Observational Study

Medicine

OPEN

Role of SNAP25 on the occurrence and development of eosinophilic gastritis

Jie Zhang, MD[a], Shiyang Hou, MD[a], Xiao-qian Chi, MD[a], Hai-feng Shan, MD[a], Xiao-wei Li, MD[a], Qi-jun Zhang, MD[a], Jin-lei Wang, MD[a], Chun-bo Kang, MD[a,*]

Abstract

Eosinophilic gastritis is characterized by gastrointestinal symptoms accompanied by peripheral eosinophilia. This study aims to explore the association between eosinophilic gastritis and Synaptosome Associated Protein 25 (SNAP25), and provide a new direction for the diagnosis and treatment of eosinophilic gastritis. GSE54043 was downloaded from the gene expression omnibus database. Differentially expressed genes (DEGs) were screened. The functions of common DEGs were annotated by Database for Annotation, Visualization and Integrated Discovery and Metascape. The protein–protein interaction network of common DEGs was obtained by Search Tool for the Retrieval of Interacting Genes and visualized by Cytoscape. Significant modules were identified from the protein–protein interaction network. A total of 186 patients with eosinophilic gastritis were recruited. The clinical data were recorded and the expression levels of CPE, SST, PCSK2, SNAP25, and SYT4 were detected. Pearson chi-square test and Spearman correlation coefficient were used to analyze the relationship between eosinophilic gastritis and related parameters. Univariate and multivariate Logistic regression were used for further analysis. 353 DEGs were presented. The top 10 genes screened by cytoHubb were shown, and Veen diagram figured out 5 mutual genes. Pearson's chi-square test showed that SNAP25 ($P < .001$) was significantly associated with eosinophilic gastritis. Spearman correlation coefficient showed a significant correlation between eosinophilic gastritis and SNAP25 ($\rho = -0.569$, $P < .001$). Univariate logistic regression analysis showed that SNAP25 (OR = 0.046, 95% CI: 0.018–0.116, $P < .001$) was significantly associated with eosinophilic gastritis. Multivariate logistic regression analysis showed that SNAP25 (OR = 0.024, 95% CI: 0.007–0.075, $P < .001$) was significantly associated with eosinophilic gastritis. The low expression of SNAP25 gene in eosinophilic gastritis is associated with a higher risk of eosinophilic gastritis.

Abbreviations: 95% CI = 95% confidence interval, DEGs = differential epigenetic genes, GEO = gene expression omnibus, MCODE = molecular complex detection, OR = odds ratio, PPI = protein-protein interaction, SNAP25 = Synaptosome Associated Protein 25.

Keywords: eosinophilic gastritis, potential targets, SNAP25

1. Introduction

Eosinophilic gastritis is a rare eosinophilic infiltrating disease in children and adults,[1] characterized by tissue infiltration of eosinophils. Eosinophilic gastritis is generally believed to be caused by degranulation of eosinophilic granulation, release of various enzymes, resulting in tissue damage. Patients often experience psychological, social and economic problems associated with the disease.[2] Eosinophilic gastritis is a specific inflammation of the digestive tract. This eosinophilic inflammation is an allergic reaction caused by some unknown antigen. Its treatment methods mainly include general treatment, drug treatment, operation treatment.[3] Among them, hormone therapy with drug therapy has a significant effect and is often the first choice. Hormone therapy remains effective in patients with relapses after hormone therapy or after surgery. Surgical treatment is suitable for patients with obstruction, but the long-term results are not good, there is still the possibility of recurrence. Eosinophilic gastritis may be involved from the esophagus to the rectum, with the small intestine and stomach being the most common.[4] Histologically, eosinophil infiltrates may be numerous and may accumulate in clumps. Eosinophil infiltrates may involve the entire gastrointestinal wall or may be dominant

JZ and SH contributed equally to this work.

This study was funded by Beijing Rehabilitation Hospital Affiliated to Capital Medical University (2022-056). The funding body had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was approved by the Beijing Rehabilitation Hospital Affiliated to Capital Medical University.

[a] *Gastrointestinal Rehabilitation Center, Beijing Rehabilitation Hospital Affiliated to Capital Medical University, Beijing, China.*

**Correspondence: Chun-bo Kang, Gastrointestinal Rehabilitation Center, Beijing Rehabilitation Hospital Affiliated to Capital Medical University, Xixiazhuang, Badachu, Shijingshan District, Beijing 100144, China (e-mail: kangchunbo220@163.com).*

How to cite this article: Zhang J, Hou S, Chi X-q, Shan H-f, Li X-w, Zhang Q-j, Wang J-l, Kang C-b. Role of SNAP25 on the occurrence and development of eosinophilic gastritis. Medicine 2023;102:29(e34377).

Received: 21 February 2023 / Received in final form: 26 June 2023 / Accepted: 27 June 2023

http://dx.doi.org/10.1097/MD.0000000000034377

in 1 layer. Eosinophil infiltrates are seen in any inflammatory process and should be identified when there is a significant increase in other inflammatory cells.[5] However, the etiology of eosinophilic gastritis is not clear, and it is generally believed to be caused by allergic reactions to exogenous or endogenous allergens.

Synaptosome Associated Protein 25 (SNAP25) is a protein-coding gene. The gene product is a presynaptic plasma membrane protein involved in the regulation of neurotransmitter release, and 2 alternative transcriptional variants encoding different protein subtypes have been described for this gene. Diseases associated with SNAP25 include myasthenic syndrome, epileptic encephalopathy, etc. The pathways involved include metabolism and neuroscience. The gene body annotations associated with this gene include calcium-dependent protein binding and SNAP receptor activity. SNAP23 is an important analogue of the gene.

