Electronic Supplementary Material (ESI) for Nanoscale.

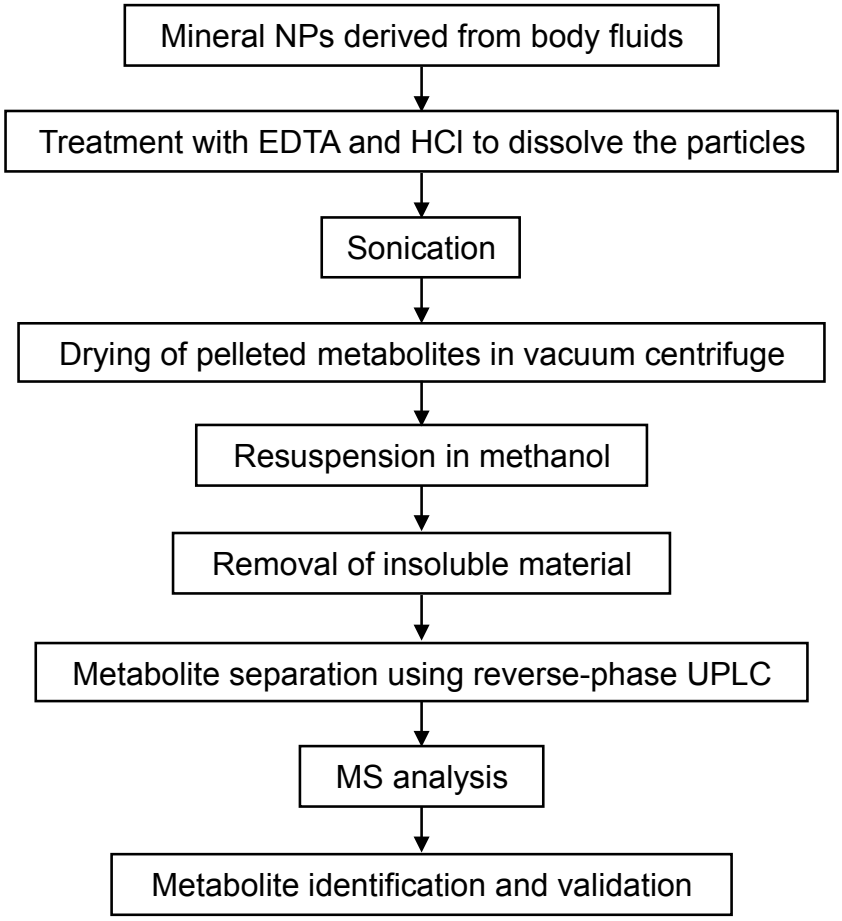

Fig. S1 Strategy used to determine the metabolite composition of mineral-organic NPs and granules. Washed mineralo-organic NPs were treated with 50 mM EDTA and 0.1 M HCl to dissolve the particles and release metabolites. The metabolites were separated on a reverse-phase LC column and submitted to LC-MS analysis as described in Experimental procedure.

