

Table S 1. tsRNA sequences screened by tRF sequencing from PRJNA415953 EVs

Name	Abbreviation	Sequence (5'to3')	Base number
tRNA-Gly-GCC-5p-tRF-921	EVs tsRNA1	GCATTGGTGGTTCAGTGGTAGAATTCTC	28
tRNA-Asp-GTC-3p-tR-half-547	EVs tsRNA2	GGAGACCGGGGTTTCGATTCCCCGACGGGGAG CCA	34
tRNA-Gly-GCC-5p-tR-half-368	EVs tsRNA3	GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTG C	34

Table S 2. List of primer sequences of the tsRNAs for real-time polymerase chain reaction (RT-qPCR).

Name	Primer sequence (5'to3')
tRNA-Gly-GCC-5p-tRF-921	F-GCATTGGTGGTTCAGTGGTAGA R-ACTGCAGGGTCCGAGGTATT RT-GTCGTATCGACTGCAGGGTCCGAGGTATTCGCAGTCGATACGACGCAGTCGATACGACGAGAAT
tRNA-Gly-GCC-5p-tR-half-368	F-TGGTGGTTCAGTGGTAGAATTCTC R-AGTGCAGGGTCCGAGGTATT RT-GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACGCAGGC
hsa-miR-16-5p	F-AGGGTAGCAGCACGTAAATA R-AACAACCAACACAACCCAAC

RT-GAACAACCAACACAACCCAACATTGGTTGTTCCGCCAA

DNMT1	F-CCTAGCCCCAGGATTACAAGG
	R-ACTCATCCGATTTGGCTCTTTC
TET1	F-CAGAACCTAAACCACCCGTG
	R-TGCTTCGTAGCGCCATTGTAA
GAPDH	F-AACTTTGGTATCGTGGAAGG
	R-GCCAGTAGAGGCAGGGATGA

Table S 3. Performance of tsRNA-based biomarker panels for PTL prediction

Biomarker(s)	AUC (95% CI)
tsRNA1+ tsRNA3	0.61 (0.46-0.76)
Exposure to smoke	0.42 (0.27-0.58)
tsRNA1+ tsRNA3+ Exposure to smoke	0.65 (0.47-0.83)
Area of house	0.63 (0.51-0.76)
tsRNA1+ tsRNA3+ Area of house	0.72 (0.58-0.85)
Early pregnancy nocturia	0.66 (0.48-0.84)
tsRNA1+ tsRNA3+ Early pregnancy nocturia	0.60 (0.38-0.83)
All combined*	0.83 (0.68-0.99)

*Combined model: tsRNA1 + tsRNA3 + Exposure to smoke + Area of house + Early pregnancy nocturia.

Note: These analyses are exploratory and require validation in larger cohorts.

Supplementary Data 1: Differentially Expressed tsRNAs in Plasma Exosomes, Exosome-Depleted Plasma, Whole Blood, and PBMCs

PRJNA415953_exosome

gene	mean.t/mean.n	pvalue	Up/Down
tRNA-Gly-GCC-5p-tRF-17	2.621862222	0.012837524	up
tRNA-Thr-CGT-3p-CCA-tRF-29	2.361772895	0.033596435	up
tRNA-Gly-GCC-misc-tRF-1281	2.114896236	0.047307182	up
tRNA-Gly-GCC-misc-tRF-1331	2.145330933	0.028065072	up
tRNA-Gly-GCC-misc-tRF-1313	3.224531826	0.005236508	up
tRNA-Gly-GCC-misc-tRF-1319	4.74730169	0.001859853	up
tRNA-Phe-GAA-3p-CCA-tRF-35	2.279255278	0.000275009	up
tRNA-Asp-GTC-3p-CCA-tRF-63	2.154622734	0.010417362	up
tRNA-Asp-GTC-misc-tRF-764	4.678034663	0.009472847	up

tRNA-Asp-GTC-3p-CCA-tRF-100	2.210976431	0.012561139	up
tRNA-Glu-TTC-3p-CCA-tRF-231	2.468217898	0.006634233	up
tRNA-Gly-GCC-misc-tRF-1812	4.732651495	0.001040497	up
tRNA-Gly-GCC-5p-tRF-72	2.178308841	0.033596435	up
tRNA-Asp-GTC-3p-tR-half-321	0.457857735	0.039975504	down
tRNA-Asp-GTC-3p-tR-half-322	2.330701204	0.006634233	up
tRNA-Gly-GCC-5p-tRF-404	2.487536361	0.019230769	up
tRNA-Gly-GCC-5p-tRF-408	2.041636409	0.039975504	up
tRNA-Gly-GCC-5p-tR-half-131	2.657024261	0.012837524	up
tRNA-Gly-GCC-5p-tR-half-134	4.082629144	0.008329648	up
tRNA-Gly-GCC-5p-tRF-489	2.438994171	0.047307182	up
tRNA-Gly-GCC-5p-tRF-490	2.387718373	0.019230769	up
tRNA-Gly-GCC-5p-tRF-834	2.111077774	0.047307182	up
tRNA-Gly-GCC-5p-tRF-835	2.128999984	0.039975504	up
tRNA-Gly-GCC-5p-tRF-877	2.31111179	0.033596435	up
tRNA-Gly-GCC-5p-tRF-903	2.210494366	0.023307704	up
tRNA-Gly-GCC-5p-tRF-908	2.0663671	0.019230769	up
tRNA-Gly-GCC-5p-tRF-918	2.637504059	0.001040497	up
tRNA-Gly-GCC-5p-tRF-921	2.226079025	0.028065072	up
tRNA-Gly-GCC-5p-tRF-924	2.502293515	0.008329648	up
tRNA-Gly-GCC-5p-tR-half-348	2.112162502	0.023307704	up
tRNA-Gly-GCC-5p-tR-half-353	3.370149877	0.015769061	up
tRNA-Gly-GCC-5p-tR-half-360	4.022701139	0.006634233	up
tRNA-Gly-GCC-5p-tR-half-367	4.303746929	0.001859853	up
tRNA-Gly-GCC-5p-tRF-1168	2.216590293	0.028065072	up
tRNA-Gly-GCC-5p-tR-half-471	3.712479854	0.005236508	up
tRNA-Gly-GCC-5p-tR-half-472	4.17961071	0.019230769	up
tRNA-Gly-GCC-misc-tRF-2111	3.79148224	0.028065072	up
tRNA-Lys-CTT-5p-tR-half-72	2.702633208	0.003181029	up
tRNA-Gly-CCC-5p-tR-half-158	2.686318418	0.001859853	up
tRNA-Gly-CCC-5p-tR-half-164	3.229962815	0.010382291	up
tRNA-Gly-TCC-5p-tRF-362	2.844191665	0.000765488	up
tRNA-Asp-GTC-3p-tR-half-545	0.38340373	0.019230769	down
tRNA-Asp-GTC-3p-tR-half-546	2.161907237	0.010222922	up
tRNA-Glu-CTC-misc-tRF-1174	2.137491452	0.015769061	up
tRNA-Glu-CTC-misc-tRF-1427	2.414439504	0.008329648	up
tRNA-Val-AAC-5p-tR-half-58	2.874233979	0.023307704	up
tRNA-Cys-GCA-3p-CCA-tRF-196	2.191321801	0.010382291	up
tRNA-Glu-TTC-5p-tRF-262	2.015449502	0.010382291	up
tRNA-Glu-CTC-5p-tRF-334	2.284719919	0.015769061	up