SNAP25 belongs to a family of evolutionarily conserved proteins whose members are critical for exocytosis.[6] Neurons and neuroendocrine cells differentially express the 2 SNAP25 subtypes in a developmentally regulated manner, and related homologies have been detected in most eukaryotic cells. SNAP25 locates on the cytoplasmic surface and secretory vesicles of the plasma membrane.[7] SNAP25 promotes subsequent recombination and may drive Ca^{2+}-triggered vesicle-plasma membrane fusion. May play an important role in synaptic function in specific neuronal systems, related to proteins involved in vesicle docking and membrane fusion.[8] However, the relationship between SNAP25 and eosinophilic gastritis is unclear.

This study hypothesized that in the occurrence and development of eosinophilic gastritis, the lower the content of SNAP25, the higher the risk of eosinophilic gastritis. Based on the above hypothesis, we recruited 186 patients with eosinophilic gastritis. These results may reveal SNAP25 as a potential molecular target of eosinophilic gastritis and provide new ideas for its molecular mechanism.

2. Methods

2.1. Dataset

We downloaded tow gene profiles, GSE54043, from the Gene Expression Omnibus (GEO) database (https://www.ncbi.nlm.nih.gov/geo/). The GSE54043 includes 5 eosinophilic gastritis samples and 5 normal samples.

2.2. Differential epigenetic genes identification

We applied GEO2R (http://www.ncbi.nlm.nih.gov/geo/geo2r), an online tool based on GEO query and limma R packages, to identify differential epigenetic genes (DEGs) between follicular thyroid carcinoma and thyroid follicular adenoma group. The cutoff criteria were that P value < .05 and a log (FC) > 1 or log (FC) < −1.

2.3. DEGs annotation

Database for Annotation, Visualization and Integrated Discovery (https://david.ncifcrf.gov/home.jsp) and Metascape (http://metascape.org/gp/index.html) are 2 powerful annotation tools which can perform the biological process, cellular component, molecular function, and Kyoto Encyclopedia of Gene

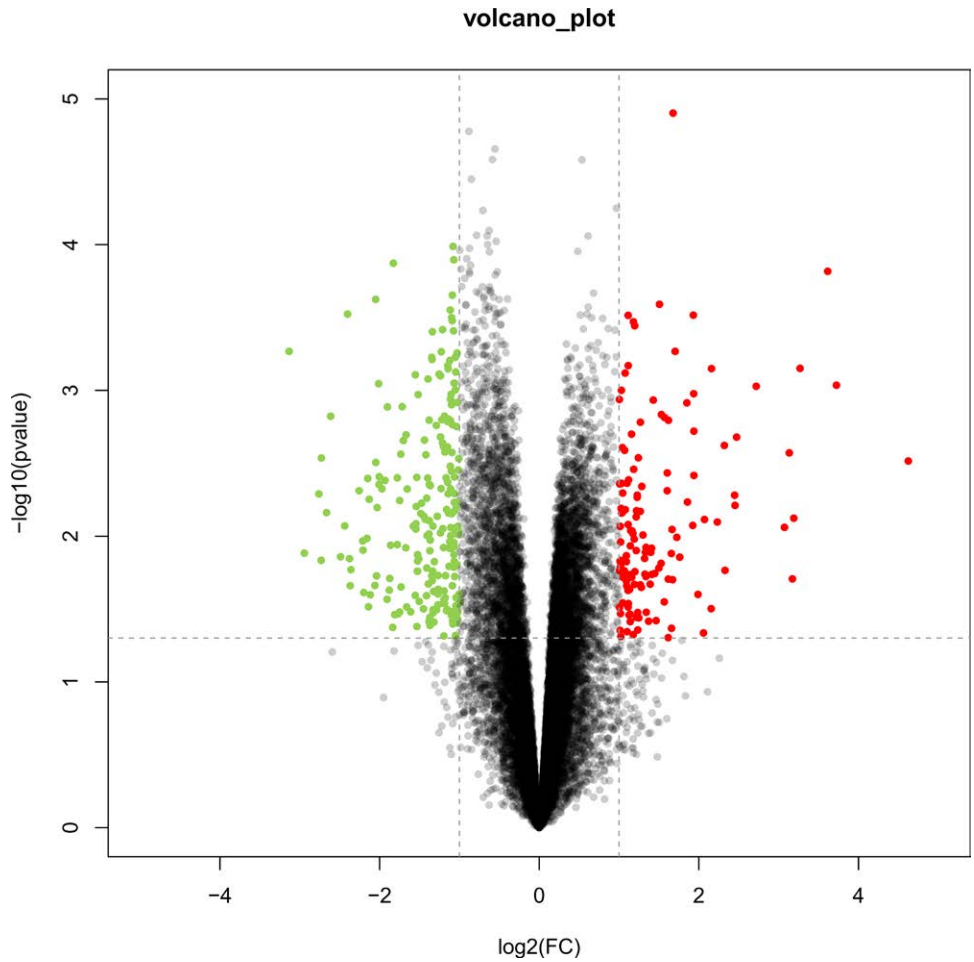

Figure 1. DEGs. The volcano plots present 353 DEGs in the GSE54043. DEGs = differential epigenetic genes.

