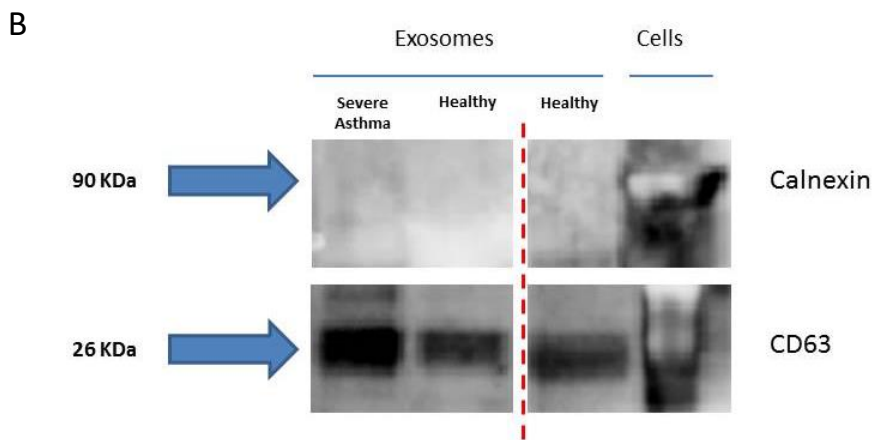
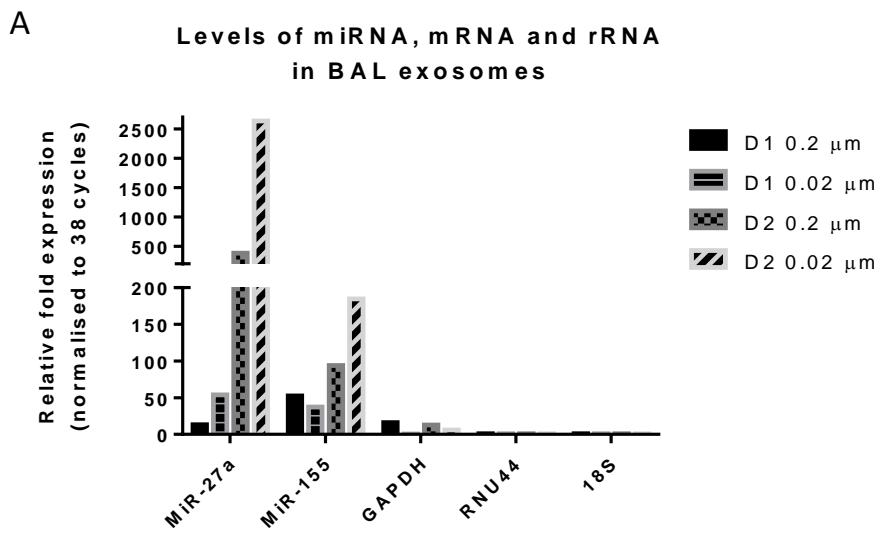
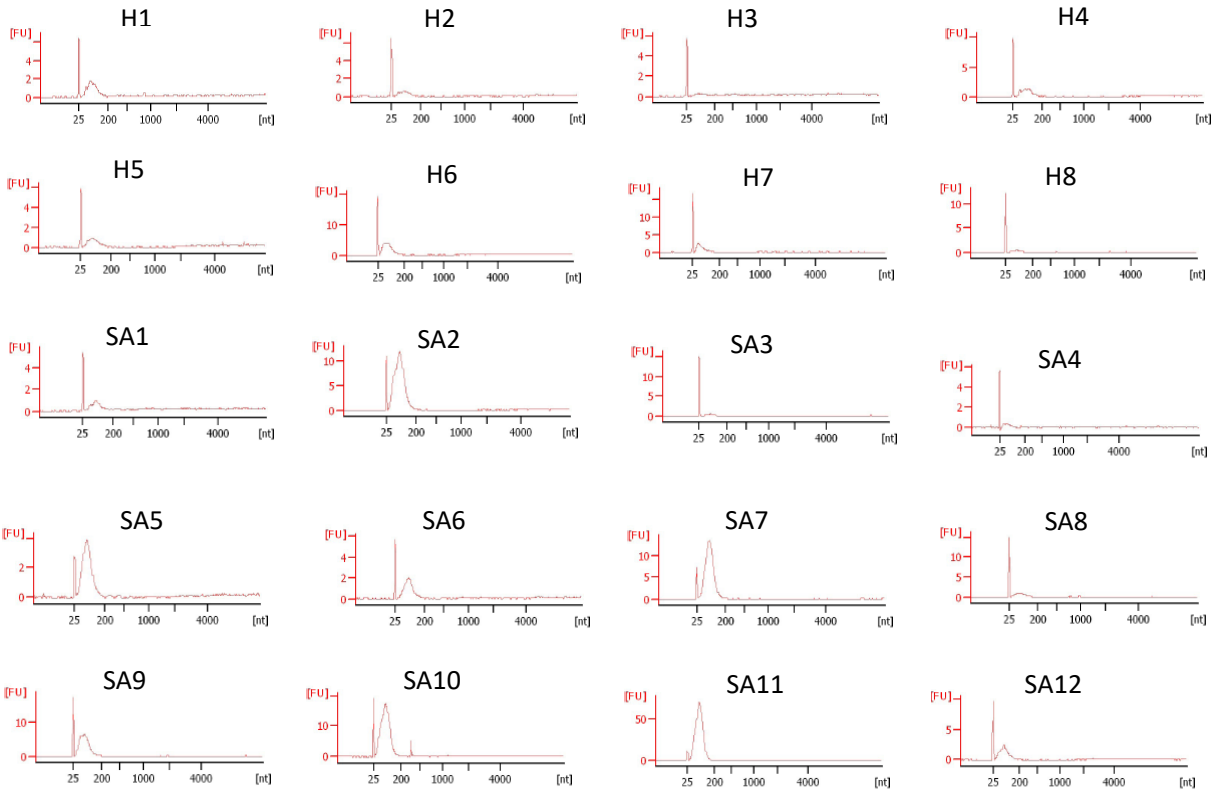


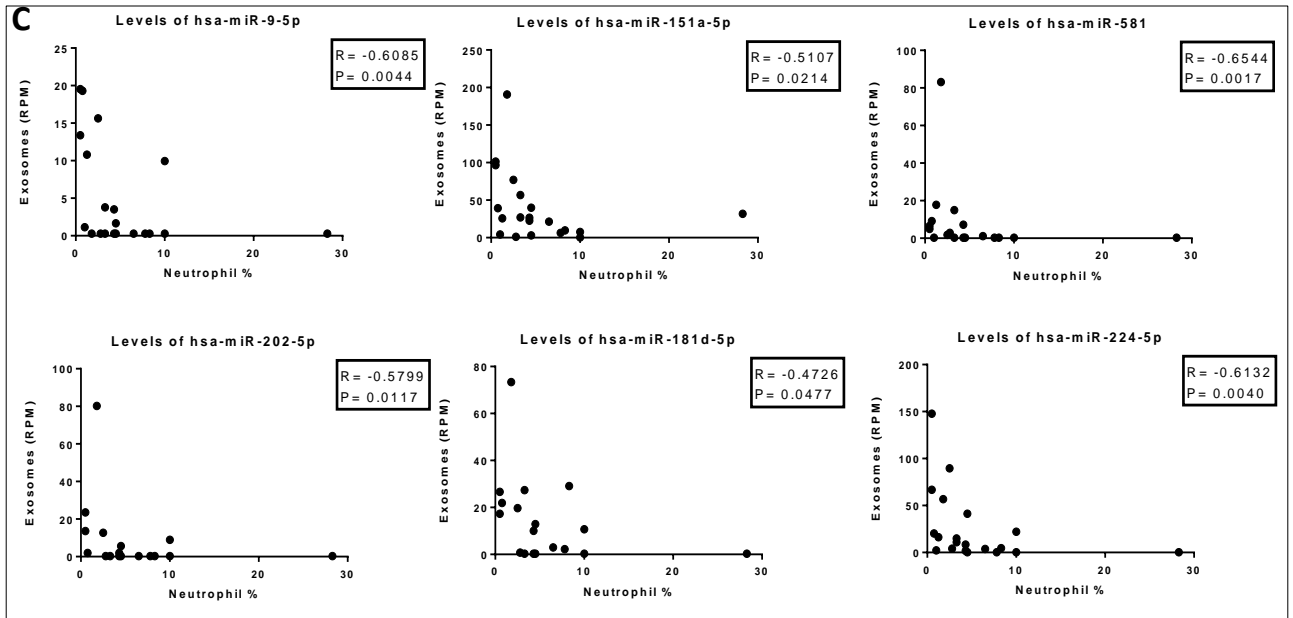
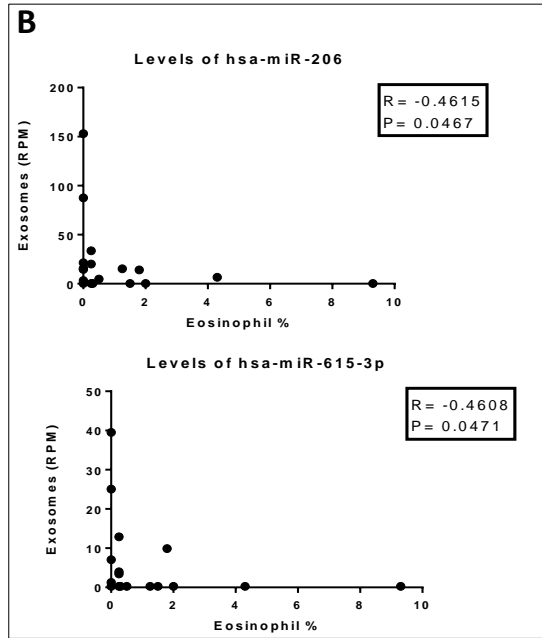
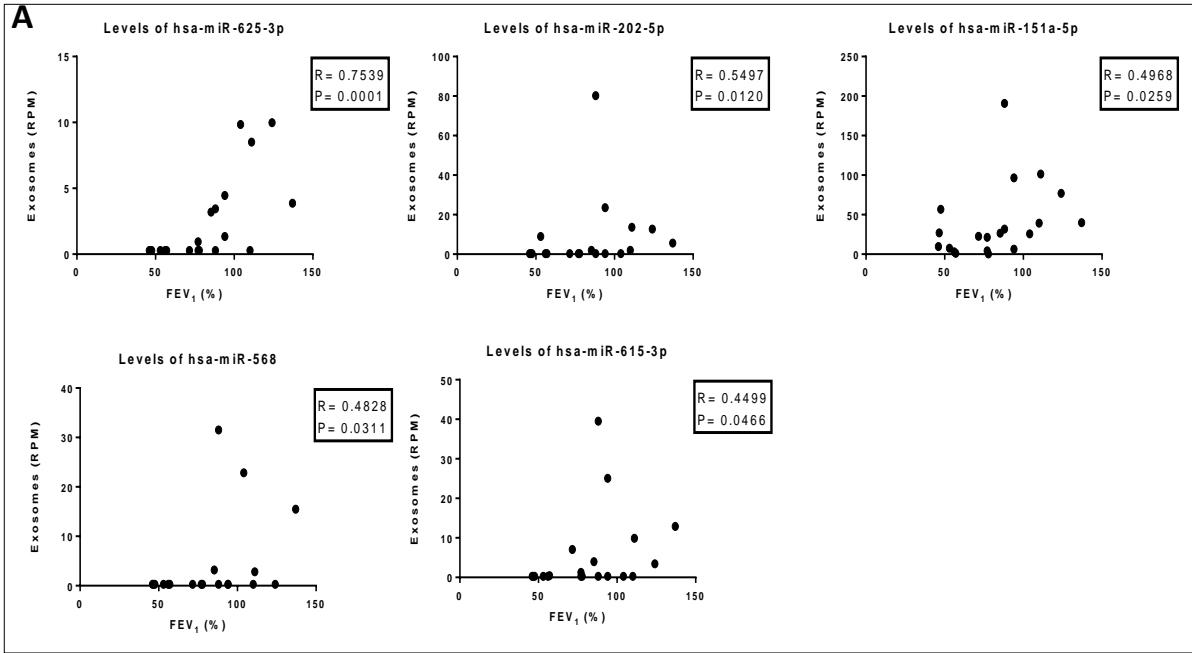
Supplementary Figures and Tables

Supplementary Figure S1



Supplementary Figure S2





Supplementary Table ST1 – 90 microRNAs are downregulated in severe asthmatic BAL exosomal microRNA

Mature miRNA Name	Anova P-value	Anova FDR	Fold Changes (Healthy vs SA)
hsa-miR-625-3p	0.00004	0.01351	12.73708735
hsa-miR-202-5p	0.00032	0.05978	17.30941106
hsa-miR-181d-5p	0.00097	0.10592	3.90773668
hsa-miR-568	0.00157	0.10592	33.6846983
hsa-miR-224-5p	0.0019	0.10592	9.17330953
hsa-miR-581	0.00196	0.10592	9.113094659
hsa-miR-1	0.00222	0.10592	5.147353113
hsa-miR-615-3p	0.00227	0.10592	12.64794731
hsa-miR-151a-5p	0.00347	0.14016	4.677970418
hsa-miR-202-3p	0.00376	0.14016	15.47127905
hsa-miR-125b-5p	0.00598	0.15237	3.646614539
hsa-miR-425-3p	0.00613	0.15237	2.859058738
hsa-miR-10b-5p	0.00615	0.15237	3.815368896
hsa-miR-500a-5p	0.00724	0.15237	5.848936075
hsa-miR-520a-3p	0.00735	0.15237	9.131554923
hsa-miR-145-5p	0.0074	0.15237	14.14228551