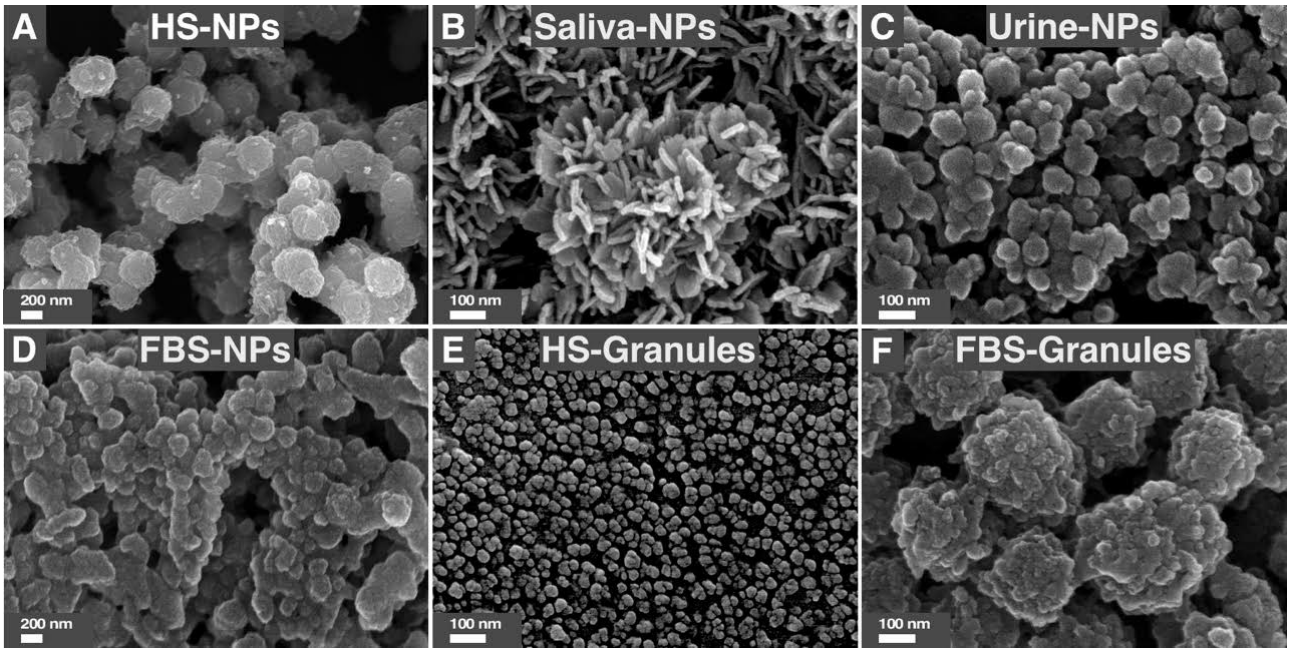

Fig. S2 Scanning electron microscopy (SEM) images of particles used in the present study. Samples were prepared for SEM observation as described in Experimental procedure. All particles show a round morphology, except for saliva-NPs which have a bacillus-like shape (B). Particle sizes are as follows: (A) 100±300 nm; (C) 50±200 nm; (D) 100±200 nm; (E) 20±50 nm; (F) 20±300 nm. Bacillus-like particles in (B) were 100±50 nm long and 20±20 nm large.