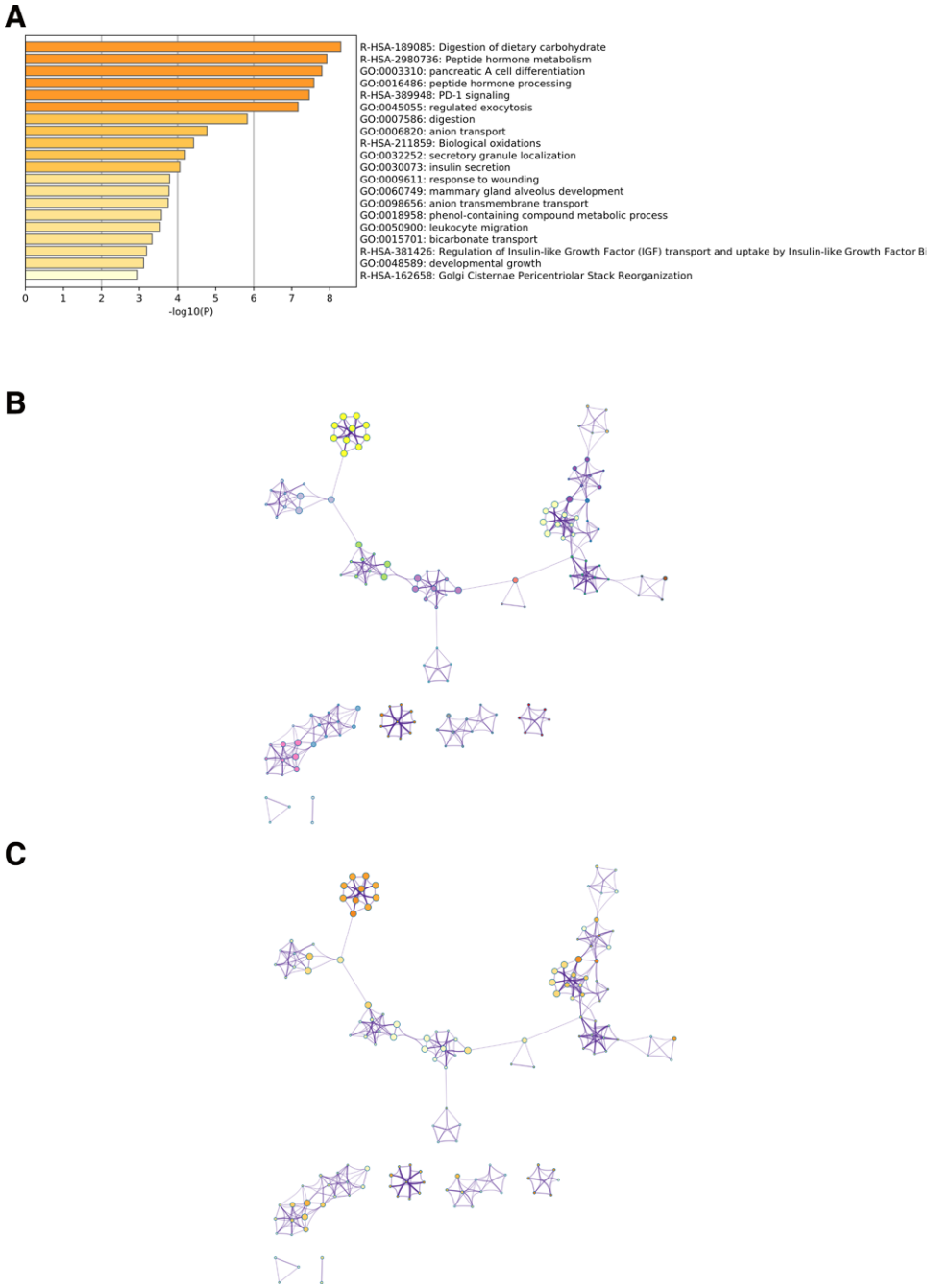

Figure 2. DEGs annotation. Enrichment analysis by Metascape was displayed. DEGs = differential epigenetic genes.

and Genome analysis on genes. We annotated the function of common DEGs through Database for Annotation, Visualization and Integrated Discovery and Metascape.

2.4. Protein–protein interaction network construction

The Search Tool for the Retrieval of Interacting Genes (http://string-db.org), can convert DEGs into expressed proteins and construct protein–protein interaction (PPI) network. We got PPI network of common DEGs through Search Tool for the Retrieval of Interacting Genes, and visualized it by Cytoscape (version 3.8.0).

2.5. Hub genes identification and expression

Molecular Complex Detection (MCODE) tool (version 1.6.1), an open plug-in of Cytoscape, was performed to identify significant module from PPI network. The criteria were that the maximum depth = 100, MCODE scores > 5, cutoff = 2, k score = 2, and node score cutoff = 0.2. Besides, we also applied cytoHubb to screened out hub genes and ranked them by maximal clique centrality and Closeness.

2.6. Patients and ethics

A total of 186 patients diagnosed with eosinophilic gastritis in Beijing Rehabilitation Hospital Affiliated to Capital Medical University from March 2015 to June 2020 were selected.

Inclusion criteria: 18 < age < 80, diagnosed as eosinophilic gastritis; cardiopulmonary function was normal; and normal coagulation.