hsa-miR-7706	0.00775	0.15237	4.251400485
hsa-miR-151a-3p	0.00777	0.15237	3.985706942
hsa-miR-628-3p	0.00807	0.15237	4.19099152
hsa-miR-206	0.00817	0.15237	8.075113169
hsa-miR-9-5p	0.0088	0.15287	6.601860461
hsa-miR-578	0.00918	0.15287	4.88633972
hsa-miR-122-5p	0.00943	0.15287	5.650117117
hsa-miR-646	0.00984	0.15295	8.332704341
hsa-miR-149-5p	0.01103	0.1615	3.565116981
hsa-miR-205-5p	0.01126	0.1615	4.494590137
hsa-miR-370-3p	0.01225	0.16518	6.672305042
hsa-miR-598-3p	0.0124	0.16518	4.296117834
hsa-miR-30a-3p	0.01357	0.1684	3.328264378
hsa-miR-552-3p	0.01372	0.1684	6.362617624
hsa-miR-493-3p	0.01541	0.1684	7.516934698
hsa-miR-502-3p	0.0161	0.1684	2.04905949
hsa-let-7e-5p	0.01641	0.1684	3.9632466
hsa-miR-516b-5p	0.01645	0.1684	8.65840658
hsa-miR-518c-5p	0.01656	0.1684	5.358308115
hsa-miR-106b-5p	0.01658	0.1684	3.279617121
hsa-miR-708-3p	0.0167	0.1684	2.284130907
hsa-miR-99b-5p	0.01759	0.17185	3.02832834
hsa-miR-708-5p	0.01797	0.17185	1.583111582
hsa-miR-339-5p	0.01872	0.17188	4.173525589

hsa-miR-125a-5p	0.01917	0.17188	2.848101262
hsa-miR-23b-3p	0.01935	0.17188	2.555333689
hsa-miR-484	0.02087	0.18106	3.094496658
hsa-miR-25-3p	0.02269	0.187	2.463719385
