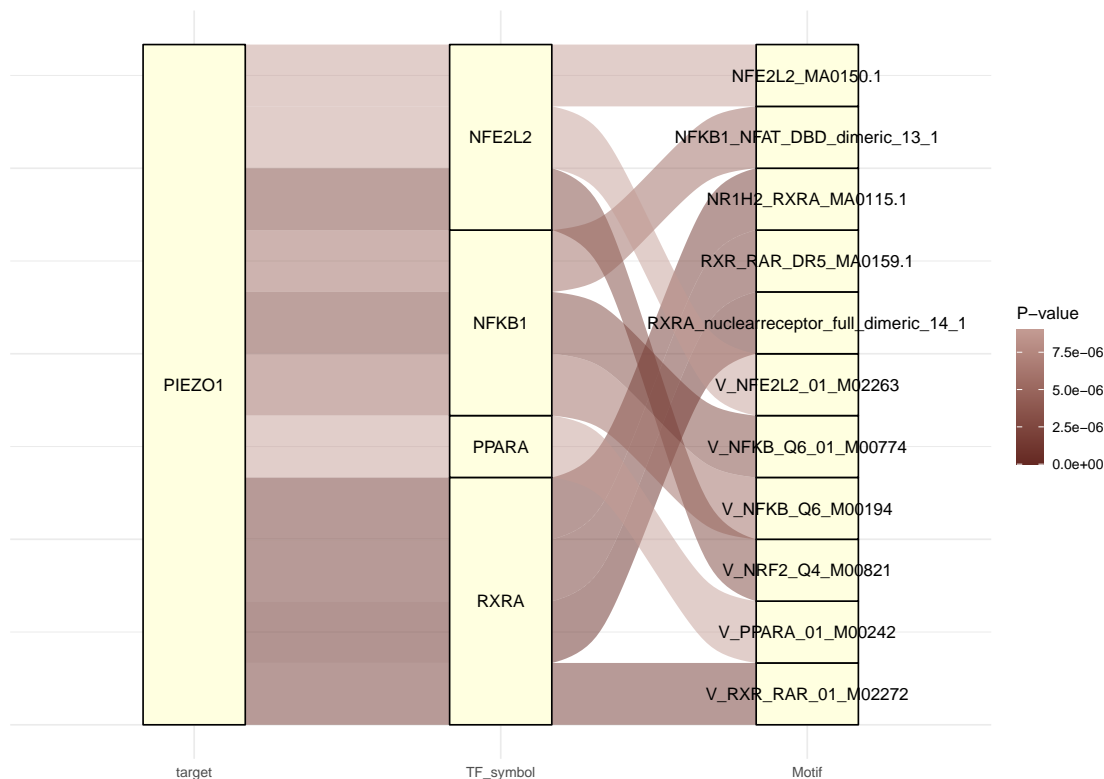**(对应文件为 `Figure+Table/The-genes-and-related-TFs.pdf`)**

Figure 7: The genes and related TFs

6.2 富集分析

Figure 8 (下方图) 为图 Ids KEGG enrichment 概览。
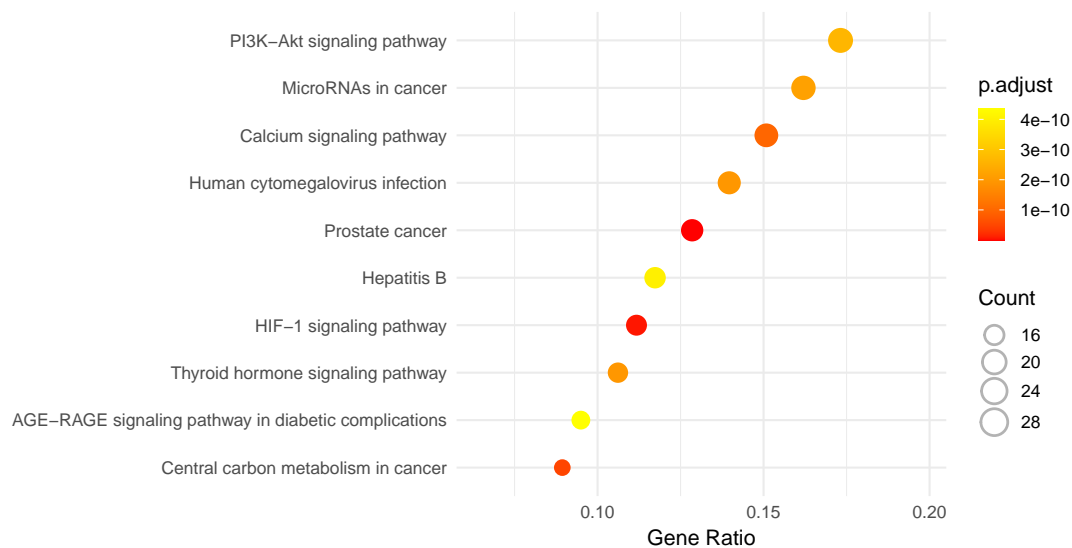
(对应文件为 Figure+Table/Ids-KEGG-enrichment.pdf)

