

Supplementary information

Shen Hong Tong Luo formula attenuates macrophage inflammation and lipid accumulation through the activation of PPAR- γ /LXR- α /ABCA1 pathway

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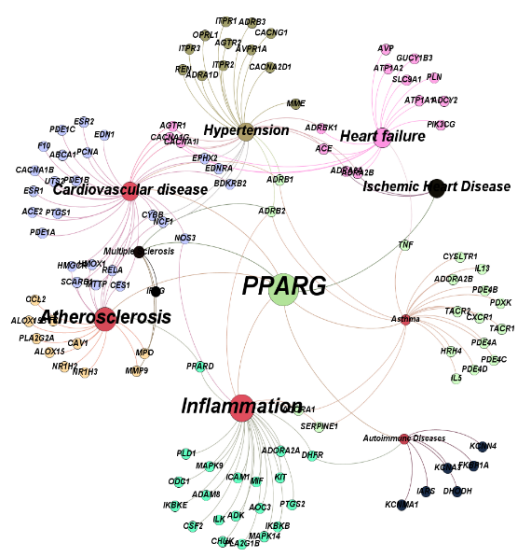
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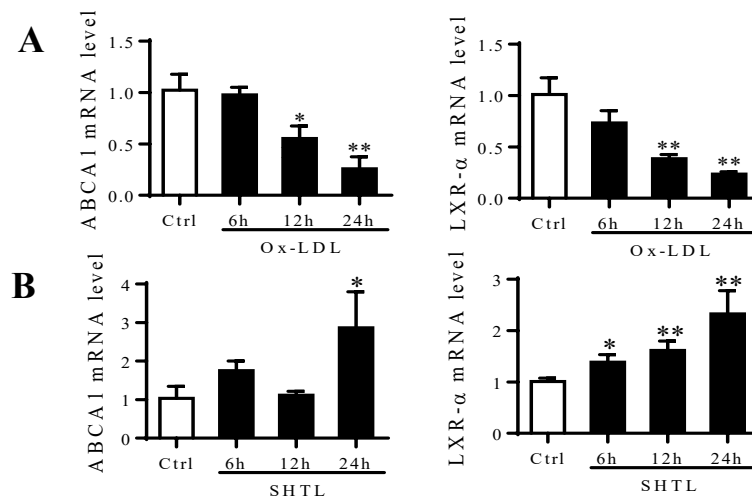
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Supplementary Figure S1



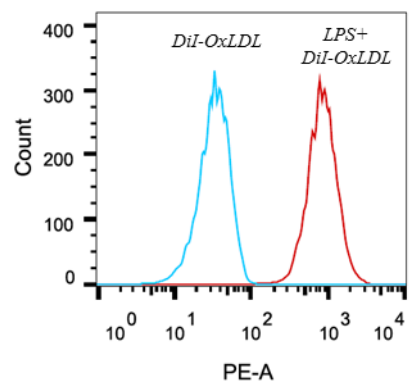
The disease-target network of SHTL was shown by Gephi. The bigger circles represented the disease and the smaller circles represented the predicted targets.

Supplementary Figure S2



(A) Mouse peritoneal macrophages (MPMs) were stimulated without or with Ox-LDL (40 μ g/mL). The time-dependent effect of Ox-LDL in MPMs was evaluated using qPCR analysis after the normalization of β -Actin. **(B)** MPMs were incubated with SHTL for 6 h, 12 h and 24 h. The time-dependent effect of SHTL in MPMs was evaluated using qPCR analysis after the normalization of β -Actin.

Supplementary Figure S3



After LPS incubation for 8 h, the lipid accumulation in MPMs was detected by DiI-Ox-
LDL staining using flow cytometry.

Supplementary Table 1 HPLC gradient elution process

Time(min)	Mobile phase A	Mobile phase B	Time(min)	Mobile phase A	Mobile phase B
0-20	10~18%	90~82%	65~85	32%	68%
20-25	18~20%	82~80%	85~95	32~90%	68~10%
25~45	20~30%	80~70%	105~110	10%	90%
45~60	30%	70%			

Supplementary Table 2 Sequences of primers used in the qRT-PCR.