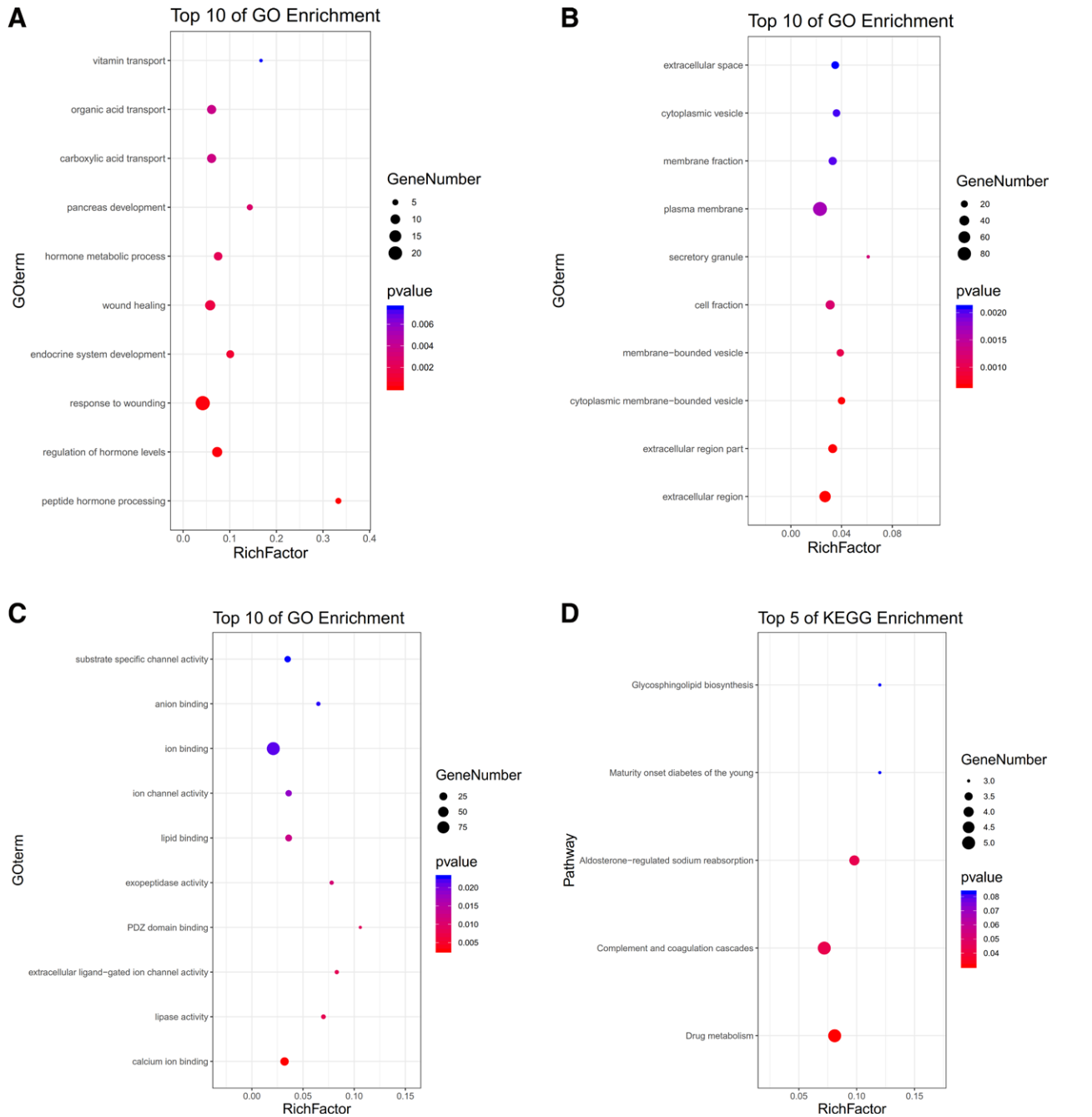

Figure 3. DEGs annotation. The DEGs related with BP, CC, MF, and KEGG enrichment analysis were displayed in bubble diagrams separately. BP = biological process, CC = cellular component, DEGs = differential epigenetic genes, KEGG = Kyoto Encyclopedia of Gene and Genome, MF = molecular function.

Exclusion criteria: patients requiring emergency surgery; poor lung, heart and liver function; and the patients and their families did not agree to participate in the trial.

This study was approved by the Ethics Committee of Beijing Rehabilitation Hospital Affiliated to Capital Medical University, and all patients signed written informed consent.

2.7. The parameter

According to the clinical data of the patients, they were classified by gender (male/female), age (≤65/>65), CPE (low/high), SST (low/high), PCSK2 (low/high), SNAP25 (low/high), and SYT4 (low/high).

2.8. Detection of blood related parameters

Venous blood samples of patients were immediately sent for examination to detect the expression levels of CPE, SST, PCSK2, SNAP25, and SYT4.

All statistical analyses were performed using SPSS software, version 21.0 (IBM, Armonk, NY). $P < .05$ was considered statistically significant.

3. Results

3.1. Differential epigenetic genes

The volcano plots present 353 DEGs in the GSE54043 (Fig. 1).