Figure 8: Ids KEGG enrichment

Figure 9 (下方图) 为图 Ids GO enrichment 概览。
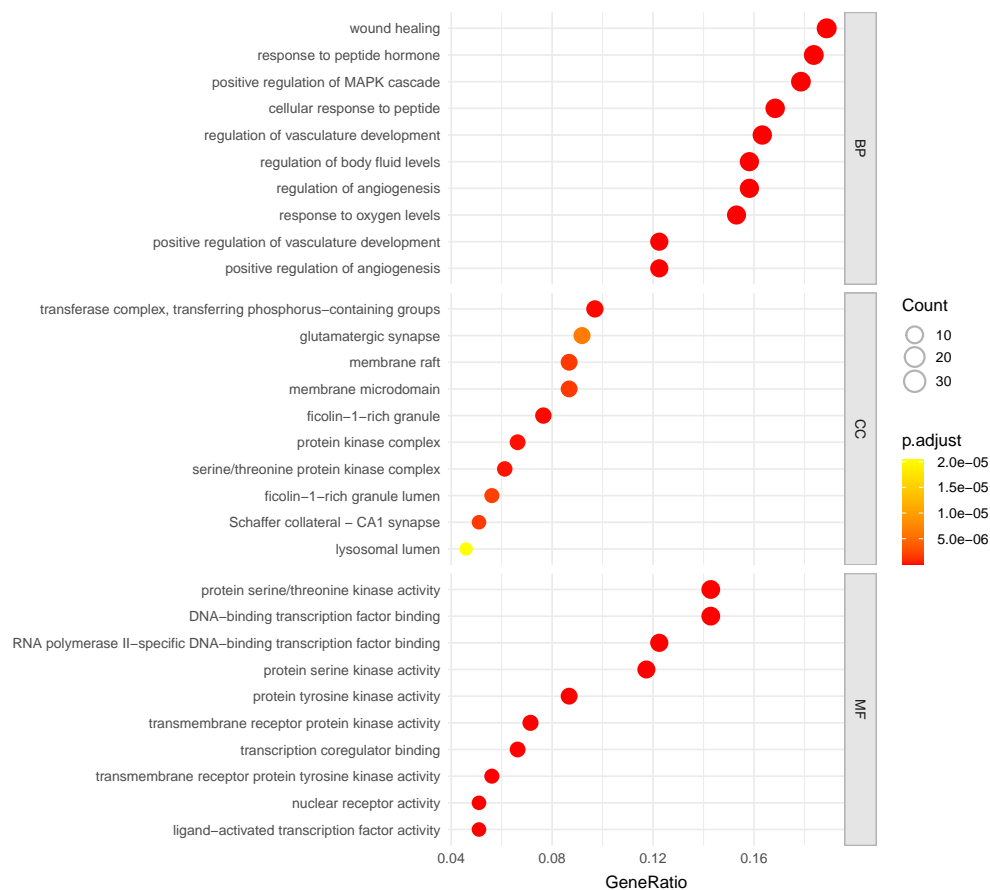
(对应文件为 Figure+Table/Ids-GO-enrichment.pdf)

Figure 9: Ids GO enrichment

6.3 分子对接

Figure 10 (下方图) 为图 Overall combining Affinity 概览。

(对应文件为 Figure+Table/Overall-combining-Affinity.pdf)
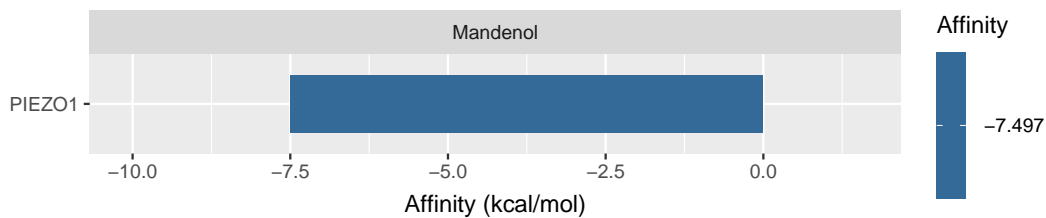

Figure 10: Overall combining Affinity

Figure 11 (下方图) 为图 Mandenol combine PIEZO1 概览。

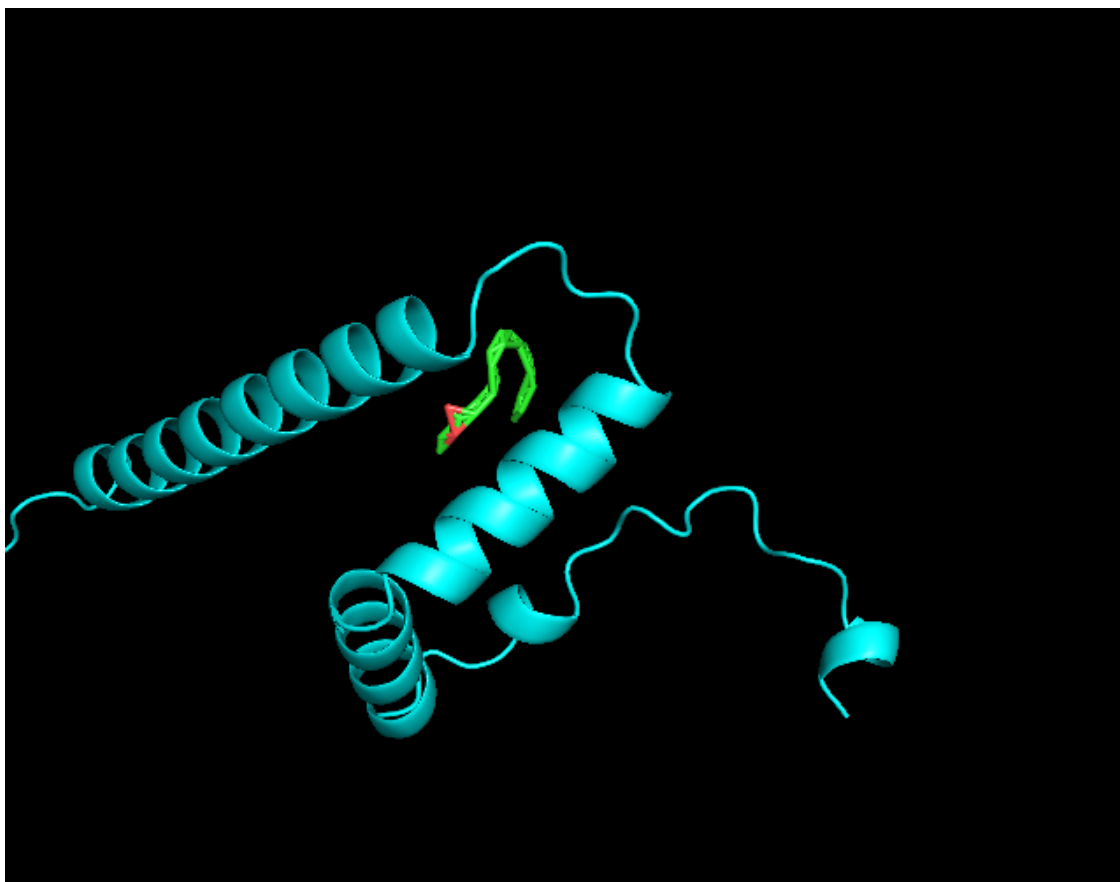**(对应文件为 Figure+Table/5282184_into_piezo1.png)**

Figure 11: Mandenol combine PIEZO1

Reference

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genetics network analysis. *Cell systems* **3**, 172–186 (2016).

8. Eberhardt, J., Santos-Martins, D., Tillack, A. F. & Forli, S. AutoDock vina 1.2.0: New docking methods, expanded force field, and python bindings. *Journal of Chemical Information and Modeling* **61**, 3891–3898 (2021).