tRNA-Glu-CTC-5p-tR-half-239	3.422127292	0.008329648	up
tRNA-Glu-CTC-5p-tR-half-245	3.045597888	0.006634233	up
tRNA-Glu-CTC-5p-tR-half-249	2.823858831	0.001859853	up
tRNA-Val-AAC-3p-CCA-tRF-267	2.071906189	0.003181029	up
tRNA-Leu-CAA-3p-CCA-tRF-66	2.636672184	0.001040497	up
tRNA-Gly-TCC-3p-CCA-tRF-172	2.472525939	0.028065072	up
tRNA-Gly-GCC-3p-tRF-253	2.140689406	0.012837524	up
tRNA-Gly-GCC-3p-CCA-tRF-264	3.143227859	0.012837524	up
tRNA-Gly-GCC-3p-CCA-tRF-278	2.719806809	0.033596435	up
tRNA-Arg-TCG-3p-CCA-tRF-385	2.100615704	0.004102451	up
tRNA-Gly-GCC-3p-CCA-tRF-302	4.030159096	0.000189955	up
tRNA-Thr-CGT-3p-CCA-tRF-216	4.064815801	0.001859853	up
tRNA-Gly-TCC-3p-CCA-tRF-199	2.480110397	0.003181029	up
tRNA-Gly-GCC-3p-tRF-315	2.768494715	0.008329648	up
tRNA-Gly-GCC-3p-tRF-316	2.875183487	0.001040497	up
tRNA-Gly-GCC-3p-tRF-317	3.498649338	0.006634233	up
tRNA-Gly-GCC-3p-CCA-tRF-304	3.482653181	0.002446728	up
tRNA-Gly-GCC-3p-CCA-tRF-305	2.755521984	0.00140056	up
tRNA-Gly-CCC-3p-tRF-247	2.167035862	0.000394085	up
tRNA-Gly-CCC-3p-tRF-249	3.131179865	0.002446728	up
tRNA-Gly-CCC-3p-CCA-tRF-255	2.655616621	0.005236508	up
tRNA-Gly-GCC-misc-tRF-3537	3.935277124	0.006634233	up
tRNA-Gly-GCC-misc-tRF-3625	3.11992763	0.003181029	up
tRNA-Gly-GCC-misc-tRF-3856	2.667586945	0.002446728	up
tRNA-Glu-CTC-misc-tRF-2172	2.367735743	0.047307182	up
tRNA-Gly-GCC-misc-tRF-4383	2.088385924	0.041731251	up
tRNA-Arg-ACG-3p-CCA-tRF-93	2.056623963	0.008329648	up
tRNA-Pro-TGG-misc-tRF-1564	2.353572645	0.033596435	up
tRNA-Gly-GCC-misc-tRF-4608	2.245303641	0.041558127	up
tRNA-Gly-CCC-3p-CCA-tRF-319	2.228167768	0.047307182	up

PRJNA415953.exosome_depleted

gene	mean.t/mean.n	pvalue	Up/Down
tRNA-Met-CAT-misc-tRF-91	3.037517922	0.001859853	up
tRNA-Ala-CGC-misc-tRF-46	2.517233157	0.039975504	up
tRNA-Cys-GCA-3p-tRF-40	0.422870115	0.00140056	down
tRNA-Pro-TGG-misc-tRF-183	0.372616471	0.012837524	down
tRNA-Ile-AAT-misc-tRF-305	3.58081616	0.001040497	up
tRNA-Cys-GCA-misc-tRF-862	3.442064082	0.003181029	up
tRNA-Gly-GCC-5p-tRF-538	3.184976867	0.000189955	up
tRNA-Gly-GCC-5p-tRF-544	3.602334043	0.000765488	up

tRNA-Ile-AAT-misc-tRF-384	2.729095257	0.005236508	up
tRNA-Ala-CGC-5p-tRF-205	0.447332014	0.019230769	down
tRNA-Leu-CAG-5p-tRF-150	2.439093133	0.028065072	up
tRNA-Glu-CTC-5p-tRF-167	2.190198341	0.028065072	up
tRNA-Ile-AAT-misc-tRF-691	2.622589253	0.012837524	up
tRNA-Pro-TGG-misc-tRF-1269	2.421156502	0.006634233	up
tRNA-Pro-TGG-misc-tRF-1320	2.701923212	0.033596435	up

PRJNA415953.plasma

gene	mean.t/mean.n	pvalue	Up/Down
tRNA-Thr-CGT-3p-CCA-tRF-34	2.097955995	0.001784167	up
tRNA-Val-AAC-3p-CCA-tRF-125	2.242313679	0.00055169	up
tRNA-Lys-CTT-misc-tRF-296	5.085866532	2.73E-07	up
tRNA-Lys-CTT-misc-tRF-274	4.912500667	1.82E-08	up
tRNA-Trp-CCA-3p-CCA-tRF-62	2.701739846	3.98E-05	up
tRNA-Cys-GCA-3p-CCA-tRF-87	4.732885578	8.32E-07	up
tRNA-Glu-TTC-3p-CCA-tRF-92	2.152723319	0.000291905	up
tRNA-Asn-GTT-3p-CCA-tRF-64	2.738892745	2.43E-05	up
tRNA-Gly-CCC-3p-CCA-tRF-65	2.063484962	0.002289289	up
tRNA-Cys-GCA-3p-CCA-tRF-144	2.990942347	1.25E-05	up
tRNA-Glu-TTC-3p-CCA-tRF-503	2.091249844	1.16E-05	up
tRNA-Gly-GCC-misc-tRF-2242	2.113019882	0.044072319	up
tRNA-Ala-TGC-5p-tRF-7	2.803316671	0.000534774	up
tRNA-Leu-AAG-5p-tRF-163	2.019892043	0.000769617	up
tRNA-Cys-GCA-3p-CCA-tRF-218	2.136708793	0.000139967	up
tRNA-Arg-TCT-3p-CCA-tRF-252	2.462576853	0.008275702	up
tRNA-Gly-CCC-3p-CCA-tRF-210	2.088938486	0.000617114	up
tRNA-Cys-GCA-3p-CCA-tRF-237	4.409387186	2.73E-07	up
tRNA-Arg-TCG-3p-CCA-tRF-397	3.192231971	0.000652411	up
tRNA-Gly-GCC-3p-CCA-tRF-320	2.564228109	3.29E-06	up
tRNA-Gly-CCC-3p-CCA-tRF-250	2.196929965	2.26E-05	up
tRNA-Arg-TCT-3p-CCA-tRF-287	2.138704117	0.000309741	up
tRNA-Gly-GCC-3p-CCA-tRF-355	2.470976001	0.00055169	up
tRNA-Gly-CCC-3p-CCA-tRF-270	2.307106671	5.79E-06	up
tRNA-Gly-TCC-3p-CCA-tRF-245	2.114178876	4.90E-05	up
tRNA-Gly-GCC-3p-tRF-403	2.248577942	0.001121015	up
tRNA-Gly-GCC-3p-tRF-404	2.360516755	0.00124522	up
tRNA-Gly-GCC-3p-CCA-tRF-357	2.709588123	7.33E-05	up
tRNA-Gly-GCC-3p-CCA-tRF-358	2.117598566	3.46E-05	up
tRNA-Gly-CCC-3p-tRF-305	2.125977282	6.42E-05	up
tRNA-Gly-CCC-3p-CCA-tRF-272	2.163810118	7.83E-05	up

tRNA-Glu-TTC-3p-CCA-tRF-1169	2.101750402	0.000115669	up
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PRJNA428989.plasma

gene	mean.t/mean.n	pvalue	Up/Down
tRNA-Gly-GCC-5p-tRF-202	3.373171027	0.002075073	up
tRNA-Gly-GCC-5p-tR-half-946	2.081650908	5.57E-06	up
tRNA-Val-CAC-5p-tRF-140	2.287840116	0.040932249	up
tRNA-Val-AAC-5p-tR-half-149	2.282365693	0.005323054	up
tRNA-Glu-TTC-5p-tRF-173	3.039523818	1.36E-05	up
tRNA-Glu-TTC-5p-tR-half-235	3.563384758	7.74E-05	up
tRNA-Glu-TTC-5p-tR-half-244	4.662618829	6.49E-06	up
tRNA-Glu-TTC-5p-tR-half-265	3.116290711	8.78E-06	up
tRNA-Glu-TTC-5p-tR-half-607	4.012713403	8.78E-06	up
tRNA-Glu-CTC-5p-tR-half-469	2.196055044	0.000349224	up
tRNA-Tyr-GTA-3p-CCA-tRF-252	3.234993168	0.002957861	up
tRNA-Leu-CAG-misc-tRF-892	2.711820931	0.034049133	up

