

Fig. S1. (A) Relative expression of serum miR-125a-5p and (B) serum CCL17 levels corresponding to each sample (58 healthy controls (HC) and 59 chronic spontaneous urticaria (CSU) patients) are plotted and the median (along with 25th-75th percentile ranges) values are shown.

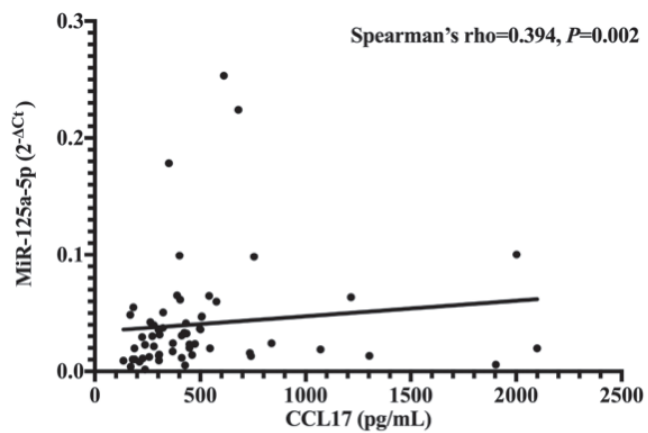


Fig. S2. Relative expression of serum miR-125a-5p was positively correlated with CCL17 in chronic spontaneous urticaria patients.

Table SI. Serum levels of miR-125a-5p within different subgroups of chronic spontaneous urticaria (CSU) patients (n = 59)

Subgroups	n	miR-125a-5p (2 ^{-ΔCt}) Median (IQR)	p-value
Sex			
Female	42	0.024 (0.013; 0.048)	0.071
Male	17	0.029 (0.016; 0.045)	
Angioedema			
With	28	0.020 (0.012; 0.035)	0.018
Without	31	0.036 (0.020; 0.055)	
Personal history of atopic diseases			
With	23	0.024 (0.020; 0.051)	0.196
Without	36	0.027 (0.011; 0.041)	
Urticaria family history			
With	19	0.024 (0.019; 0.042)	0.658
Without	40	0.027 (0.013; 0.050)	
Atopic diseases family history			
With	17	0.019 (0.010; 0.035)	0.069
Without	42	0.031(0.016; 0.052)	
Anti-TG/anti-TPO antibodies			
Positive	15	0.024 (0.011; 0.062)	0.897
Negative	44	0.027 (0.014; 0.047)	
Total IgE			
0–100 IU/ml	28	0.024 (0.013; 0.041)	0.646
>100 IU/ml	31	0.029 (0.014; 0.055)	
Serum specific IgE			
Positive	17	0.036 (0.022; 0.053)	0.099
Negative	42	0.022 (0.012; 0.044)	
CCL17 ^a			
>263.0 pg/ml	46	0.032 (0.018; 0.053)	0.002
≤263.0 pg/ml	13	0.011 (0.009; 0.026)	

^a263.0 pg/ml was the cut-off value of CCL17.

TG: thyroglobulin; TPO: thyroid peroxidase.

Table SII. Therapeutic regimens of 10 refractory chronic spontaneous urticaria (CSU) patients

Dosage	<i>n</i>	Therapeutic regimens
4-fold dose	2	
	1	Desloratadine 10 mg twice daily
4-fold equivalent dose	1	Olopatadine 10 mg twice daily
	4	
	1	Desloratadine 5 mg, loratadine 10 mg once daily, olopatadine 5 mg twice daily
	1	Ebastine 20 mg, fexofenadine 180 mg, loratadine 10 mg once daily
4-fold equivalent dose and LRA	1	Desloratadine 5 mg, ebastine 20 mg, fexofenadine 180 mg once daily
	1	Desloratadine 5 mg, ebastine 20 mg, loratadine 10 mg once daily
	1	Ebastine 20 mg, fexofenadine 180 mg, loratadine 10 mg, montelukast 10 mg once daily
4-fold equivalent dose and LRA and H ₂ -antihistamine	1	Ebastine 20 mg, fexofenadine 180 mg, loratadine 10 mg, montelukast 10 mg daily, ranitidine 350 mg twice daily
4-fold equivalent dose and Chinese traditional medication	2	
	1	Olopatadine 5 mg twice daily, fexofenadine 120 mg thrice daily, TGP 2 capsules thrice daily
	1	Ebastine 20 mg once daily, desloratadine 5 mg twice daily, TGP 2 capsules thrice daily

LRA: leukotriene receptor antagonist; TGP: total glucosides of paenony.