Primer		Sequence
PPAR- γ	forward	GCAGCTACGCTCCTTTCTTG
	reverse	TGTTGCCCTCTTTAGTGCA
LXR- α	forward	ATCGCCTTGCTGAAGACCTCTG
	reverse	GATGGGGTTGATGAACTCCACC
ABCA1	forward	GCTTGTTGGCCTCAGTTAAGG
	reverse	GTAGCTCAGGCGTACAGAGAT
IL-6	forward	CCAAGAGGTGAGTGCTTCCC
	reverse	CTGTTGTTCAGACTCTCTCCCT
TNF- α	forward	CCCTCACACTCAGATCATCTTCT
	reverse	GCTACGACGTGGGCTACAG
β -Actin	forward	GGCTGTATTCCCCTCCATCG
	reverse	GCTACGACGTGGGCTACAG

Supplementary Table 3 The Top20 pathway Enrichment of Shen Hong Tong Luo formula

Term description	P-value	Benjamini-value	Coverage	EnrichRatio
beta-Alanine metabolism	1.12E-05	9.00E-05	17	2.8
Serotonergic synapse	2.86E-06	2.38E-05	44	1.9
PPAR signaling pathway	2.61E-06	2.25E-05	31	2.2
Alanine, aspartate and glutamate metabolism	5.23E-07	4.67E-06	21	2.9
TGF-beta signaling pathway	3.90E-07	3.76E-06	36	2.3
Tryptophan metabolism	2.14E-07	2.15E-06	23	2.8
Propanoate metabolism	2.01E-07	2.11E-06	20	3.1
Cysteine and methionine metabolism	1.74E-07	1.91E-06	22	2.9
Cardiac muscle contraction	3.20E-08	3.86E-07	37	2.3
cGMP - PKG signaling pathway	1.25E-08	1.59E-07	65	1.9
Biosynthesis of amino acids	5.05E-09	7.16E-08	37	2.5
Purine metabolism	1.48E-09	2.23E-08	68	2
Phenylalanine metabolism	7.02E-10	1.13E-08	16	4.4
Glycine, serine and threonine metabolism	3.52E-10	6.06E-09	26	3.3
Valine, leucine and isoleucine degradation	5.05E-11	9.36E-10	29	3.3
Tyrosine metabolism	4.15E-11	8.33E-10	27	3.4
Carbon metabolism	1.09E-12	2.63E-11	54	2.6
Arginine and proline metabolism	2.57E-16	1.03E-14	41	3.4
Calcium signaling pathway	2.94E-22	2.36E-20	94	2.6
Neuroactive ligand-receptor interaction	7.81E-37	9.41E-35	148	2.7

Supplementary Table 4 Significant enrichment of diseases and their targets belong to Shen Hong Tong Luo formula

Disease	Target
Atherosclerosis	ABCA1, ADIPOQ, CREB1, ROCK1, SCARB1, ALOX15, ALOX15B, CAV1, CCL2, CES1, HMGCR, HMOX1, MMP9, MPO, NR1H2, NR1H3, PLA2G2A, PPARD, PPARG
Inflammation	ADAM8, ADK, ADORA1 ,ADORA2A, AOC3, CHUK, DHFR, ICAM1, IKBKB, IKBKE, ILK, KIT, MAPK14, MAPK9, NOS3, ODC1, PLA2G1B, PLD1, PPARD, PPARG, PTGS2, SERPINE1
Cardiovascular disease	ABCA1, ADRB1, AGTR1, BDKRB2, CACNA1B, CES1, EDN1, EDNRA, EPHX2, ESR1, ESR2, F10, HMGCR, , HMOX1, NOS3, PCNA, PDE1B, PTGS1, SCARB1, SCD, UTS2
Myocardial infarction	BDKRB2, HMGCR, NPR2, PIK3CG, PTGS2, UTS2R
Hypertension	ACE, ADRA1D, ADRA2A, ADRA2B, ADRB1, ADRBK1, AGTR1, AGTR2, AVPR1A, BDKRB2, CACNA2D1, CACNG1, EDNRA, EPHX2, MME, OPRL1
Heart failure	ACE, ADCY2, ADRA2A, ADRA2B, ADRBK1, AGTR1, ATP1A1, ATP1A2, AVP, GUCY1B3, PIK3CG, PLN, SLC9A1, TNF