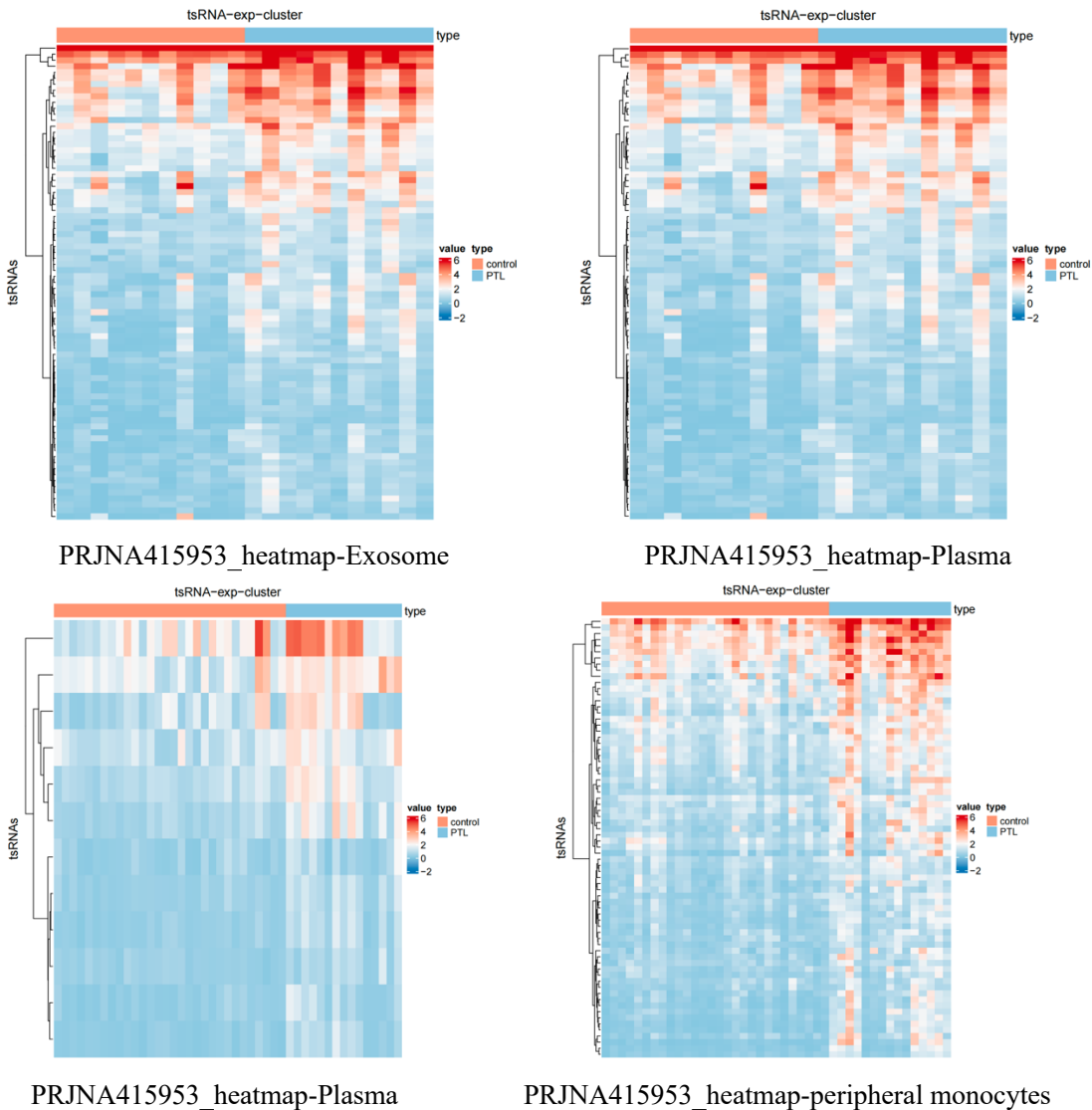
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gene	mean.t/mean.n	pvalue	Up/Down
tRNA-Val-AAC-3p-CCA-tRF-38	2.261032696	1.68E-06	up
tRNA-Val-AAC-3p-tRF-55	2.251565536	0.000246929	up
tRNA-Val-AAC-3p-tRF-117	2.932400855	0.001041961	up
tRNA-Val-AAC-3p-CCA-tRF-82	4.778261158	1.19E-07	up
tRNA-Val-AAC-3p-tRF-125	7.68099641	4.68E-05	up
tRNA-Lys-CTT-misc-tRF-276	2.614225412	3.54E-05	up
tRNA-Lys-CTT-misc-tRF-237	2.071796841	0.000440108	up
tRNA-Cys-GCA-3p-CCA-tRF-46	3.076633629	1.26E-05	up
tRNA-Asp-GTC-3p-tR-half-292	3.035562229	1.68E-06	up
tRNA-Gly-GCC-3p-CCA-tRF-34	2.198302375	0.000492189	up
tRNA-Gly-CCC-3p-CCA-tRF-27	2.070394451	1.98E-05	up
tRNA-Phe-GAA-3p-CCA-tRF-25	3.611737035	0.00010396	up
tRNA-Val-AAC-3p-CCA-tRF-129	3.717784651	2.41E-06	up
tRNA-Cys-GCA-3p-CCA-tRF-92	2.899757421	2.88E-06	up
tRNA-Arg-CCT-misc-tRF-543	2.033842887	0.000134048	up
tRNA-Gly-GCC-5p-tRF-663	2.092174033	0.000312338	up
tRNA-Gly-GCC-5p-tR-half-608	4.724195609	1.98E-05	up
tRNA-Gly-GCC-5p-tR-half-614	6.450694558	2.02E-06	up
tRNA-Gly-GCC-5p-tR-half-619	5.539200322	2.30E-05	up
tRNA-Gly-GCC-5p-tR-half-631	4.4715694	0.000277895	up
tRNA-Gly-GCC-5p-tR-half-632	3.403542957	1.47E-05	up
tRNA-Gly-GCC-5p-tR-half-644	3.715441227	0.00333251	up
tRNA-Gly-GCC-5p-tR-half-704	4.069164498	8.01E-05	up