Table SIII. Therapeutic regimens of 49 non-refractory chronic spontaneous urticaria (CSU) patients

Dosage	<i>n</i>	Therapeutic regimens
Licensed dose	15	Loratadine 10 mg once daily, <i>n</i> = 6; fexofenadine 180 mg once daily, <i>n</i> = 5; ebastine 10 mg once daily, <i>n</i> = 3; mizolastine 10 mg once daily, <i>n</i> = 1
2-fold dose	8	Ebastine 20 mg once daily, <i>n</i> = 8
2-fold equivalent dose	6	Fexofenadine 180 mg, loratadine 10 mg once daily, <i>n</i> = 4; fexofenadine 180 mg, desloratadine 5 mg once daily, <i>n</i> = 2
3-fold dose	1	Fexofenadine 180 mg thrice daily, <i>n</i> = 1
3-fold equivalent dose	19	Ebastine 20 mg, fexofenadine 180 mg once daily, <i>n</i> = 12; ebastine 20 mg, loratadine 10 mg once daily, <i>n</i> = 4; desloratadine 5 mg, fexofenadine 180 mg and loratadine 10 mg once daily, <i>n</i> = 1; fexofenadine 180 mg once daily and olopatadine 5 mg twice daily, <i>n</i> = 1; ebastine 20 mg, desloratadine 5 mg once daily, <i>n</i> = 1

Table SIV. Characteristics of the 12 chronic spontaneous urticaria (CSU) patients with serum samples collected in the remission phase

Age, years, median (IQR)	33 (30; 41)
Sex (female/male)	9/3
Female age, years, median (IQR)	35 (31.5; 45)
Male age, years, median (IQR)	30 (27; 33)
Disease duration, months, median (IQR)	3.5 (2.3; 5.0)
Personal history of atopic diseases, <i>n</i> (%)	2 (16.7)
Urticaria/atopic diseases family history, <i>n</i> (%)	8 (66.7)
Urticaria family history, <i>n</i>	4
Atopic diseases family history, <i>n</i>	4
Urticaria and atopic diseases family history, <i>n</i>	0
UAS, median; (IQR)	5 (4; 6)
Total IgE, IU/ml, median (IQR)	142.7 (39.6; 365.7)
MiR-125a-5p ($2^{-\Delta\Delta Ct}$), median (IQR)	
Active phase	0.028 (0.007; 0.058)
Remission phase	0.004 (0.002; 0.009)
CCL17, pg/ml, median (IQR)	
Active phase	597.1 (346.3; 976.6)
Remission phase	343.3 (256.6; 488.9)
Positive anti-TG/anti-TPO antibodies, <i>n</i> (%)	2 (16.7)
Positive serum specific IgE, <i>n</i> (%)	4 (33.3)

HC: healthy control; IQR: interquartile ranges; UAS: urticaria activity score; TG: thyroglobulin; TPO: thyroid peroxidase.

Table SV. Treatment and follow up of the 12 chronic spontaneous urticaria (CSU) patients with serum samples collected in the remission phase

Case	Sex	Age, years	Disease duration, months	Therapeutic regimens	Refractory	Time interval (m)	Outcome
1	F	39	5	2-fold dose	No	12.3	Medication withdrawal for 8 months
2	F	52	3	2-fold equivalent dose	No	15.2	Medication withdrawal for 3 months
3	F	33	2	4-fold equivalent dose and montelukast and ranitidine	Yes	20.3	Medication withdrawal for 6 months
4	F	49	4	4-fold equivalent dose	Yes	4.5	Fexofenadine 120 mg once daily
5	M	30	2	4-fold equivalent dose and ranitidine	Yes	5.9	Olopatadine 5 mg once daily, ranitidine 350 mg twice daily
6	F	31	5	3-fold equivalent dose	No	6.3	Licensed dose
7	F	41	6	2-fold dose	No	6.5	Licensed dose
8	F	32	3	4-fold equivalent dose	Yes	8.4	Licensed dose
9	M	27	4	4-fold equivalent dose and ranitidine	Yes	8.6	Licensed dose
10	F	30	2	4-fold equivalent dose and ranitidine and TGP	Yes	10.3	Licensed dose
11	F	35	12	4-fold equivalent dose	Yes	18.9	Licensed dose
12	M	33	3	4-fold dose	Yes	21.5	Licensed dose

Time interval: refers to the time interval between two time point of serum collections; TGP: total glucosides of peony.

Table SVI. Chronic spontaneous urticaria (CSU)-associated targeted genes of miR-125a-5p with known canonical signal pathways

Genes	Complete names of the genes	Canonical signal pathways
<i>BCL2</i>	B-cell/lymphoma 2	AGE-RAGE signaling pathway FoxO signaling pathway JAK-STAT signaling pathway EGFR tyrosine kinase inhibitor resistance Neurotrophin signaling pathway NF-kappa B signaling pathway Ras signaling pathway
<i>STAT3</i>	Signal transducer and activator of transcription 3	AGE-RAGE signaling pathway FoxO signaling pathway JAK-STAT signaling pathway EGFR tyrosine kinase inhibitor resistance Chemokine signaling pathway Inflammatory bowel disease Signaling pathways regulating pluripotency of stem cells Th17 cell differentiation
<i>TGFBR1</i>	Transforming growth factor-beta receptor, type 1	AGE-RAGE signaling pathway FoxO signaling pathway Adherens junction Cytokine-cytokine receptor interaction MAPK signaling pathway TGF-beta signaling pathway

AGE-RAGE: advanced glycation end products and receptor for advanced glycation end products; FoxO: forkhead box O; JAK-STAT: janus kinase and signal transducer and activator of transcription; EGFR: epidermal growth factor receptor; MAPK: mitogen-activated protein kinase.