

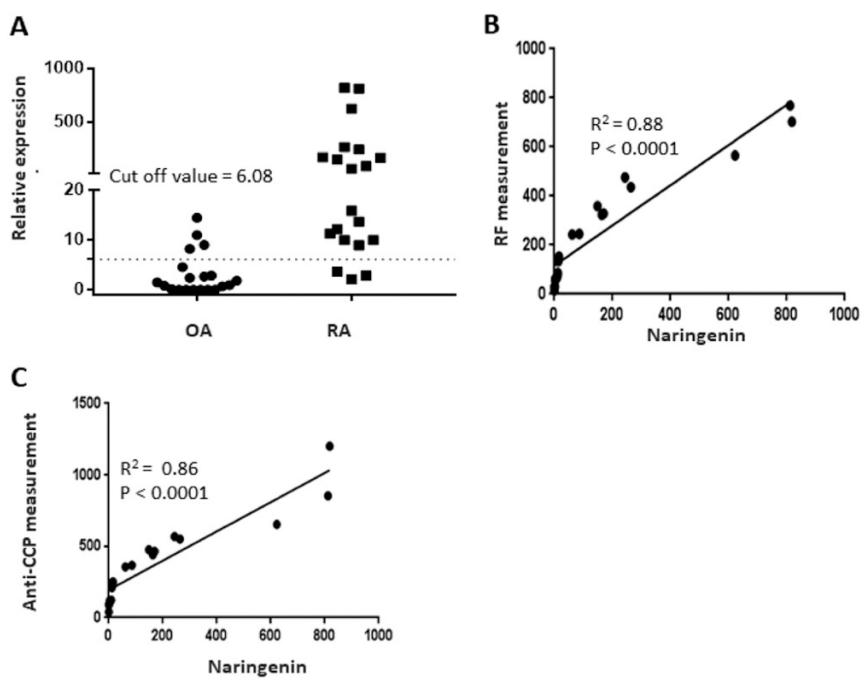
**Supplementary Table S1.** Clinical and biochemical parameter in OA and RA patients.

Parameters	OA patients	RA patients	<i>p</i> -value
Number (n)	20	20	
Female/male	13 / 7	16 / 4	0.30
Age (years)	67 ± 8	57 ± 15	0.01
BMI (kg/m <sup>2</sup> )	26 ± 4	22 ± 4	0.0015
Duration of disease (years)	5 ± 3	6 ± 4	0.33
Laboratory findings			
ESR (mm/h)	31 ± 35	65 ± 35	0.004
CRP (mg/L)	15 ± 34	48 ± 40	0.008
Rheumatoid factor (IU)	4 ± 5	258 ± 231	<0.0001
Anti-CCP antibody (U)	2 ± 2	381 ± 292	<0.0001
SF WBC (count/mm <sup>3</sup> )	98 ± 36	15000 ± 12000	<0.0001
DAS28	5 ± 1		
Kellgren-Lawrence grading scale	3 ± 0.5		
Treatment agents (n)			
DMARDs	0	20	
NSAID	20	11	
SYSADOAs	5	0	
Traditional Chinese medicine	2	3	

RA: rheumatoid arthritis; OA: osteoarthritis; BMI: body mass index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; anti-CCP: anticyclic citrullinated peptide; SF WBC: synovial fluid white blood cell; DAS28: Disease Activity Score 28; DMARDs: disease-modifying anti-rheumatic drugs; NSAIDs: non-steroidal anti-inflammatory drugs; SYSADOAs: symptomatic slow-acting drugs for osteoarthritis.

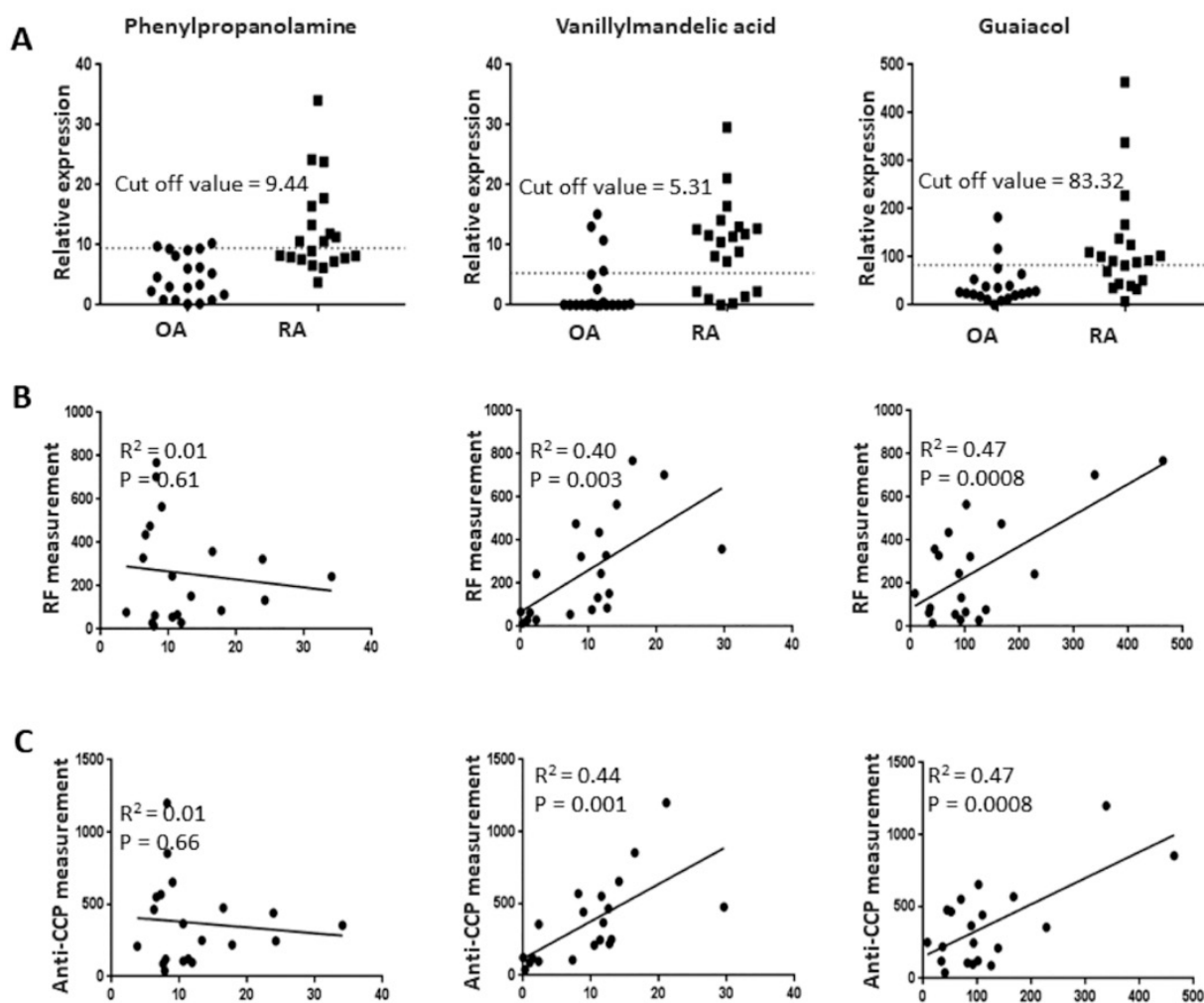
**Supplementary Table S2.** Differential metabolite in SF samples of OA and RA subjects.

Metabolites	OA	RA	<i>p</i> -value	FC	VIP
Phenylpropanolamine	4.72 ± 3.58	12.33 ± 7.54	0.0002	2.61	2.84335
Vanillylmandelic acid	2.65 ± 4.80	9.81 ± 7.53	0.0009	3.69	2.64042
L-Aspartyl-L-phenylalanine	8.51 ± 11.09	33.09 ± 31.89	0.0023	3.89	2.43553
Tauroursodeoxycholic acid	179.23 ± 192.17	514.17 ± 428.83	0.0028	2.87	2.36018
Quinolinic acid	41.35 ± 27.29	105.71 ± 87.43	0.0032	2.56	2.376
Guaiacol	41.66 ± 42.67	120.45 ± 110.36	0.0050	2.89	2.21216
Naringenin	3.04 ± 4.23	172.91 ± 265.20	0.0067	56.83	2.09422
Cytosine	20.37 ± 30.41	48.56 ± 35.82	0.0107	2.38	2.00985
1-Methylhistidine	7.41 ± 8.77	42.45 ± 61.15	0.0154	5.72	1.96858
Palmitoleic acid	229.64 ± 212.52	109.47 ± 45.26	0.0179	0.48	1.91649
L-3-Phenyllactic acid	36.92 ± 49.31	9.76 ± 7.26	0.0196	0.26	1.90933
Paraxanthine	17.48 ± 18.38	76.41 ± 112.67	0.0265	4.37	1.89929
Linoleic acid	2334.69 ± 2246.7	1119.13 ± 918.34	0.0310	0.48	1.79213
Deoxyuridine	0.087 ± 0.13	2.46 ± 4.83	0.0341	28.11	1.77119
L-Fucose	3.47 ± 5.62	9.11 ± 10.03	0.0346	2.62	1.67672
Inosine	346.24 ± 238.37	703.38 ± 696.73	0.0364	2.03	1.7013
Guanosine	48.63 ± 57.90	148.13 ± 197.69	0.0371	3.05	1.71261
N-Acetyl-L-aspartic acid	35.34 ± 51.70	9.11 ± 16.82	0.0373	0.26	1.71817
α-N-Phenylacetyl-L-glutamine	336.41 ± 426.10	666.38 ± 567.44	0.0443	1.98	1.68087
Methionine sulfoxide	6.85 ± 9.25	19.79 ± 26.48	0.0459	2.89	1.6623
Guanosine monophosphate	2.58 ± 4.82	80.13 ± 169.15	0.0473	31.05	1.66561
Glutaric acid	0.84 ± 2.50	3.72 ± 5.80	0.0492	4.38	1.6087



**Supplementary Fig. S1.** Correlation of naringenin with serum RF or anti-CCP levels.

**A:** Naringenin level in RA SF.  
**B:** Association analysis of naringenin with the serum RF level in RA.  
**C:** Association analysis of naringenin with the serum anti-CCP level in RA.  
 RA: rheumatoid arthritis; OA: osteoarthritis; SF: synovial fluid; cut-off value = 2 \* (candidate mean value in SF of OA patients); RF: rheumatoid factor; anti-CCP: anti-cyclic citrullinated peptide.



**Supplementary Fig. S2.** Correlation of phenylpropanolamine, vanillylmandelic acid and guaiacol levels with RF or anti-CCP levels.

**A:** Phenylpropanolamine, vanillylmandelic acid and guaiacol level in RA SF. **B:** Association analysis of phenylpropanolamine, vanillylmandelic acid and guaiacol levels with the serum RF level in RA. **C:** Association analysis of PPA, VMA and guaiacol levels with the serum anti-CCP level in RA.  
 RA: rheumatoid arthritis; OA: osteoarthritis; SF: synovial fluid; cut-off value = 2 \* (candidate mean value in SF of OA patients); RF: rheumatoid factor; anti-CCP: anti-cyclic citrullinated peptide.