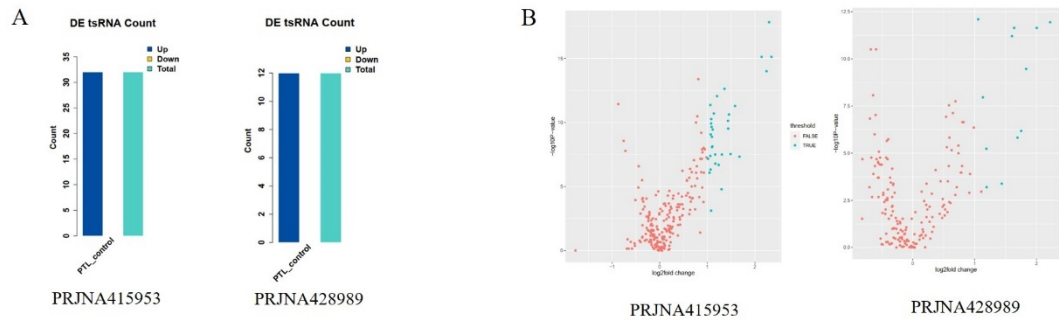
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tRNA-Ala-CGC-5p-tRF-204	2.134024166	0.004358395	up
tRNA-Ala-CGC-5p-tRF-515	2.340116712	8.01E-05	up
tRNA-Leu-CAG-5p-tRF-135	2.340635493	0.011758188	up
tRNA-Lys-CTT-misc-tRF-1818	2.067099721	0.000277895	up
tRNA-Glu-TTC-5p-tRF-206	3.019783644	0.001154576	up
tRNA-Glu-TTC-5p-tRF-212	2.071231741	0.014783716	up
tRNA-Glu-TTC-5p-tRF-216	2.710452176	0.013708494	up
tRNA-Glu-TTC-5p-tR-half-333	3.799187576	9.14E-05	up
tRNA-Glu-TTC-5p-tR-half-347	5.380632885	5.34E-07	up
tRNA-Glu-TTC-5p-tR-half-368	7.773194941	2.88E-06	up
tRNA-Glu-TTC-5p-tR-half-372	8.064202318	0.000194192	up
tRNA-Glu-TTC-5p-tR-half-379	3.858628198	0.001898079	up
tRNA-Glu-TTC-5p-tR-half-391	10.96103639	4.23E-06	up
tRNA-Glu-TTC-5p-tR-half-398	11.35296563	9.21E-06	up
tRNA-Gly-GCC-3p-CCA-tRF-168	2.522560723	0.000118136	up
tRNA-Gly-CCC-3p-CCA-tRF-129	2.824430836	6.51E-07	up
tRNA-Glu-CTC-5p-tR-half-510	3.205146779	0.000246929	up
tRNA-Glu-CTC-5p-tR-half-519	2.504206841	0.003041548	up
tRNA-Glu-CTC-5p-tR-half-543	2.325753402	0.007895426	up
tRNA-Glu-CTC-5p-tR-half-566	2.521609201	0.002773303	up
tRNA-Glu-CTC-5p-tR-half-571	2.10541839	0.007895426	up
tRNA-Glu-CTC-5p-tR-half-634	2.689476443	0.00010396	up
tRNA-Glu-CTC-5p-tR-half-665	3.005296426	0.000277895	up
tRNA-Cys-GCA-3p-tRF-165	3.617213807	5.34E-07	up
tRNA-Cys-GCA-3p-CCA-tRF-159	3.204314678	2.02E-06	up
tRNA-Cys-GCA-3p-tRF-171	4.917704133	0.00010396	up
tRNA-Cys-GCA-3p-tRF-172	6.859367007	5.36E-05	up
tRNA-Cys-GCA-3p-tRF-175	8.353846188	1.40E-06	up
tRNA-Leu-CAG-3p-CCA-tRF-106	2.54454544	0.001154576	up
tRNA-Gly-GCC-3p-CCA-tRF-214	2.600562479	0.003647817	up
tRNA-Lys-CTT-misc-tRF-2406	2.100175528	0.000549768	up
tRNA-Gly-TCC-3p-CCA-tRF-118	4.232732657	1.86E-07	up
tRNA-Gly-GCC-3p-tRF-211	5.999686936	1.16E-06	up
tRNA-Gly-GCC-3p-CCA-tRF-255	4.413544675	7.85E-06	up
tRNA-Gly-GCC-3p-CCA-tRF-256	4.464796023	1.47E-05	up
tRNA-Gly-CCC-3p-CCA-tRF-183	3.540653461	6.51E-07	up
tRNA-Tyr-GTA-3p-CCA-tRF-115	39.85105471	4.23E-06	up
tRNA-Glu-CTC-misc-tRF-4711	3.082889149	8.01E-05	up
tRNA-Glu-CTC-misc-tRF-4741	3.020441885	7.02E-05	up

tRNA-Glu-CTC-misc-tRF-4844	2.513413634	4.07E-05	up
tRNA-Glu-CTC-misc-tRF-4886	3.811933555	2.30E-05	up
tRNA-Gly-GCC-3p-CCA-tRF-279	2.008429478	0.000134048	up
tRNA-Gly-CCC-3p-CCA-tRF-207	2.596903917	1.16E-06	up
tRNA-Arg-CCT-misc-tRF-1306	2.931886133	2.66E-05	up
tRNA-Pro-TGG-misc-tRF-1301	11.00152065	0.003989176	up
tRNA-Pro-TGG-misc-tRF-1311	5.408707616	0.000350602	up
tRNA-Pro-TGG-misc-tRF-1320	4.714991275	0.000760764	up
tRNA-Pro-TGG-misc-tRF-1531	5.726927269	0.000312338	up

Supplementary Data 2: Clustering analysis

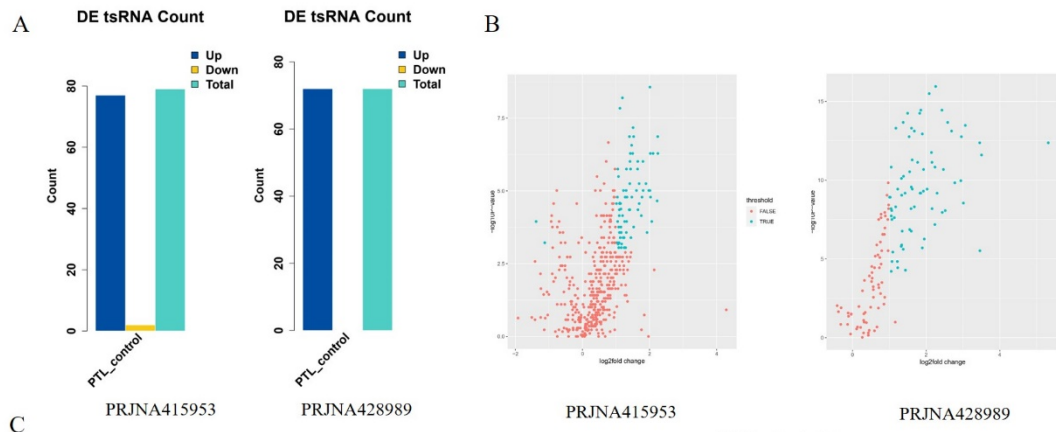


Detailed analyses of other samples from PRJNA415953 and PRJNA428989



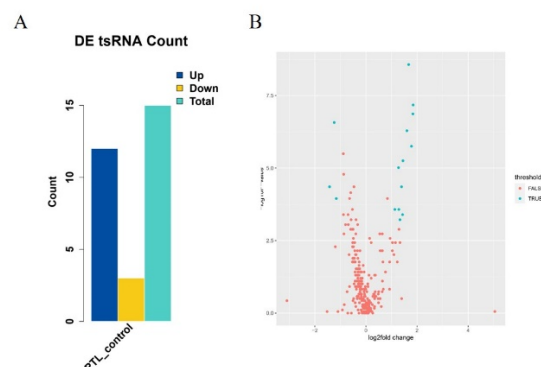
Differential expression of tRNA fragments and volcano plot between PRJNA415953 and PRJNA428989 in whole blood plasma