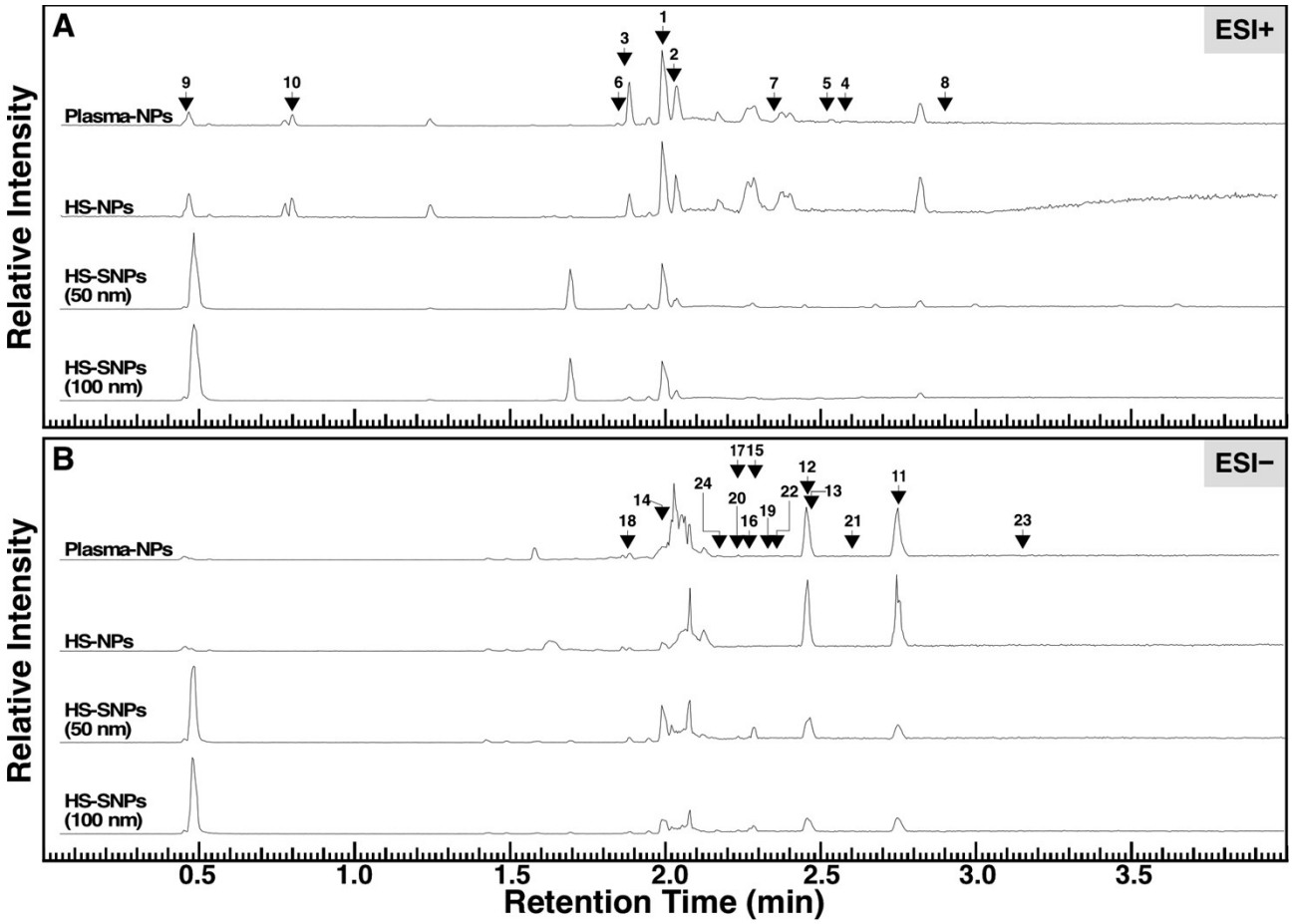

Fig. S3 LC/MS chromatograms of biological and synthetic NPs prepared in human body fluids. Calcium phosphate NPs ("Plasma-NPs" and "HS-NPs") were prepared by adding $CaCl_2$ and NaH_2PO_4 at 3 mM each in DMEM containing human plasma or human serum (HS), prior to incubation overnight and preparation for LC/MS analysis. Commercial synthetic NPs (SNPs) with a diameter of 50 or 100 nm were incubated into HS and prepared for LC/MS analysis as described in Experimental procedure. Samples were analyzed in (A) ESI^+ and (B) ESI^- modes. Peak numbers correspond to the compounds listed in Supplementary Tables S1 and S2.

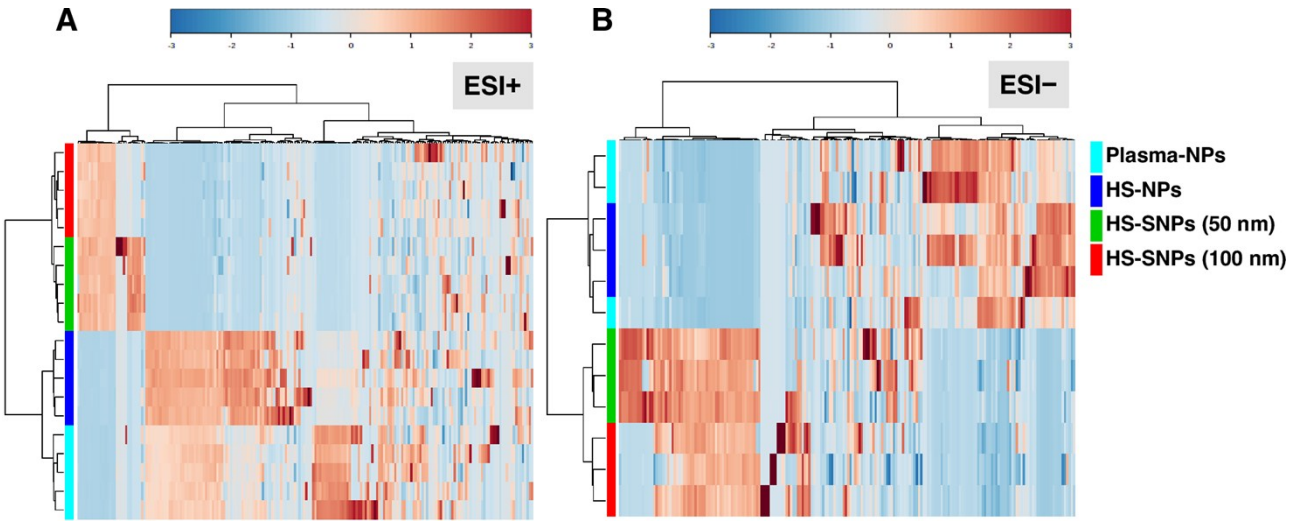

Fig. S4 Heat map diagrams of metabolites identified in the organic corona of biological and synthetic NPs. Calcium phosphate NPs ("Plasma-NPs" and "HS-NPs") were prepared and processed as described in Supplementary Fig. S3 and Experimental procedure. Synthetic NPs (SNPs) of 50 or 100 nm were incubated into HS and prepared for LC/MS analysis as described in Experimental procedure. Particle specimens were analyzed in (A) ESI^+ and (B) ESI^- modes. For each sample, 3–5 specimens were prepared and analyzed in the same manner. The diagrams illustrate the color-based intensity (legend on top) for the various metabolite candidates (dendrogram on top) and their grouping based on the specimens analyzed (dendrogram on the left).