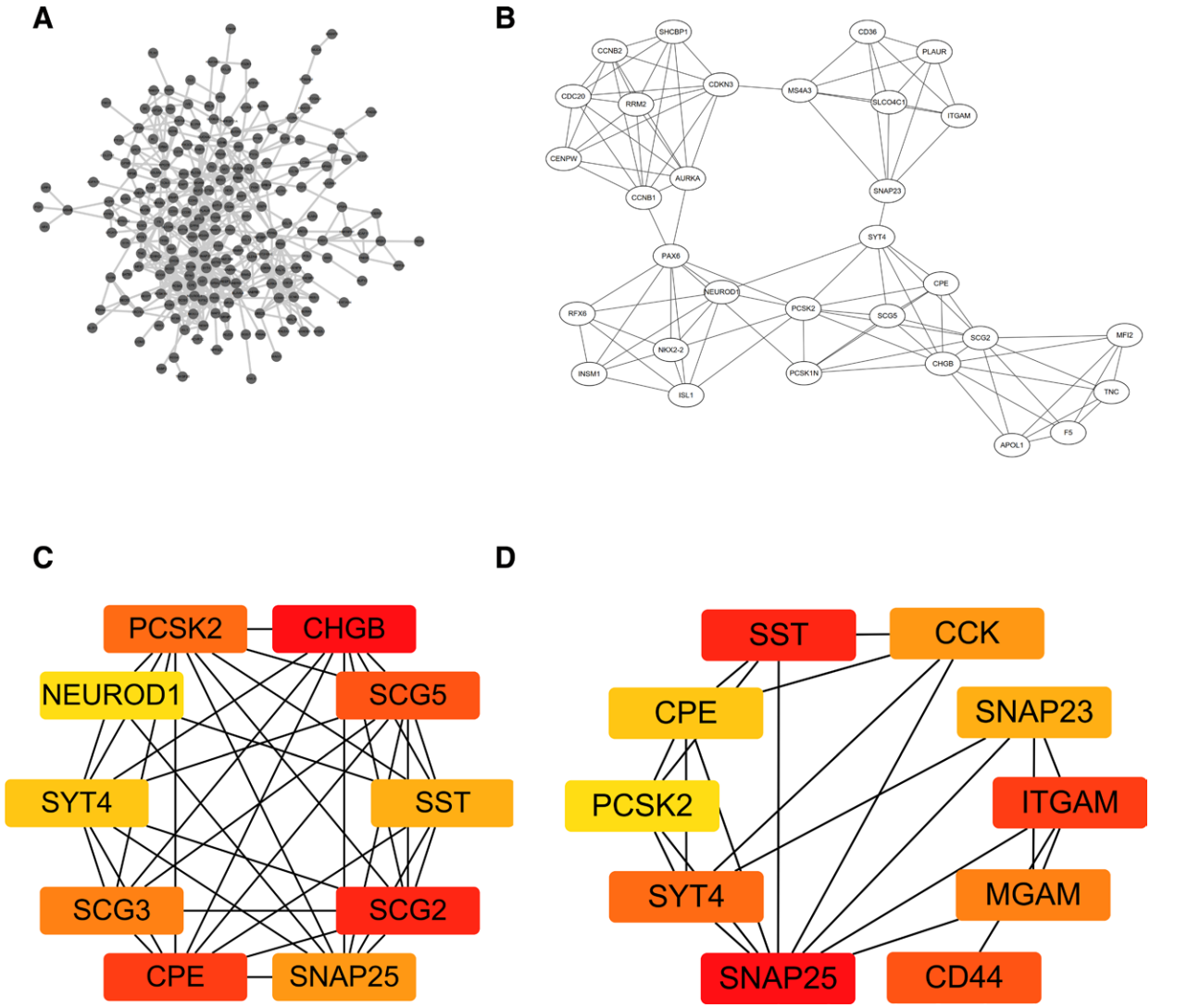

Figure 4. PPI network and hub genes. (A) PPI was displayed in. (B) The key module of MCODE analysis. (C and D) The top 10 genes screened by cytoHubb were shown. MCODE = molecular complex detection, PPI = protein–protein interaction.

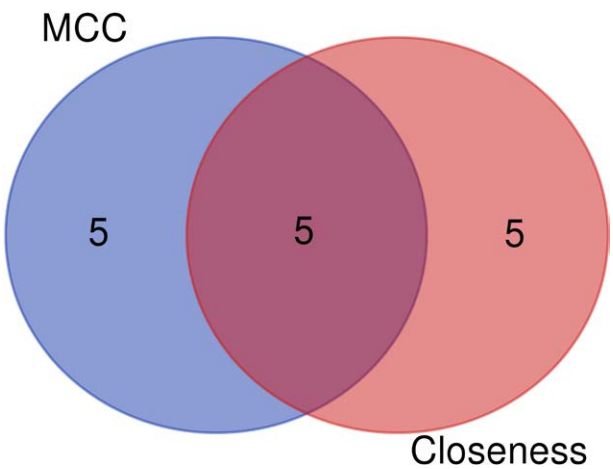

Figure 5. Veen diagram figured out 5 mutual genes.

3.2. DEGs annotation

Enrichment analysis by Metascape was displayed in Figure 2. The DEGs related with biological process, cellular component, molecular function, and Kyoto Encyclopedia of Gene and Genome enrichment analysis were displayed in bubble diagrams separately (Fig. 3A–D).

3.3. PPI network and hub genes

PPI was displayed in Figure 4A. The key module of MCODE analysis was shown (Fig. 4B). The top 10 genes screened by cytoHubb were shown (Fig. 4C and D), and Veen diagram figured out 5 mutual genes (Fig. 5). The heat map showed the expressions of the hub genes in GSE54043 (Fig. 6).

3.4. Pearson's chi-square test was used to analyze the correlation between eosinophilic gastritis and related factors

Pearson's chi-square test was used to summarize the relationship between eosinophilic gastritis and related clinical factors. SNAP25 ($P < .001$) was significantly associated with eosinophilic gastritis. However, sex ($P = .244$), age ($P = .994$), CPE ($P = .882$), SST ($P = .608$), PCSK2 ($P = .710$), and SYT4 ($P = .894$) had no significant correlation with eosinophilic gastritis (Table 1).

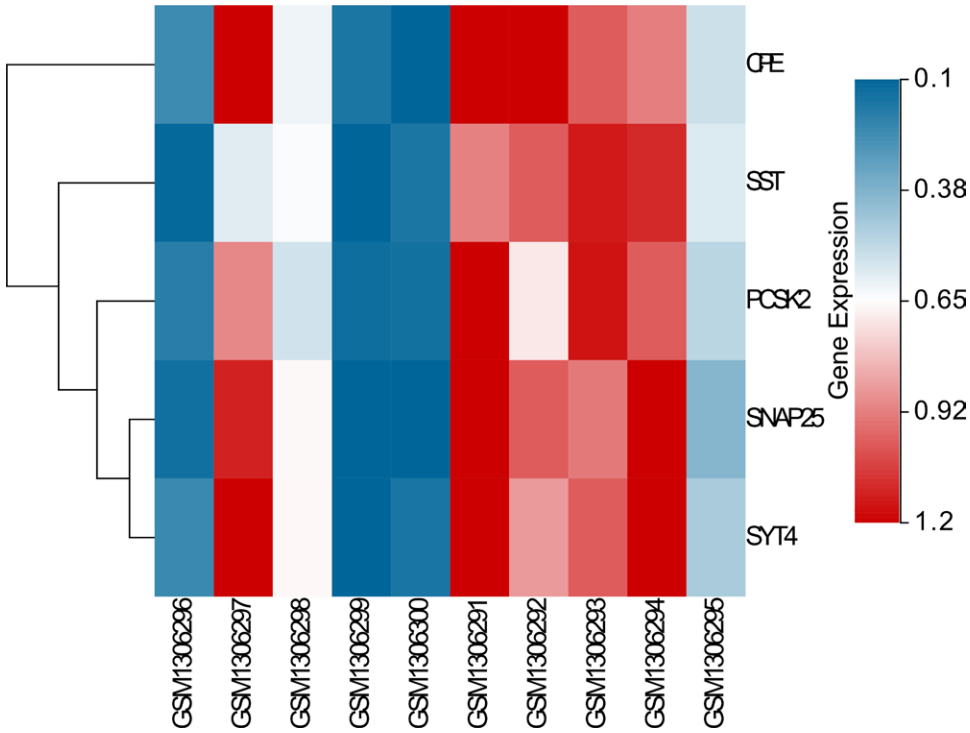

Figure 6. The heat map showed the expressions of the hub genes in GSE54043.