A. Number of differentially expressed tRNA fragments; B. Volcanic diagram of differentially expressed tRNA fragments



Differential expression of tRNA fragments and volcano plot between PRJNA415953 and PRJNA428989 in exosomes and peripheral monocytes

A. Number of differentially expressed tRNA fragments; B. Volcanic diagram of differentially expressed tRNA fragments



Differential expression of tRNA fragments, volcano plot, and cluster plot of PRJNA415953 in exocrine plasma

A. Number of differentially expressed tRNA fragments; B. Volcanic diagram of differentially expressed tRNA fragments

Supplementary Data 3: GO and KEGG enrichment analyses were performed on the predicted targets (results for datasets PRJNA415953 and PRJNA428989

PRJNA415953plasma

tRNA-Gly-CCC-3p-CCA-tRF-TCGATTCCCGGGCGGCGCACCA		
Name	p	q
Type II diabetes mellitus	0.00463097	0.829667149
Adipocytokine signaling pathway	0.006078148	0.829667149
Insulin signaling pathway	0.017800289	1
tRNA-Gly-GCC-misc-tRF-GCCACGCGGGAGGCC		
Name	p	q
RNA degradation	0.029575606	1
Folate biosynthesis	0.042142233	1
Synaptic vesicle cycle	0.013298775	1
Glutamatergic synapse	0.024628791	1
Adipocytokine signaling pathway	0.007792907	1

PRJNA415953 exosome

tRNA-Gly-GCC-5p-tRF-GCATTGGTGGTTCAGTGGTAGAATTC				
Description	Gene_DE	q_value	Rich_Ratio	Size
Allograft rejection	2	0.0187410 67	69.747474 75	3
Graft-versus-host disease	2	0.0187410 67	78.689458 69	3
Asthma	2	0.0187410 67	85.246913 58	3
Type I diabetes mellitus	2	0.0203758 5	43.841269 84	3
Intestinal immune network for IgA production	2	0.0203758 5	46.498316 5	3
Influenza A	3	0.0203758 5	14.994571 12	4
Autoimmune thyroid disease	2	0.0203758 5	49.498207 89	3
Inflammatory bowel disease (IBD)	2	0.0204618 48	40.918518 52	3
Staphylococcus aureus infection	2	0.0227988 1	36.534391 53	3
Leishmaniasis	2	0.0331949 1	28.681204 57	3

Rheumatoid arthritis	2	0.0404515 31	22.902155 89	3
Antigen processing and presentation	2	0.0404515 31	22.732510 29	3
Viral myocarditis	2	0.0404515 31	23.975694 44	3
tRNA-Gly-GCC-5p-tRF-GCATTGGTGGTTCAGTGGTAGAATTCT				
Description	Gene_DE	q_value	Rich_Ratio	Size
Allograft rejection	2	0.0399160 85	52.310606 06	3
Graft-versus-host disease	2	0.0399160 85	59.017094 02	3
Asthma	2	0.0399160 85	63.935185 19	3
Type I diabetes mellitus	2	0.0433862 38	32.880952 38	3
Autoimmune thyroid disease	2	0.0433862 38	37.123655 91	3
Inflammatory bowel disease (IBD)	2	0.0433862 38	30.688888 89	3
Influenza A	3	0.0433862 38	11.245928 34	4
Intestinal immune network for IgA production	2	0.0433862 38	34.873737 37	3
Staphylococcus aureus infection	2	0.0482785 59	27.400793 65	3
tRNA-Gly-GCC-5p-tRF-GCATTGGTGGTTCAGTGGTAGAATTCTC				
Description	Gene_DE	q_value	Rich_Ratio	Size
Antigen processing and presentation	3	0.0437302 32	21.920634 92	4
Asthma	2	0.0437302 32	54.801587 3	3
Graft-versus-host disease	2	0.0437302 32	50.586080 59	3
Allograft rejection	2	0.0437302 32	44.837662 34	3
tRNA-Asp-GTC-3p-tR-half-GGAGACCGGGTTCGATTCCCCGACGGGGAGCCA				

Description	Gene_DE	q_value	Rich_Ratio	Size
Calcium signaling pathway	4	0.0122992 62	14.805682 12	5
Neuroactive ligand-receptor interaction	4	0.0122992 62	12.954971 86	5
Dopaminergic synapse	3	0.0302112 58	17.705128 21	4
tRNA-Gly-GCC-5p-tR-half- GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTGC				
Description	Gene_DE	q_value	Rich_Ratio	Size
Antigen processing and presentation	6	0.0068908 04	9.8996415 77	4
tRNA-Gly-GCC-5p-tRF- GCATTGGTGGTTCAGTGGTAGAATTCTCG				
Description	Gene_DE	q_value	Rich_Ratio	Size
Antigen processing and presentation	4	0.0051267 06	21.536062 38	5

PRJNA415953 exosome_depleted

tRNA-Gly-GCC-5p-tRF- GCATTGGTGGTTCAGTGGTAGAATTC				
Description	Gene_DE	q_value	Rich_Ratio	Size
Allograft rejection	2	0.01874106 7	69.7474747 5	3
Graft-versus-host disease	2	0.01874106 7	78.6894586 9	3
Asthma	2	0.01874106 7	85.2469135 8	3
Autoimmune thyroid disease	2	0.02037585	49.4982078 9	3
Type I diabetes mellitus	2	0.02037585	43.8412698 4	3
Influenza A	3	0.02037585	14.9945711 2	4
Intestinal immune network for IgA production	2	0.02037585	46.4983165	3
Inflammatory bowel disease (IBD)	2	0.02046184 8	40.9185185 2	3
Staphylococcus aureus infection	2	0.0227988	36.5343915 3	3

Leishmaniasis	2	0.03319491	28.68120457	3
Viral myocarditis	2	0.040451531	23.97569444	3
Antigen processing and presentation	2	0.040451531	22.73251029	3
Rheumatoid arthritis	2	0.040451531	22.90215589	3
tRNA-Gly-GCC-5p-tRF-GCATTGGTGGTTCAGTGGTAGAATTCT				
Description	Gene_DE	q_value	Rich_Ratio	Size
Asthma	2	0.039916085	63.93518519	3
Graft-versus-host disease	2	0.039916085	59.01709402	3
Allograft rejection	2	0.039916085	52.31060606	3
Influenza A	3	0.043386238	11.24592834	4
Intestinal immune network for IgA production	2	0.043386238	34.87373737	3
Type I diabetes mellitus	2	0.043386238	32.88095238	3
Inflammatory bowel disease (IBD)	2	0.043386238	30.68888889	3
Autoimmune thyroid disease	2	0.043386238	37.12365591	3
Staphylococcus aureus infection	2	0.048278559	27.40079365	3

PRJNA428989 plasma

tRNA-Gly-GCC-5p-tRF-GCATGGGTGGTTCAGTGGTAGAATT		
Name	p	q
Influenza A	0.002865245	0.782211952
Primary bile acid biosynthesis	0.006929131	0.945826321
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0.041877463	1
Viral myocarditis	0.036540138	1
Bacterial invasion of epithelial cells	0.048308732	1
Phototransduction - fly	0.01668368	1
Hypertrophic cardiomyopathy (HCM)	0.039352028	1
Salmonella infection	0.049702538	1
Dilated cardiomyopathy	0.041597106	1