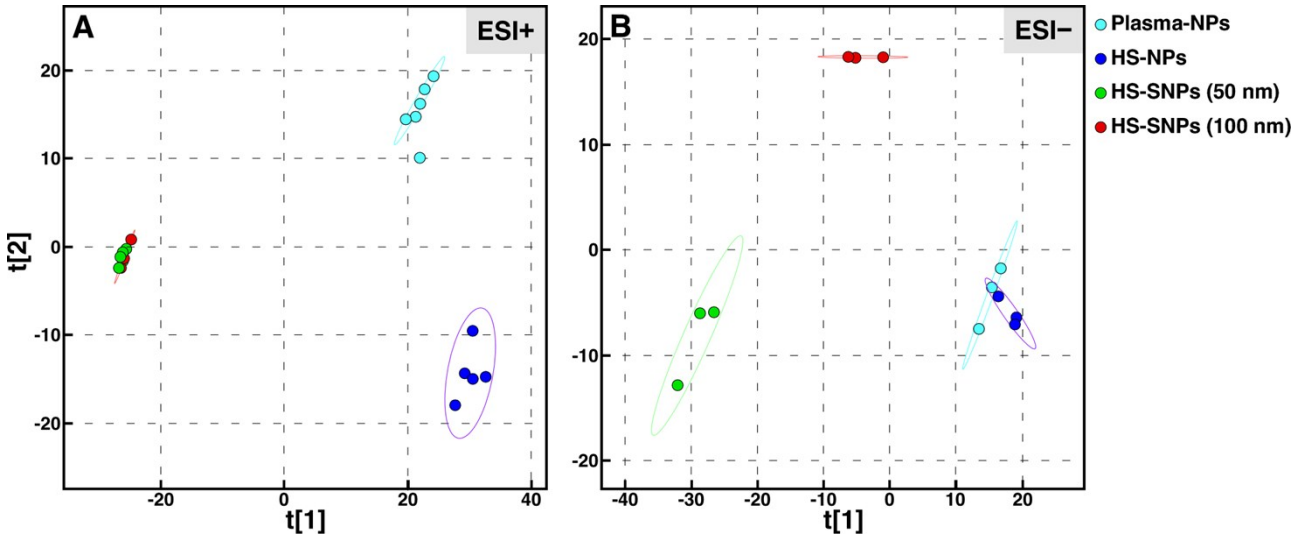

Fig. S5 PCA analysis of biological and synthetic NPs prepared in human body fluids. Calcium phosphate NPs ("Plasma-NPs" and "HS-NPs") were prepared and processed as described in Supplementary Fig. S3 (see also Experimental procedure). Synthetic NPs (SNPs) of 50 or 100 nm were incubated into HS and prepared for LC/MS analysis as described in Experimental procedure. Samples were analyzed in (A) ESI^+ and (B) ESI^- modes. The diagrams illustrate the level of similarity between the metabolite candidates identified in the samples (represented by circles).

Table S2 List of validated organic compounds identified in mineralo-organic particles and synthetic nanoparticles in the ESI^+ mode

#	Compound	ID Number	Formula	RT	*m/z*	Plasma-NPs	HS-NPs	50-nm SNPs	100-nm SNPs
1	Lyso-PC (16:0)	HMDB10382	$C_{24}H_{50}NO_7P$	1.99	496.3409	94.3	91.2	75.4	75.3
2	Lyso-PC (18:1)	HMDB02815	$C_{26}H_{52}NO_7P$	2.03	522.3556	25.2	31.0	46.7	45.8
3	Lyso-PC (20:4)	HMDB10395	$C_{28}H_{50}NO_7P$	1.87	544.3392	3.2	1.6	2.4	1.5
4	MG (18:0)	HMDB11535	$C_{21}H_{42}O_4$	2.58	359.3133	0.2	0.3	0.6	1.9
5	Stearamide	HMDB34146	$C_{18}H_{37}NO$	2.52	284.2955	2.0	0.7	–	–
6	Lyso-PC (22:6)	HMDB10404	$C_{30}H_{50}NO_7P$	1.85	568.3407	0.7	0.4	0.8	0.3
7	MG (16:0)	HMDB11564	$C_{19}H_{38}O_4$	2.35	331.2856	0.2	0.3	0.1	1.1
8	MG (18:2)	HMDB11538	$C_{21}H_{38}O_4$	2.58	355.0718	–	0.5	–	–
9	Glucose	HMDB06564	$C_6H_{11}O_6Na$	0.46	203.0525	0.3	0.1	–	–
10	Niacinamide	HMDB01406	$C_6H_6N_2O$	0.80	123.0550	–	–	–	–

Metabolites were validated by comparing the LC-MS spectrum of the candidate metabolite with the spectrum of the corresponding pure standard and website database. Alternatively, the metabolites were validated by LC-MS analysis. The compound numbers given in the left column correspond to the peaks numbered in Fig. S3. The numbers given within parentheses in the "Compound" column correspond respectively to the number of carbons and double bonds found in the fatty acid molecule. Ion intensity for each compound was normalized by multiplying the ion intensity of each entry by the average of total ion intensities for the six samples shown, and then dividing by the sum of ion intensities for the corresponding sample. The compounds were ranked based on the sum of ion intensity of each compound. ESI, electrospray ionization; HMDB, Human Metabolome Database; ID, identification; MG, monoacylglycerol; NPs, nanoparticles; PC, phosphatidylcholine; RT, retention time (min), SNPs, synthetic nanoparticles.

Table S3 List of validated organic compounds identified in mineralo-organic particles and synthetic nanoparticles in the ESI^- mode

#	Compound	ID Number	Formula	RT	*m/z*	Plasma-NPs	HS-NPs	50-nm SNPs	100-nm SNPs
11	Stearic acid (C18:0)	HMDB00827	$C_{18}H_{36}O_2$	2.75	283.2629	46.4	35.5	74.4	56.2
12	Palmitic acid (C16:0)	HMDB00220	$C_{16}H_{32}O_2$	2.46	255.2310	34.0	33.9	61.2	78.3
13	Oleic acid (C18:1)	HMDB00207	$C_{18}H_{34}O_2$	2.47	281.2459	34.0	41.5	23.0	27.4
14	Lyso-PC (16:0)	HMDB10382	$C_{24}H_{50}NO_7P$	1.99	480.3090	21.1	23.1	7.2	5.7
15	Linolenic acid (C18:3)	HMDB00673	$C_{18}H_{32}O_2$	2.29	279.2304	15.8	20.7	5.4	5.6
16	Palmitoleic acid (C16:1)	HMDB03229	$C_{16}H_{30}O_2$	2.27	253.2148	12.3	10.4	4.5	4.6
17	Myristic acid (C14:0)	HMDB00806	$C_{14}H_{28}O_2$	2.23	227.2000	7.7	7.7	5.4	6.0
18	Lyso-PC (18:2)	HMDB10386	$C_{27}H_{48}N_7O_4P$	1.88	564.3318	4.9	5.6	7.1	3.6
19	Pentadecanoic acid (C15:0)	HMDB00826	$C_{15}H_{30}O_2$	2.33	241.2153	6.3	5.7	3.2	3.6
20	Arachidonic acid (C20:4)	HMDB01043	$C_{20}H_{32}O_2$	2.23	303.2317	4.6	5.8	0.8	0.9
21	Margaric acid (C17:0)	HMDB02259	$C_{17}H_{34}O_2$	2.60	269.2478	3.8	3.3	2.3	2.2
22	9-Heptadecenoic acid (C17:0)	HMDB31046	$C_{17}H_{32}O_2$	2.36	267.2328	3.7	1.7	0.4	1.0
23	Arachidic acid (C20:0)	HMDB02212	$C_{20}H_{40}O_2$	3.15	311.2960	1.2	0.5	1.7	1.5
24	DHA (C22:6)	HMDB02183	$C_{22}H_{32}O_2$	2.18	327.2342	1.3	1.7	0.5	0.6

Metabolites were validated by comparing the LC-MS spectrum of the candidate metabolite with the spectrum of the corresponding pure standard and website database. Alternatively, the metabolites were validated by LC-MS analysis. The compound numbers given in the left column correspond to the peaks numbered in Fig. S3. The numbers given within parentheses in the "Compound" column correspond respectively to the number of carbons and double bonds found in the fatty acid molecule. Ion intensity for each compound was normalized by multiplying the ion intensity of each entry by the average of total ion intensities for the six samples shown, and then dividing by the sum of ion intensities for the corresponding sample. The compounds were ranked based on the sum of ion intensity of each compound. DHA, docosahexaenoic acid; ESI, electrospray ionization; HMDB, Human Metabolome Database; ID, identification; NPs, nanoparticles; PC, phosphatidylcholine; RT, retention time (min), SNPs, synthetic nanoparticles.