Table 1

Relevant characteristics of patients with eosinophilic gastritis body.

Characteristic			Eosinophilic gastritis		
			No	Yes	*P*
Sex	Male	94	16 (8.6%)	78 (41.9%)	.244
	Female	92	22 (11.8%)	70 (37.6%)	
Age	≤65	88	18 (9.7%)	70 (37.6%)	.994
	>65	98	20 (10.8%)	78 (41.9%)	
CPE	Low	91	19 (10.2%)	72 (38.7%)	.882
	High	95	19 (10.2%)	76 (40.9%)	
SST	Low	91	20 (10.8%)	71 (38.2%)	.608
	High	95	18 (9.7%)	77 (41.4%)	
PCSK2	Low	88	19 (10.2%)	69 (37.1%)	.710
	High	98	19 (10.2%)	79 (42.5%)	
SNAP25	Low	130	7 (23.3%)	123 (26.4%)	<.001*
	High	56	31 (22.1%)	25 (28.2%)	
SYT4	Low	85	17 (9.1%)	68 (36.6%)	.894
	High	101	21 (11.3%)	80 (43.0%)	

Pearson's chi-square test.
*$P < .05$.

3.5. Spearman's correlation coefficient was used to analyze the correlation between eosinophilic gastritis and related factors

Further analysis of Spearman's correlation coefficient showed that eosinophilic gastritis was significantly correlated with SNAP25 ($\rho = -0.569$, $P < .001$). However, sex ($\rho = 0.085$, $P = .246$), age ($\rho = 0.001$, $P = .994$), CPE ($\rho = 0.011$, $P = .883$), SST ($\rho = 0.038$, $P = .611$), PCSK2 ($\rho = 0.027$, $P = .712$), SYT4 ($\rho = -0.010$, $P = .895$) had no significant correlation with eosinophilic gastritis (Table 2).

3.6. Univariate logistic regression analysis of eosinophilic gastritis and related factors

Binary logistic regression was used to determine the relationship between relevant parameters and eosinophilic gastritis,

Table 2

Relationship between patient characteristics and eosinophilic gastritis.

Characteristic	Eosinophilic gastritis	
	ρ	*P*
Sex	−0.085	.246
Age	0.001	.994
CPE	0.011	.883
SST	0.038	.611
PCSK2	0.027	.712
SNAP25	−0.569	<.001*
SYT4	−0.010	.895

Spearman correlation analysis.
*$P < .05$.

Table 3

Influence of relevant parameters on eosinophilic gastritis based on univariate logistic regression analysis.

Characteristic			Eosinophilic gastritis		
			OR	95% CI	*P*
Sex	Male	94	1		.246
	Female	92	0.653	0.318–1.341	
Age	≤65	88	1		.994
	>65	98	1.003	0.491–2.048	
CPE	Low	91	1		.882
	High	95	1.056	0.517–2.153	
SST	Low	91	1		.609
	High	95	1.205	0.590–2.460	
PCSK2	Low	88	1		.710
	High	98	1.145	0.561–2.336	
SNAP25	Low	130	1		<.001*
	High	56	0.046	0.018–0.116	
SYT4	Low	85	1		.894
	High	101	0.952	0.465–1.950	

95% CI = 95% confidence interval, OR = odds ratio.
*$P < .05$.

Table 4

Multivariate logistic regression analysis of eosinophilic gastritis and its influence.

Characteristic	Eosinophilic gastritis		
	OR	95% CI	*P*
Sex	0.562	0.218–1.444	.231
Age	1.578	0.602–4.136	.353
CPE	2.785	1.001–7.746	.050
SST	0.872	0.344–2.215	.774
PCSK2	2.290	0.853–6.149	.100
SNAP25	0.024	0.007–0.075	<.001*
SYT4	0.886	0.345–2.278	.802

95% CI = 95% confidence interval, OR = odds ratio.
*$P < .05$.

odds ratio (OR), and 95% confidence interval (95% CI). Table 3 describes the SUBJECTS 'OR and 95% CI at the univariate Logistic regression level, showing that SNAP25 (OR = 0.046, 95% CI: 0.018–0.116, $P < .001$) was significantly associated with eosinophilic gastritis. However, sex (OR = 0.653, 95% CI: 0.318–1.341, $P = .246$), age (OR = 1.003, 95% CI: 0.491–2.048, $P = .994$), CPE (OR = 1.056, 95% CI: 0.517–2.153, $P = .882$), SST (OR = 1.205, 95% CI: 0.590–2.460, $P = .609$), PCSK2 (OR = 1.145, 95% CI: 0.561–2.336, $P = .710$), SYT4 (OR = 0.952, 95% CI: 0.465–1.950, $P = .894$) and eosinophilic gastritis were not significantly correlated (Table 3).

3.7. Multivariate logistic regression analysis of eosinophilic gastritis related factors

Multivariate logistic regression was used to describe the OR and 95% CI of the subjects at the multivariate level. SNAP25 (OR = 0.024, 95% CI: 0.007–0.075, $P < .001$) was significantly associated with eosinophilic gastritis, while sex (OR = 0.562, 95% CI: 0.218–1.444, $P = .231$), age (OR = 1.578, 95% CI: 0.602–4.136, $P = .353$), CPE (OR = 2.785, 95% CI: 1.001–7.746, $P = .050$), SST (OR = 0.872, 95% CI: 0.344–2.215, $P = .774$), PCSK2 (OR = 2.290, 95% CI: 0.853–6.149, $P = .100$), and SYT4 (OR = 0.886, 95% CI: 0.345–2.278, $P = .802$) were not significantly correlated with eosinophilic gastritis (Table 4).