Adherens junction	0.039352028	1
Steroid hormone biosynthesis	0.030897842	1
Hippo signaling pathway - fly	0.038509108	1
Lysine degradation	0.028633998	1
tRNA-Gly-GCC-5p-tR-half-GCATTGGTGGTTCAGTGGTAGAATTCTCGT		
Name	p	q
Antigen processing and presentation	5.56E-05	0.015170744
Graft-versus-host disease	0.001729743	0.149991368
Allograft rejection	0.002197676	0.149991368
Asthma	0.001474887	0.149991368
Type I diabetes mellitus	0.005471785	0.213399627
Autoimmune thyroid disease	0.004317607	0.213399627
Intestinal immune network for IgA production	0.004878753	0.213399627
Inflammatory bowel disease (IBD)	0.006257323	0.213531154
Staphylococcus aureus infection	0.007792907	0.236384833
NOD-like receptor signaling pathway	0.009093022	0.248239504
Influenza A	0.012226578	0.282118607
Leishmaniasis	0.012400818	0.282118607
Viral myocarditis	0.017419673	0.345589912
Rheumatoid arthritis	0.018988457	0.345589912
Prostate cancer	0.018988457	0.345589912
Estrogen signaling pathway	0.028619738	0.469809787
Progesterone-mediated oocyte maturation	0.029255554	0.469809787
Cell adhesion molecules (CAMs)	0.032519478	0.493212076
Toxoplasmosis	0.039816772	0.572104151
Systemic lupus erythematosus	0.04424287	0.603915182
tRNA-Val-CAC-5p-tRF-GCTTCTGTAGTGTAGTGGTTATC		
Name	p	q
ECM-receptor interaction	0.030332252	1
Amoebiasis	0.039913667	1
Aminoacyl-tRNA biosynthesis	0.017826531	1
Small cell lung cancer	0.043558318	1
Ovarian steroidogenesis	0.018968386	1
Biosynthesis of unsaturated fatty acids	0.009518248	1
Protein digestion and absorption	0.028633998	1
GnRH signaling pathway	0.039352028	1
Fatty acid elongation	0.010954457	1

tRNA-Val-AAC-5p-tR-half-GTTTCCGTAGTGTAGTGGTTATCACGTTTCGC		
Name	p	q
Fat digestion and absorption	0.011112628	1
Pancreatic secretion	0.023021639	1
Steroid biosynthesis	0.004336979	1
Hippo signaling pathway - fly	0.01944218	1
Glycerolipid metabolism	0.012838874	1
tRNA-Glu-TTC-5p-tRF-TCCCACATGGTCTAGCGGTTAGGATTCCT		
Name	p	q
Glutamatergic synapse	0.004219029	0.575897471
GABAergic synapse	0.002758894	0.575897471
Terpenoid backbone biosynthesis	0.027664805	1
Vasopressin-regulated water reabsorption	0.044060357	1
Mucin type O-glycan biosynthesis	0.03083707	1
Nitrogen metabolism	0.04218119	1
Glyoxylate and dicarboxylate metabolism	0.035262785	1
tRNA-Glu-TTC-5p-tR-half-TCCCACATGGTCTAGCGGTTAGGATTCCTG		
Name	p	q
Mucin type O-glycan biosynthesis	0.047564399	1
Other glycan degradation	0.027019575	1
GABAergic synapse	0.006772275	1
Terpenoid backbone biosynthesis	0.042709644	1
Galactose metabolism	0.049499892	1
Biosynthesis of amino acids	0.025893997	1
Glutamatergic synapse	0.010282408	1
tRNA-Glu-TTC-5p-tR-half-TCCCACATGGTCTAGCGGTTAGGATTCCTGG		
Name	p	q
Peroxisome	0.026279476	0.911652868
Arginine and proline metabolism	0.03005449	0.911652868
Staphylococcus aureus infection	0.009238152	0.911652868
N-Glycan biosynthesis	0.00881948	0.911652868
GABAergic synapse	0.019375754	0.911652868
Glutamatergic synapse	0.029004364	0.911652868
Pertussis	0.020264524	0.911652868
Thiamine metabolism	0.010376418	0.911652868
tRNA-Glu-TTC-5p-tR-half-TCCCACATGGTCTAGCGGTTAGGATTCCTGGTT		

Name	p	q
GABAergic synapse	0.012359329	1
Glutamatergic synapse	0.018632199	1
Thiamine metabolism	0.008222097	1
Biosynthesis of amino acids	0.045862817	1
tRNA-Glu-TTC-5p-tR-half-607		
Name	p	q
Bile secretion	0.028067418	1
tRNA-Glu-CTC-5p-tR-half-TCCCTGGTGGTCTAGTGGTTAGGATTCGGCGCC		
Name	p	q
MAPK signaling pathway	0.0463643	1
Protein digestion and absorption	0.012603619	1
Caffeine metabolism	0.028743132	1
Steroid hormone biosynthesis	0.015484022	1
Ovarian steroidogenesis	0.004007776	1

PRJNA428989 peripheral_monocytes

tRNA-Gly-GCC-5p-tRF-GCATTGGTGGTTCAGTGGTAGAATTCT				
Description	Gene_DE	q_value	Rich_Ratio	Size
Asthma	2	0.039916085	63.93518519	3
Allograft rejection	2	0.039916085	52.31060606	3
Graft-versus-host disease	2	0.039916085	59.01709402	3
Type I diabetes mellitus	2	0.043386238	32.88095238	3
Intestinal immune network for IgA production	2	0.043386238	34.87373737	3
Influenza A	3	0.043386238	11.24592834	4
Inflammatory bowel disease (IBD)	2	0.043386238	30.68888889	3
Autoimmune thyroid disease	2	0.043386238	37.12365591	3
Staphylococcus aureus infection	2	0.048278559	27.40079365	3
tRNA-Gly-GCC-5p-tR-half-GCATTGGTGGTTCAGTGGTAGAATTCTCGT				

Description	Gene_DE	q_value	Rich_Ratio	Size
Antigen processing and presentation	4	0.0151707 44	17.049382 72	5
tRNA-Gly-GCC-5p-tR-half- GCATTGGTGGTTCAGTGGTAGAATTCTCGCT				
Description	Gene_DE	q_value	Rich_Ratio	Size
Antigen processing and presentation	4	0.0350447 58	14.109833 97	5
tRNA-Gly-GCC-5p-tR-half- GCATTGGTGGTTCAGTGGTAGAATTCTCGCCTGCC				
Description	Gene_DE	q_value	Rich_Ratio	Size
Antigen processing and presentation	6	0.0068908 04	9.8996415 77	4
tRNA-Gly-GCC-5p-tR-half- GCATTGGTGGTTCAGTGGTAGAATTCTCGCA				
Description	Gene_DE	q_value	Rich_Ratio	Size
Antigen processing and presentation	4	0.0350447 58	14.109833 97	5