hsa-miR-340-3p	0.02323	0.187	3.808979069
hsa-miR-222-3p	0.02481	0.187	3.523702049
hsa-miR-135b-5p	0.02524	0.187	2.409671607
hsa-miR-610	0.02542	0.187	7.660760307
hsa-miR-421	0.02625	0.187	5.084263677
hsa-miR-154-5p	0.02631	0.187	5.324262368
hsa-miR-339-3p	0.02667	0.187	2.772589834
hsa-miR-141-3p	0.02826	0.187	4.522902385
hsa-miR-642a-3p	0.02872	0.187	3.962289923
hsa-miR-512-3p	0.0296	0.187	5.740633397
hsa-miR-29c-5p	0.02977	0.187	1.861863266
hsa-miR-432-3p	0.0298	0.187	4.747031935
hsa-miR-393a-5p	0.02992	0.187	3.412651069
hsa-miR-27b-3p	0.03009	0.187	3.029741361
hsa-miR-196b-5p	0.03045	0.187	5.258139059
hsa-miR-361-3p	0.03075	0.187	3.19312995
hsa-miR-223-3p	0.03087	0.187	2.002770697
hsa-miR-219a1-3p	0.03371	0.187	2.487512138
hsa-miR-618	0.03374	0.187	3.005812985
hsa-miR-181b-5p	0.03404	0.187	3.306539992
hsa-miR-330-3p	0.03443	0.187	4.323106426
hsa-miR-590-3p	0.03487	0.187	4.493258792
hsa-miR-532-5p	0.03513	0.187	2.039622436
hsa-miR-345-5p	0.03536	0.187	1.769460107
hsa-miR-10a-5p	0.03561	0.187	3.225234328
hsa-miR-30c-5p	0.03761	0.187	2.82521551
hsa-miR-210-3p	0.03765	0.187	6.707880135
hsa-miR-508-5p	0.03825	0.187	6.434115532
hsa-miR-187-3p	0.03858	0.187	4.374361733
hsa-miR-186-5p	0.03868	0.187	2.934362441
hsa-miR-143-3p	0.03872	0.187	1.749772468
hsa-miR-607	0.03878	0.187	7.362377653
hsa-miR-193b-3p	0.03902	0.187	9.503401498
hsa-miR-3622a-5p	0.0396	0.187	5.058152899
hsa-miR-99a-5p	0.04001	0.187	3.460720561
hsa-miR-28-3p	0.0406	0.187	2.012607232
hsa-miR-3909	0.04153	0.187	5.77088053
hsa-miR-328-3p	0.04208	0.187	1.233765577
hsa-miR-875-3p	0.04209	0.187	5.917943392
hsa-miR-486-5p	0.04331	0.187	2.124673179
hsa-miR-489-3p	0.0435	0.187	5.386910932
hsa-miR-200b-5p	0.0435	0.187	3.416159075
hsa-miR-483-3p	0.04362	0.187	5.053249029
hsa-miR-93-5p	0.04759	0.20172	2.754331525
hsa-miR-27a-5p	0.0494	0.20551	0.155014724
hsa-miR-375	0.04959	0.20551	2.487893854

Supplementary Table ST2: Pathways dysregulated in severe asthma

Adjusted p-value	Pathway	Highlighted targets
0.0059	Chronic myeloid leukemia	PI3K, Sos, Ras, ERK, NFKB, TGF- β , TGF β RI, TGF β RII, Smad3, Smad4, p53
0.0059	Adherens junction	IGF-1R, INSR, MET, Actin, p120ctn, α -Catenin, Rac, TGF β R, ERK, Smad3, Smad4
0.0059	MAPK signalling pathway	SOS, Ras, PKA, MEK1, ERK, NFKB, TNF, IL1, TGF β , TGF β R, p38, MKP, NLK
0.0059	Focal adhesion	ECM, ITGA, ITGB, Filamin, Paxillin, Actin PI3K, Rac, PAK, Sos, MEK1, ERK1/2
0.0059	Neurotrophin signalling pathway	PI3K, SOS, Ras, Raf, MEKK3, MEK1/2, p38, Erk1/2, NFKB
0.0059	mTOR signalling pathway	INS/IGF, PI3K, mTOR, ERK1/2, VEGF, eIF4B, eIF4E, REDD1, AMPK, BRAF
0.0101	TGF-beta signalling pathway	TGF β , TNF α , TGF β RI, TGF β RII, Smad1/5/8, Smad4, Smad 6/7, Smad2/3, ERK, Activin
0.0133	Regulation of actin cytoskeleton	MEK, ERK, Sos, Ras, PI3K, F-Actin, Rac, PAK, MLCK
0.0138	Endocytosis	TGF β , TGF β R, Smad2/3, RTK, dynamin, clathrin, Smurf2, Smad7, Rab11, rabaptin5, Rab5, Rab22, Alix, VPS25, CHMP1, VPS, Arf
0.0231	Prostate cancer	GF, GFR, PI3K, SOS, Ras, Raf, MEK, ERK, p27, NFKB, mTOR
0.0231	Pancreatic cancer	PI3K, NFKB, Raf, Rac, MEK, ERK, VEGF, p16, Rb, p53, BRCA2, TGF β , TGF β RI, Smad2/3, Smad4,
0.0231	Melanoma	GF, RTK, Ras, BRAF, Raf, PI3K, MEK, ERK, p53, Rb, E2F
0.0231	Insulin signalling pathway	SOCS, PI3K, GLUT4, PKA, mTOR, SOS, Ras, Raf, MEK1/2, ERK 1/2
0.0266	Glioma	IGF-1, EGFR, PDGFR, Shc, Sos, Ras, PI3K, Raf, MEK, ERK, mTOR, Rb, E2F, p53, PDGF
0.0295	Dilated cardiomyopathy	ITGA, ITGB, Desmin, Titin, SGCD, β 1AR, AC, PKA, DHPR, SERCA2a, NCX, TNF α , TGF β , IGF-1, Lamin, Titn, ACTC1, TPM