4. Discussion

In this study, Pearson's card test showed that SNAP25 ($P < .001$) was significantly associated with eosinophilic gastritis. Spearman correlation coefficient showed a significant correlation between Eosinophilic gastritis and SNAP25 ($\rho = -0.569$, $P < .001$). Univariate logistic regression analysis showed that SNAP25 (OR = 0.046, 95% CI: 0.018–0.116, $P < .001$) was significantly associated with eosinophilic gastritis. Multivariate logistic regression analysis showed that SNAP25 (OR = 0.024, 95% CI: 0.007–0.075, $P < .001$) was significantly associated with eosinophilic gastritis.

Eosinophilic gastritis is a gastrointestinal disease characterized by increased eosinophils in peripheral blood. The gastrointestinal tract may have various degrees of eosinophils infiltration.[9] The etiology is not clear, and is related to allergic reaction, parasitic infection, etc., and responds well to glucocorticoid treatment. The disease lacks specificity and can be acute due to gastric outflow tract obstruction, with symptoms lasting for many years in some patients.[10] This type of disease mainly involves the muscular layer, and its clinical manifestations are obstruction, including pyloric obstruction and intestinal obstruction.

SNAP25, a member of SNARE family, is also a membrane binding protein in neurons and plays an indispensable role in the occurrence and development of various synaptic lesions.[11,12] The SNAP25 protein subfamily also plays an important role in autophagy. Autophagy is the process of removing damaged, denatured and senescent proteins or organelles in cells. It is the metabolic needs of cells themselves and also the renewal of some organelles. Autophagy involves membrane fusion. SNAP25 subfamily members can interact with other SNARE complexes to form SNARE complexes and thus participate in autophagy. It has been shown that NUPR1 maintains autolysosomal excretion in cancer cells by activating SNAP25 transcription, and snap25-mediated autophagolysosomal processes play an unexpectedly broad role in autophagolysosomal biogenesis and excretion.[13] Because of its pro-survival effect under adverse conditions, autophagy protects cancer cells from stress such as nutrient deprivation or chemotherapy.[14,15]

SNAP25 plays an important role in neuronal exocytosis pathway.[16] Another member of the SNAP25 protein family is SNAP23, which is derived from a separate gene of SNAP25a/B and shares 60% of the amino acid level with the SNAP25 subtype. SNAP23 has universal tissue distribution and function in cell types such as mast cells and adipocytes, and may play a

role in constitutive exocytosis pathways throughout the body. SNAP23 is 60% the same as SNAP25, and both SNAP25a and SNAP25b have unique cysteine-rich regions. SNAP25a and SNAP25b are highly expressed SNARE proteins in the brain, which play an important role in presynaptic neurotransmitter release. In addition to neurons, SNAP25A/B has limited distribution and function in tissues outside the nervous system, most notably in the regulated exocrine pathways of pancreatic beta cells and pheochromocytoma in the adrenal medulla.[17]

SNAP25 is a microenvironment-related and immune-related gene involved in metabolic processes. Bioinformatics analysis showed that SNAP25 is involved in tumor-related signaling pathways as well as immune and metabolic processes. SNAP25 performs different functions depending on the type of cancer. In addition, SNAP25, which is critical for dendritic formation and is associated with the effectiveness of targeted chemotherapy, was found to be significantly reduced in medulloblastoma.[18] SNAP25 expression is down-regulated in glioma tissues and cells, and low expression of SNAP25 is detrimental to the prognosis of glioma patients. Downregulation of SNAP25 accelerated cell proliferation, migration, and invasion, and reduced glutamine hydrolysis of glioma cells. SNAP25 may serve as a biomarker for glioblastoma inhibitors and glioblastoma therapy.[19,20] Since SNAP25 basically plays a key role in regulating synaptic activity of alveolar metastasis between adjacent cells in the nervous system,[19,20] SNAP25 may play a role in activation of glioma cell interactions, thereby affecting the growth of brain cancer. SNAP25 has also been shown to be a potential prognostic biomarker for prostate cancer.[21]

SNAP25 was significantly correlated with lymphocytes (NK, macrophages, mast cells and NKT), and the potential prognostic value of SNAP25 in colon cancer was explored based on matrix immune score.[22] SNAP25 was positively correlated with immune infiltration of various types of T cells, B cells, macrophages, NK cells, monocytes, neutrophils, fibroblasts, etc. In recent years, more and more studies have confirmed the association between SNAP25 level and gastric cancer[23] and thyroid papillary carcinoma.[24]

SNAP25 is essential for the regulation of neurotransmitter release, synaptic information transmission, secretory vesicle extravasation, intercellular signaling and ion channel opening.[25,26] SNAP25 is considered to be a potentially important factor in normal vesicle fusion and lysosomal transport[27] and plays a key role in endosomal fusion.[28] Therefore, SNAP25 is speculated to be related to the occurrence and development of eosinophilic gastritis.

However, there are some shortcomings in this study. Although clinical data have been examined and analyzed, the molecular mechanism of SNAP25 expression levels on vertebral compression fractures has not been validated in animal models. Therefore, future studies should focus on animal experiments to explore the molecular pathway and mechanism of SNAP25 in vertebral compression fractures.

5. Conclusion

The expression level of SNAP25 was significantly correlated with the occurrence of eosinophilic gastritis. The low expression of SNAP25 gene in eosinophilic gastritis is associated with a higher risk of eosinophilic gastritis. As a potential target of eosinophilic gastritis, SNAP25 provides a new idea for the molecular mechanism of its occurrence and development.

Author contributions

Conceptualization: Jie Zhang, Shiyang Hou.
Data curation: Xiao-qian Chi, Xiao-wei Li, Qi-jun Zhang, Chun-bo Kang.
Formal analysis: Xiao-qian Chi, Chun-bo Kang.
Investigation: Jin-lei Wang.
Methodology: Xiao-qian Chi, Xiao-wei Li, Qi-jun Zhang.
Software: Xiao-qian Chi, Hai-feng Shan, Xiao-wei Li, Qi-jun Zhang, Jin-lei Wang.
Supervision: Hai-feng Shan, Jin-lei Wang.
Validation: Jie Zhang, Shiyang Hou.
Visualization: Jie Zhang, Shiyang Hou.
Writing – original draft: Chun-bo Kang.
Writing – review & editing: Jie Zhang, Shiyang Hou.

References

[1] Chen PH, Anderson L, Zhang K, et al. Eosinophilic gastritis/gastroenteritis. Curr Gastroenterol Rep. 2021;23:13.
[2] Dellon ES, Peterson KA, Murray JA, et al. Anti-Siglec-8 antibody for eosinophilic gastritis and duodenitis. N Engl J Med. 2020;383:1624–34.
[3] Zhang M, Li Y. Eosinophilic gastroenteritis: a state-of-the-art review. J Gastroenterol Hepatol. 2017;32:64–72.
[4] Uppal V, Kreiger P, Kutsch E. Eosinophilic gastroenteritis and colitis: a comprehensive review. Clin Rev Allergy Immunol. 2016;50:175–88.
[5] Bobrova VI, Horobets AO, Proshchenko JI, et al. Eosinophilic gastritis in children: morphological and immunohistochemical diagnostic criteria. Wiad Lek. 2021;74:1722–7.
[6] Söderqvist S, McNab F, Peyrard-Janvid M, et al. The SNAP25 gene is linked to working memory capacity and maturation of the posterior cingulate cortex during childhood. Biol Psychiatry. 2010;68:1120–5.
[7] Gosso MF, de Geus EJ, Polderman TJ, et al. Common variants underlying cognitive ability: further evidence for association between the SNAP-25 gene and cognition using a family-based study in two independent Dutch cohorts. Genes Brain Behav. 2008;7:355–64.
[8] Lochman J, Balcar VJ, Šťastný F, et al. Preliminary evidence for association between schizophrenia and polymorphisms in the regulatory regions of the ADRA2A, DRD3 and SNAP-25 genes. Psychiatry Res. 2013;205:7–12.
[9] Otowa Y, Mitsutsuji M, Urade T, et al. Eosinophilic gastroenteritis associated with multiple gastric cancer. Eur J Gastroenterol Hepatol. 2012;24:727–30.
[10] Hirano I, Collins MH, King E, et al.; CEGIR investigators. Prospective endoscopic activity assessment for eosinophilic gastritis in a multisite cohort. Am J Gastroenterol. 2022;117:413–23.
[11] Wang Q, Wang Y, Ji W, et al. SNAP25 is associated with schizophrenia and major depressive disorder in the Han Chinese population. J Clin Psychiatry. 2015;76:e76–82.
[12] Antonucci F, Corradini I, Morini R, et al. Reduced SNAP-25 alters short-term plasticity at developing glutamatergic synapses. EMBO Rep. 2013;14:645–51.
[13] Mu Y, Yan X, Li D, et al. NUPR1 maintains autolysosomal efflux by activating SNAP25 transcription in cancer cells. Autophagy. 2018;14:654–70.
[14] Amaravadi RK, Yu D, Lum JJ, et al. Autophagy inhibition enhances therapy-induced apoptosis in a Myc-induced model of lymphoma. J Clin Invest. 2007;117:326–36.
[15] Cai Q, Lu L, Tian JH, et al. Snapin-regulated late endosomal transport is critical for efficient autophagy-lysosomal function in neurons. Neuron. 2010;68:73–86.
[16] Greaves J, Gorleku OA, Salaun C, et al. Palmitoylation of the SNAP25 protein family: specificity and regulation by DHHC palmitoyl transferases. J Biol Chem. 2010;285:24629–38.
[17] Zurawski Z, Rodriguez S, Hyde K, et al. Gβγ binds to the extreme C terminus of SNAP25 to mediate the action of Gi/o-coupled G protein-coupled receptors. Mol Pharmacol. 2016;89:75–83.
[18] Choi J, Choi JA. Influence of leisure competence and level of leisure activity on life satisfaction in low-income older adults in Rural South Korea. Res Gerontol Nurs. 2017;10:67–75.
[19] Olbrich K, Costard L, Möser CV, et al. Cleavage of SNAP-25 ameliorates cancer pain in a mouse model of melanoma. Eur J Pain. 2017;21:101–11.
[20] Yu C, Yin J, Wang X, et al. Association between SNAP25 and human glioblastoma multiform: a comprehensive bioinformatic analysis. Biosci Rep. 2020;40:BSR20200516.
[21] Di L, Gu M, Wu Y, et al. SNAP25 is a potential prognostic biomarker for prostate cancer. Cancer Cell Int. 2022;22:144.
[22] Zou J, Duan D, Yu C, et al. Mining the potential prognostic value of synaptosomal-associated protein 25 (SNAP25) in colon cancer based on stromal-immune score. PeerJ. 2020;8:e10142.
[23] Rabben HL, Andersen GT, Olsen MK, et al. Neural signaling modulates metabolism of gastric cancer. iScience. 2021;24:102091.

[24] Yu X, Zhong P, Han Y, et al. Key candidate genes associated with BRAF(V600E) in papillary thyroid carcinoma on microarray analysis. J Cell Physiol. 2019;234:23369–78.
[25] Baker RW, Hughson FM. Chaperoning SNARE assembly and disassembly. Nat Rev Mol Cell Biol. 2016;17:465–79.
[26] Wang T, Li L, Hong W. SNARE proteins in membrane trafficking. Traffic. 2017;18:767–75.
[27] Manca P, Mameli O, Caria MA, et al. Distribution of SNAP25, VAMP1 and VAMP2 in mature and developing deep cerebellar nuclei after estrogen administration. Neuroscience. 2014;266:102–15.
[28] Aikawa Y, Lynch KL, Boswell KL, et al. A second SNARE role for exocytic SNAP25 in endosome fusion. Mol Biol Cell. 2006;17:2113–24.