Supplementary Data 4: targetscan|miRDB|HTR8_DEG

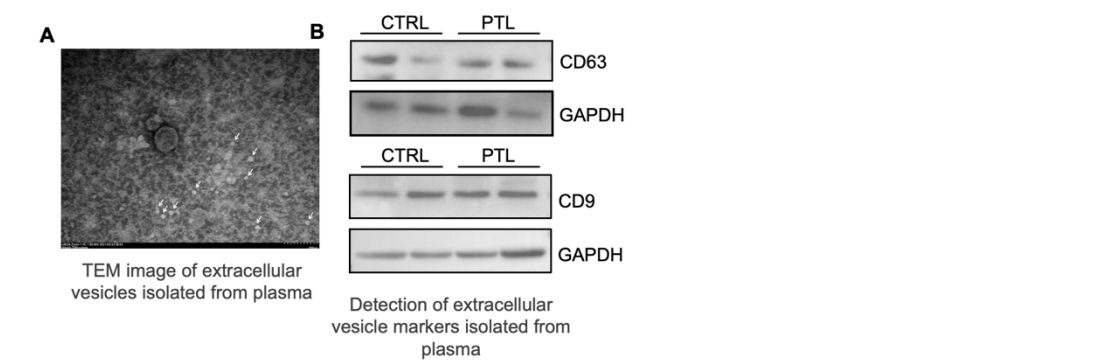
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PFN2		SMCO4		ATP2C1		CLCN3		FCHO2		MFAP3
ITGB1		MBNL1		KLHL24		AP3M1		CEP97		DPP8
TMEM184C		GNG12		CDK5R1		GLRA3		RPS6KA3		MAP3K2
IDH2		PRKCI		PTPN4		KCNJ14		SRSF10		GPAM
EEF2		RAB30		PCGF5		PLEKHA5		SIRPA		KLHL23
CTDSP1		KIF2A		BRMS1L		ENAH		SPRY3		SEL1L
DUSP10		FRS2		SACS		COL25A1		TCF12		ARHGEF18
RHPN2		KLHL28		NCK2		PDCD6		PDE4D		RAB43
SLC25A15		CEP170B		RABGAP1L		SESN1		TAB3		PKD2
TMSB4X		MTA1		PDCD4		ARHGAP21		FAT1		GPCPD1
FOXN2		EZR		PNPT1		PHF3		CELF1		KCTD2
REV1		RBMS1		ATP2B4		DGCR2		NCS1		GNAQ
TCF7L2		MAPK8IP1		FOXO1		TMED7		SMPD3		HECTD2

DAGLA		ABI2		SGMS2		SLC35C1		SPAST		FAM8A1
TAOK1		NFE2L1		CHIC1		CIAPIN1		TARBP1		RAB9B
STK38L		SKIL		SPIN3		TMEM115		L1CAM		TSPAN4
SLC6A6		SOX6		SLC39A9		FAM78A		PFN1		DENND6A
TET1		CAND1		DCUN1D1		OSBPL2		PBX2		ANKRD52
PRUNE2		CNOT6L		BCL2L12		GK		TBXA2R		SLITRK4
RORA		AFF4		SLC2A8		PPP4R2		TNS1		DOK4
SIDT2		MED12L		GLB1L		AJUBA		SNAP23		CDC42BPA
SLC25A36		SYT1		ADRA2C		PPM1L		CERS2		KLF15
PRKACB		SPRED1		FZD3		BRPF3		MBNL2		PAFAH1B1
NRBF2		RNF217		AK3		FMR1		TRIM37		PRRT3
AJAP1		KAZALD1		CFL1		SPAG1		RWDD4		CD47
NR3C1		REPS2		SLC39A1		ARF4		MYO19		PAIP1
ITGB8		NUFIP2		DENR		PPP1R13L		CHST1		ANK3
ACVR2B		HLTF		CLPTM1L		FOXO3		RMND5A		KDELRL1
PPM1E		SNX13		GPC1		PTAR1		PCDH18		CLOCK
DAAM1		PLAGL2		GXYLT1		CTDSP2		NOVA2		DPY19L3
AAK1		PLCB4		CHMP1A		CAMSAP2		ORC5		COG3
QKI		OSBPL8		MAK		CNNM3		MET		THBS1
HBEGF		AZIN1		SETD7		MYO1D		ACER3		MYB
FLRT3		PSD3		RASA2		SLC33A1		CCDC88A		GRB2
RAB8B		ERP44		CD2AP		BNIP3		AATK		PHIP
ATP13A3		LHX1		CUL5		TSPAN9		RFTN1		CBX2
CERS6		CTTN		PC		STOX2		PDZD8		JAZF1
MED1		FLOT1		ADD3		SNX17		DOCK9		S100BPB
SH3BGR12		PEG10		SLC1A1		LCA5		KPNA3		NUDT3
AMD1		JMJD1C		SC5D		KLHDC10		IGDCC3		CSRNP3
SNCB		ATF7IP		PREPL		DSG2		SHOC2		MYO1C
PHF6		TRIQK		CACNA2D1		FAM167A		MLX		GNA13
CELSR3		LPP		SPIN1		SH3PXD2B		NAMPT		GIT2
RNF157		FOXF2		DTNBP1		MISP		REEP1		SYPL1
PRKAR2A		RASA1		APBA2		SNX4		FXR1		CASP2
NCKAP1		ADCY6		SH3BP5		LRRC7		THBS2		DIXDC1
BRD4		STK19		PAN2		CBFA2T3		ATOH8		FEM1B
GMFB		RAB6B		PHF21B		BCAT2		ELL		SCRT1
EVI5		ARCN1		FAM171A1		CHAMP1		SMAD7		SH3KBP1
DGKH		LRCH2		CORO1C		CCDC92		PDGFRA		HOOK3
BNC2		ACTR2		EGLN1		AVP1		PHF13		EEA1
FAM168A		RAPGEF5		ROCK1		TMEM198		CEBPA		ABHD13
GNB1		KTN1		TNS3		SEPHS1		ANGPTL1		CCND3
NRXN3		SP3		TMEM47		MEOX1		ONECUT2		ARMC1
CSNK1G3		RARG		BOD1L1		EGR3		PTPRG		HECW2
DMXL1		EPAS1		NAGPA		INTS6		MED14		DDAH1

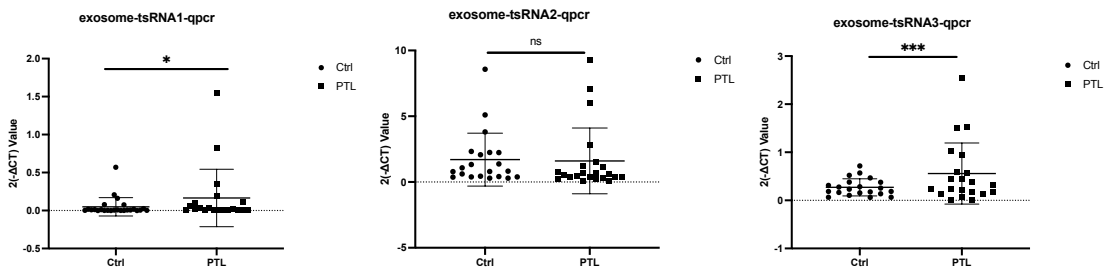
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EIF3A		SPEN		RALGAPB		DCP2		CLPSL2		KCTD5
HES1		ADAM22		TACC1		CHST10		ELAC2		TRIM44
RCC2		ACER2		PPP1R11		ANXA11		CDCA4		BSCL2
RPS6KA6		ARRDC3		RNF44		SESN3		RIC8B		MSTO1
RAVER2		MYADM		BRWD1		DDHD1		RBL2		FUT2
STAG1		RAB23		BRWD3		PDK3		GPN2		PDLIM1
SYNE2		MAP1B		FIGN		NHS		TIPARP		MEX3A
PLEKHA8		AMOTL2		ARHGDI4		INO80D		DESI2		PID1
TMEM170B		PRKAA2		RNF208		PHF12		R3HDM1		ENG
RUNDC3B		PKN2		DENND5B		SCN8A		RAB7A		ARC
FEM1C		ELAVL2		PYGO2		ASAP1		SENP1		ARHGEF5
CEP250		ANLN		RALGDS		CYLD		TEAD3		KLF11
PIK3R1		SLC43A2		PLOD2		FLNB		DPH1		DISP2
ANKIB1		FBXO41		NF1		RAB3B		PURB		SHC1
PAN3		PLEKHG3		GALNT2		ALDH6A1		IGF2BP2		C1orf116
STARD13		TRIM8		QSER1		COL5A1		THAP11		POGLUT1
EIF4EBP2		FAM91A1		IER5L		LRRC8C		C6orf120		NFATC2
OCRL		FOXP2		RIMS3		PPM1A		MXRA7		RNF41
DAB2IP		RDX		SLC4A7		TBC1D12		LRRC58		GPR153
PCMTD1		RAB10		OGT		CREB3L1		TIGD5		CSNK1E
CCDC117		TP73		SDC1		SOS1		DCAF10		DNAJA2
SLC30A7		TP53INP1		PARPBP		ALG9		ORC2		PIK3R5
CGGBP1		SESN2		BICD2		EIF5A2		PSIP1		PLCXD2
RALGPS1		RICTOR		ABLIM1		METTL8		RAD9A		CCP110
KIAA0513		EPHA3		H6PD		BPTF		TESK2		PICALM
SH3BGR13		NLGN2		PLD1		SLC8A1		C5orf51		LITAF
FGD4		MLLT1		LARP1		NAP1L1		RHOG		ERMP1
PPP1R12A		ARID4A		IGSF10		PAFAH1B2		EMILIN3		PTEN
SPRY4		TCP11L2		TENM4		NIPBL		LYPD1		GNAO1
ADAM10		MORC3		GJC1		RHD		CCDC142		PAX8
CHMP1B		TMOD1		POU2F1		SMARCA5		CCNE2		FAM189B
SLC44A2		CLCN5		CDK6		CACNA1B		PIK3CB		NR2C2
FBXO27		SEZ6L2		RGS5		S100B		PLCH2		PFKFB4
TMEM245		DYRK1A		PSME4		LAMTOR3		MRPS10		RPAP1
SLC7A8		PPM1F		NFIC		SOX15		DHX35		ENPP1
PPP1R9B		ATP8A1		MRAS		CYB561D1		LYPD5		SLC35E4
LRP10		KPNA1		MCFD2		TMEM229B		NFYC		KIF1B
ARHGAP29		N4BP1		CNOT6		NUP153		PPP2R5E		CDKL1
C2orf72		RALGPS2		RAPGEF6		ARPC1A		SERHL2		RFX7
ABCA2		KCNN3		ATAD2B		CHTF8		SPARCL1		BIN3
MMP16		SLC22A23		FAT3		CHD6		CEP57L1		PDIA6

HELZ2		CLDN5		SYP		RAB3IP		SESTD1		AZI2
BACE1		ATXN2L		FER		C5orf22		LCORL		CPD
ST3GAL1		CMTR1		SLC26A1		CDCP1		POLDIP3		MPZ
CNOT8		PIK3R3		MCOLN3		TMEM164		TRDMT1		MRPL43
PDS5A		GLCCI1		HIPK3		SMAD2		LRP3		MYBL1
PARP8		HK1		TMEM64		C12orf4		EFHC1		PFKFB3
LRRC14		EFCAB2		SIN3B		CHRNA4		OSER1		SEC14L2
MSANTD1		CLN8		LZTS3		LRRC27		GDF11		ASH1L
RPS6KB1		PADI1		BBX		NCAM2		PIK3CA		CNTNAP1
KAT6A		FBXO11		DDX51		NOTCH2		RPS23		NPAS2
TLL1		FBXL20		MACF1		PTGR2		C22orf39		PCCA
PLEKHG2		FMNL3		TMEM108		ASXL1		MGMT		PTPRF
SYT5		SLC39A10		SLC9A8		CCDC115		PPIL4		RAP1B
STK40		KMT2C		RTKN2		ABHD2		MRPS18C		SEMA3D
FAM117B		POLR2C		DNMT3A		ATF6		SLC25A4		GTF2IRD1
DHDDS		PRKAA1		POM121		STRN		SETX		PGAP1
MCPH1		SHANK3		ERI2		RPAP2		SERPINH1		
PADI2		ATM		NUDC		PIAS2		FARSB		
CNTLN		SERTAD4		MRPS26		SCAI		DHX40		
HCFC2		SYDE1		APOL6		RGS9BP		EFTUD2		
SNTB2		DOCK1		RSBN1		PDCL		GPATCH2L		

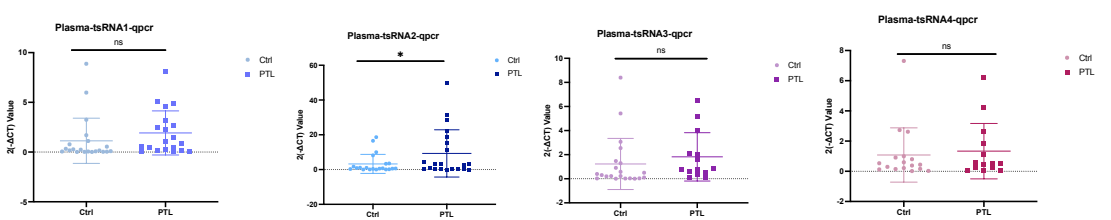
Supplementary Data 5: Successfully extracted maternal plasma extracellular vesicles using an exosome kit



Supplementary Data 6: Upregulation of plasma EVs tsRNA1 and plasma EVs tsRNA3 in preterm labor group



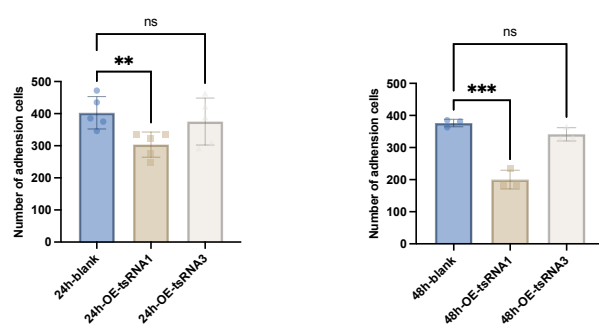
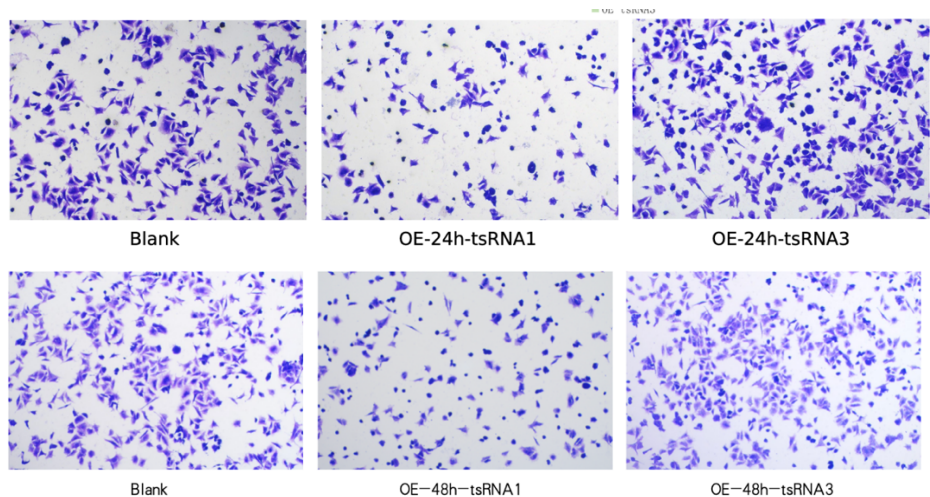
Supplementary Data 7: There was no significant difference in the expression level of plasma tsRNA in preterm labor group



Supplementary Data 8: HTR8/SVneo cells can secrete extracellular vesicles



Supplementary Data 9: Overexpression of tsRNA3 does not affect the function of HTR8/SVneo Adhesion:



Angiogenesis:

