

Supplementary Figures 1, 2, 3 and 4
Supplementary Tables 1a,b,c, 2, 3, 4 and 5

A heritable profile of miRNAs in autistic patients and mouse models.

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Supplementary Table 1a EVRENA Clinics

Patients	Gender	Age	Diagnosis	Clinical Findings	ADSI	Family History	Consanguinity
14-101	Female	5	Autism	ID, Epilepsy		None	Positive
14-102	Female	3	Autism	ID, Epilepsy		None	Positive
15-101	Male	9	Autism	ID		Epilepsy, Deafness	Positive
15-102	Male	9	Autism	ID		Epilepsy, Deafness	Positive
16-101	Female	9	Autism	ID		Autism	Positive
16-102	Male	9	Autism	ID		Autism	Positive
16-103	Male	5	Autism	ID		Autism	Positive
17-101	Female	8	Autism	ID		None	Positive
17-102	Female	12	Autism	ID		None	Positive
19-101	Male	5	Autism	ID		MR	Positive
20-101	Male	2	Autism	ID		None	Positive
21-101	Male	12	Autism	ID		Schizophrenia	Negative
22-101	Female	11	Autism	ID		None	Negative
24-101	Male	4	Autism	ID		None	Negative
28-101	Female	13	Autism	ID, Epilepsy		None	Positive
29-101	Male	6	Autism	ID, Epilepsy		None	Positive
31-101	Female	6	Autism	ADHD		Autism	Positive
32-101	Male	3	Autism	ID, Epilepsy	Suspicious	Deafness	Negative
37-101	Male	10	Autism			None	Positive
41-101	Male	5	Autism	ID, ADHD		None	Negative
H10-103	Male	3	Autism	ID	Abnormal	Acromegaly, Deafness	Negative
H10-102	Male	3	Autism	ID	Abnormal	Acromegaly, Deafness	Negative
H13-101	Female	3	Autism	ID		Deafness	Negative
H33-102	Female	3	Autism	ID		Schizophrenia, Asperger	Negative
H34-101	Male	9	Autism			Schizophrenia	Negative
H36-101	Male	9	Autism	ID	Abnormal	None	Positive
H37-101	Male	4	Autism	ID	Abnormal	None	Positive
18-101	Male	6	Atypic Autism		Abnormal	Epilepsy, MS	Negative
25-101	Male	7	Atypic Autism	ADHD	Suspicious	MR	Negative
26-101	Female	3	Atypic Autism			None	Negative
27-101	Male	7	Atypic Autism	ID, ADHD	Suspicious	None	Negative
30-101	Male	7	Atypic Autism	ID	Abnormal	None	Positive
34-101	Male	5	Atypic Autism	ID		None	Negative
35-101	Male	9	Atypic Autism	ID, ADHD		None	Positive
36-101	Female	7	Atypic Autism			None	Negative
38-101	Female	9	Atypic Autism			None	Negative
40-101	Male	5	Atypic Autism	ID, ADHD		None	Negative
42-101	Male	5	Atypic Autism	ID, ADHD		None	Positive
H10-101	Male	6	Atypic Autism	ID, ADHD		Acromegaly, Deafness	Negative
H17-101	Male	6	Atypic Autism	ID, ADHD	Suspicious	None	Positive
H18-101	Male	6	Atypic Autism			None	Negative
H33-101	Male	3	Atypic Autism	ID	Abnormal	Schizophrenia, Asperger	Negative
H34-102	Female	9	Atypic Autism			Schizophrenia	Negative
H38-101	Male	3	Atypic Autism	ID	Abnormal	Autism	Negative
H39-101	Male	3	Atypic Autism	ID	Abnormal	Schizophrenia	Negative
				ID: intellectual disability	(Ankara Developmental Screening Inventory (ADSI))		

Supplementary Table 1c (Dataset A2) Six miRNAs in autism

		Gender		sub 2023-10	sub 2023-11	sub 2023-12	sub 2024-01	sub 2024-02	sub 2024-03	sub 2024-04	sub 2024-05	sub 2024-06
Parent Group	40-50	F	1	0.0462016	2.259489	0.0278127	0.0324627	0.0324627	0.0324627	0.0324627	0.0324627	0.0324627
	40-50	F	1	0.0462016	1.7624871	0.0278127	0.0324627	0.0324627	0.0324627	0.0324627	0.0324627	0.0324627
	40-50	F	1	0.0376574	0.8076713	0.0376574	0.0376574	0.0376574	0.0376574	0.0376574	0.0376574	0.0376574
	40-50	F	1	0.0323776	0.0468611	0.0323776	0.0323776	0.0323776	0.0323776	0.0323776	0.0323776	0.0323776
	40-50	F	1	0.0323776	1.0842094	0.0323776	0.0323776	0.0323776	0.0323776	0.0323776	0.0323776	0.0323776
	40-50	F	1	0.0377369	2.1173989	0.0377369	0.0377369	0.0377369	0.0377369	0.0377369	0.0377369	0.0377369
	40-50	F	1	0.0232663	0.6237475	0.0232663	0.0232663	0.0232663	0.0232663	0.0232663	0.0232663	0.0232663
	40-50	F	1	0.1747651	0.0000000	0.1747651	0.1747651	0.1747651	0.1747651	0.1747651	0.1747651	0.1747651
	40-50	F	1	0.0458004	0.0000000	0.0458004	0.0458004	0.0458004	0.0458004	0.0458004	0.0458004	0.0458004
	40-50	F	13	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	2	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	11	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	4	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	7	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	2	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	10	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
	40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	0.0368643	
40-50	F	1	0.0368643	0.0000000	0.0368643	0.0368643	0.0368643					

Supplementary Figure 1 The serum miRNA expression profiles.

($p < 0.05$), (log fold change, Unpaired t-test).

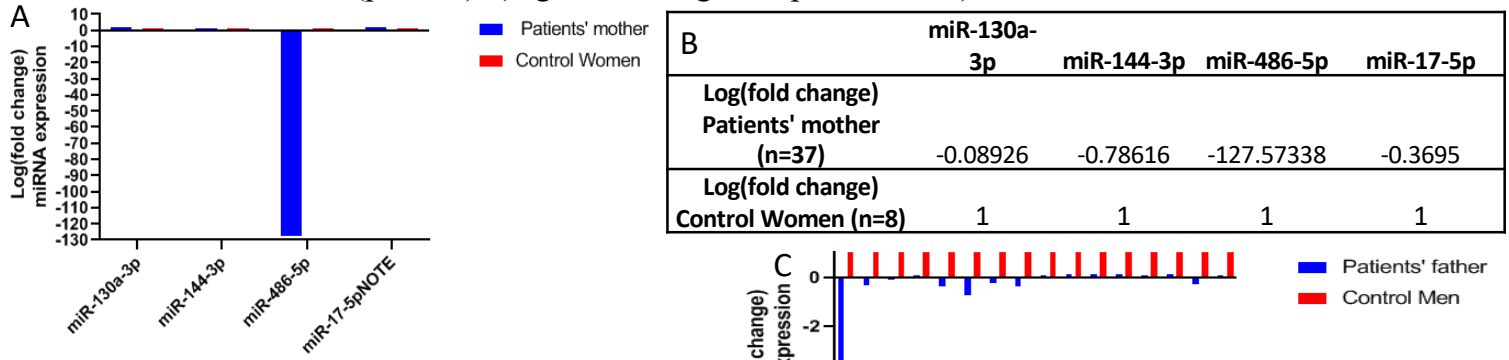


Fig.1a Patients' mothers compared to healthy female control.

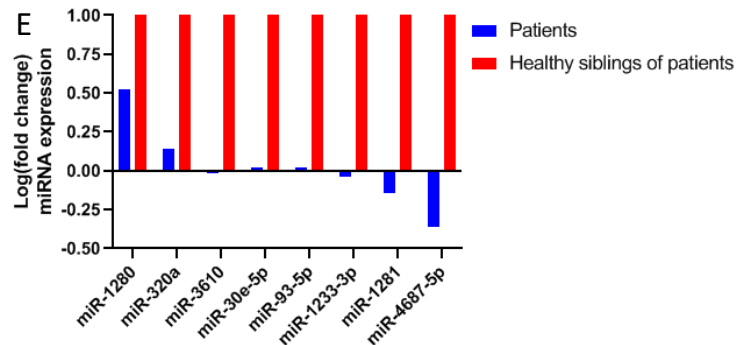
4 miRNAs (downregulated) were found as shown in the graph (A) and table (B).

Fig.1b Patients' fathers compared to healthy male controls. 16 miRNAs (downregulated) were found as shown in the graph (C) and table (D).

D	Log(fold change)		Log(fold change)	
	miRNA	Patients' fathers (n=37)	miRNA	Patients' fathers (n=37)
				Control Men (n=8)
	miR-3613-3p	-6.80606	miR-30a-5p	-0.03665
	miR-150-5p	-0.31346	miR-191-5p	-0.02524
	miR-18a-5p	-0.09276	miR-4770	-0.01006
	miR-4301	-0.04901	miR-30e-5p	-0.03094
	miR-19b-3p	-0.37706	miR-23a-3p	-0.04609
	miR-19a-3p	-0.71662	miR-374a-5p	-0.02271
	miR-15b-5p	-0.25856	miR-197-3p	-0.26137
	miR-17-3p	-0.3618	miR-30c-5p	-0.05194

Fig.1c miRNA Autism patients compared to their healthy siblings.

8 miRNAs (3 up- and 5 downregulated) were found as shown in the graph (E) and table (F).



F	miR-1280	miR-320a	miR-3610	miR-30e-5p	miR-93-5p	miR-1233-3p	miR-1281	miR-4687-5p
Log(fold change) Patients (n=45)	0.523376	0.141137	0.008134	-0.00237	-0.00445	-0.03715	-0.14263	-0.36016
Log(fold change) Healthy siblings of patients (n=33)	1	1	1	1	1	1	1	1

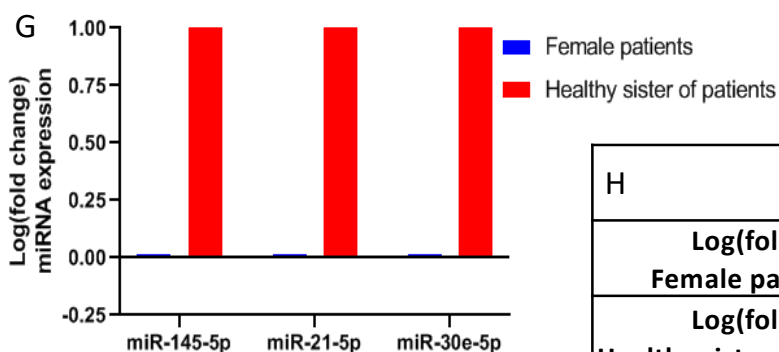
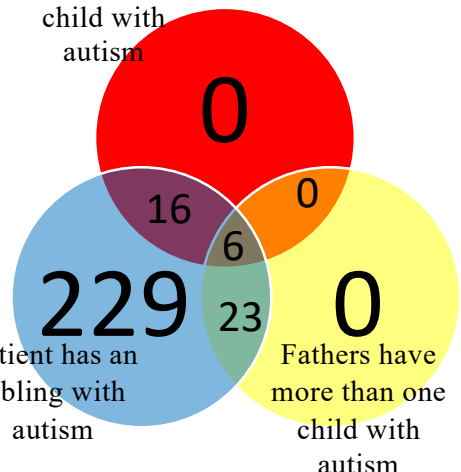


Fig.1d Female autism patients compared to the patients' sisters. 3 miRNAs (2 up- and 1 downregulated) were found as shown in the graph (G) and table (H).

H	miR-145-5p	miR-21-5p	miR-30e-5p
Log(fold change) Female patients (n=14)	0.013661	0.013045	-0.00342
Log(fold change) Healthy sister of patients (n=16)	1	1	1

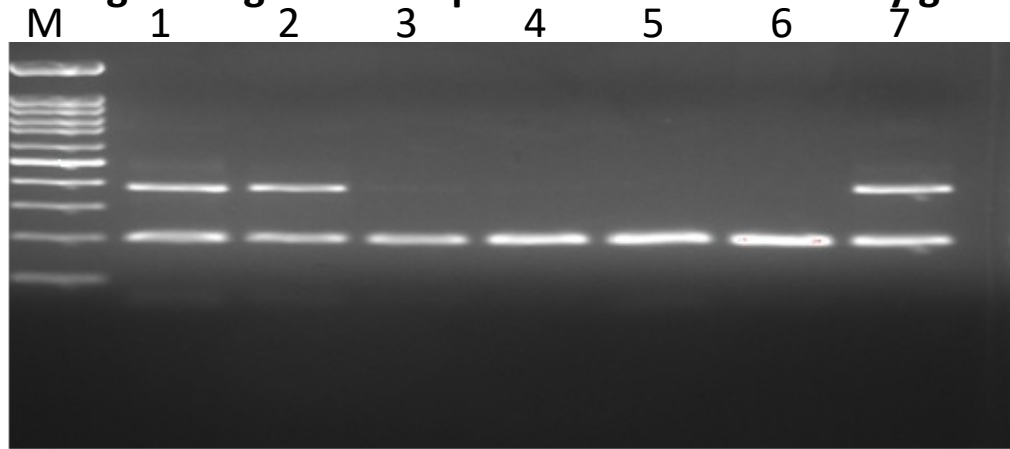
Groups	Number of common miRNAs	miRNAs
Fathers have more than one child with autism	6	miR-19a-3p (downregulated)
		miR-361-5p (downregulated)
Mothers have more than one child with autism		miR-3613-3p (downregulated)
		miR-150-5p (downregulated)
Patient has an sibling with autism		miR-126-3p (downregulated) miR-499a-5p (downregulated)
Fathers have more than one child with autism	23	miR-363-3p, miR-17-3p, miR-32-5p, miR-1193 miR-18a-3p, let-7b-5p, miR-3159, miR-1280 miR-202-3p, miR-605-5p, miR-9-5p, miR-143-3p, miR-1307-3p, miR-421, miR-126-3p, miR-11111, miR-18a-5p, miR-576-5p, miR-660-5p, miR-151a-3p, miR-1301-3p, miR-4301 and miR-4732-5p
Patient has an sibling with autism		
Mothers have more than one child with autism	16	miR-92a-3p, miR-130a-3p, miR-192-5p, miR-130b-3p, miR-16-5p, miR-19b-3p, miR-195-5p, miR-144-3p, miR-17-5p,NOTE miR-140-3p, miR-25-3p, miR-486-5p, miR-451a miR-425-5p, miR-30e-5p, miR-93-5p miR-629-5p, miR-942-5p, miR-181b-5p, miR-373-5p, miR-30a-3p, miR-495-3p, miR-4770 miR-548d-5p, miR-631 miR-337-3p, miR-1281 miR-433-3p, miR-34a-5p, miR-100-5p, miR-223-5p, miR-324-5p, miR-542-3p, miR-671-3p, miR-10a-5p, miR-1 miR-424-5p, miR-574-3p, miR-30e-3p, miR-378a-5p, miR-486-3p, miR-7-5p, miR-128-3p, miR-374b-5p,NOTE miR-4286 miR-103a-3p, miR-320b miR-339-3p, miR-184 miR-28-3p, miR-190a-5p, miR-26a-5p, miR-769-5p, miR-503-5p, miR-627-5p, miR-320e miR-183-5p, miR-422a miR-134-5p, miR-222-3p, miR-3911 miR-106b-5p miR-122-5p, miR-378g miR-324-3p, miR-744-5p, let-7i-5p, miR-3689a-5p,NOTE miR-423-3p, miR-375 miR-487a-3p, miR-181a-5p, miR-454-3p, miR-3646 miR-378h miR-29b-3p, miR-191-5p, miR-497-5p, miR-183-3p, miR-382-5p, miR-21-5p, miR-28-5p, miR-133b miR-4524a-3p, miR-15b-3p, miR-374a-5p, miR-181d-5p, miR-362-3p, miR-27a-3p, miR-101-3p, miR-1260a miR-4651 miR-152-3p, miR-3183 miR-329-3p, miR-125a-5p, miR-425-3p, miR-1180-3p, miR-4323 miR-1260b miR-615-5p, let-7e-5p, miR-151bNOTE miR-139-5p, miR-7-2-3p, miR-214-3p, miR-625-3p, miR-342-5p, miR-339-5p, miR-487b-3p, miR-550a-5p, miR-16-2-3p, miR-145-5p, miR-2110 miR-1976 miR-345-5p, miR-1207-5p, miR-146b-5p, miR-628-3p, miR-27b-3p, miR-505-3p, miR-365a-3p,NOTE miR-224-5p, miR-4732-3p, miR-3651 miR-301a-3p, miR-145-3p, let-7c-5p, miR-3191-3p, let-7a-3p, miR-4274 miR-125b-5p, miR-22-5p, miR-4422 miR-1587 miR-489-3p, miR-3120-3p, let-7f-1-3p, miR-1910-5p, miR-30d-5p, miR-7-1-3p, miR-23a-3p, miR-376c-3p, miR-369-3p, miR-181c-3p, miR-3131 miR-15a-5p, miR-532-5p, miR-185-5p, miR-199a-5p, miR-29a-3p, miR-4454 miR-188-5p, miR-99b-5p, miR-3610 miR-98-5p, miR-26b-5p, miR-296-5p miR-664a-3p, miR-219a-1-3p, miR-378a-3p, miR-590-5p, miR-338-3p, miR-20a-5p, miR-381-3p, miR-1237-3p, miR-331-3p, miR-92b-3p, let-7g-5p, miR-142-3p, miR-373-3p, miR-1287-5p, miR-30a-5p, miR-186-5p, miR-197-3p, miR-29c-3p, miR-223-3p, miR-15b-5p, miR-4538 miR-30c-5p, miR-4306 miR-15a-3p, miR-20b-5p, miR-22-3p, miR-328-3p, miR-4296 miR-885-5p, miR-340-5p, miR-342-3p, miR-326 miR-191-3p, miR-3200-5p, miR-23b-3p, miR-490-3p, miR-126-5p, miR-409-3p, miR-4505 miR-637 miR-485-3p, miR-4687-5p, miR-4291 miR-148b-3p, miR-21-3p, miR-1913 miR-215-5p, miR-132-3p, miR-200c-3p, miR-378b miR-877-5p, miR-200b-3p, miR-1233-3p, miR-502-3p, miR-148a-3p, miR-99a-5p, let-7d-3p, miR-194-5p, miR-151a-5p, miR-142-5p, miR-3923 miR-378i miR-4516 miR-335-5p, miR-301b miR-144-5p, miR-766-3p, miR-596 miR-484 miR-3185 miR-24-3p, miR-675-3p, miR-130b-5p, miR-652-3p, miR-199b-5p, miR-30b-5p, miR-146a-5p, miR-877-3p, miR-1247-5p, miR-1225-3p, let-7f-5p, miR-181c-5p, miR-206 let-7a-5p, miR-199a-3p,NOTE miR-519b-5p,NOTE miR-370-3p,
Patient has an sibling with autism		
Mothers have more than one child with autism	229	
Patient has an sibling with autism		
Fathers have more than one child with autism	229	

According to a p value<0.001 in the microRNA analysis, six common the “Six-miRNAs” were identified.

Supplementary Figure 11

Supplementary Figure 2

Agarose gel images of PCR products: *Cc2d1a* family genotyping.



Supplementary Fig.2 Lines 1, 2 and 7 are heterozygous for *Cc2d1a* gene (see primer in Materials and Methods). Two fragments are produced (200 and 400 base pair (bp)), lines 3, 4, 5 and 6 wild type normal diploid genotypes with only 200 bp fragment.

Normal (200 bp), heterozygote (200 and 400 bp), M: Marker (100-1500 bp)

Supplementary Fig. 3 miRNAs analysis in mouse Blood and Hippocampus

Raw data are presented in a graph and table for the 5p strand (6) and the 3p premicroRNA (5) of the “Six-miRNAs” differentially expressed. (founder generation).

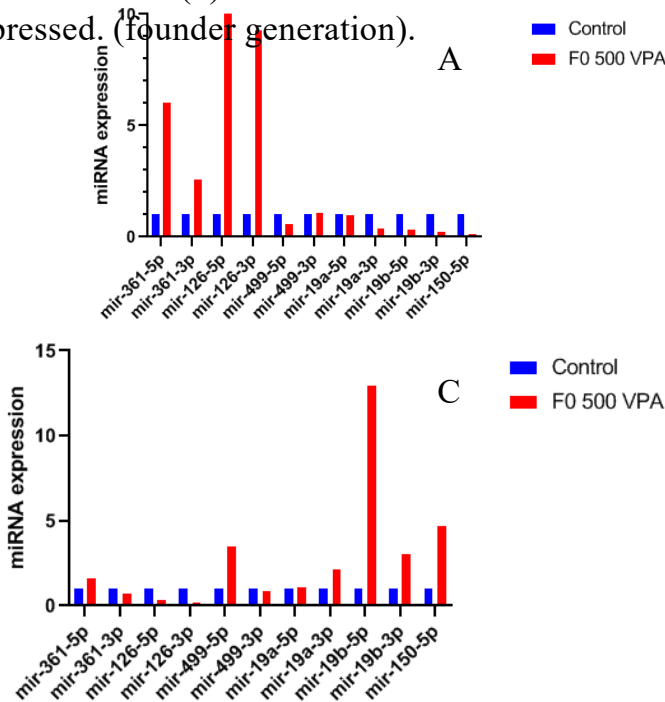
Supplementary

Fig.3a samples from VPA-treated males 500 mg/ml (founder generation).

Blood samples (A) graph (B) Table

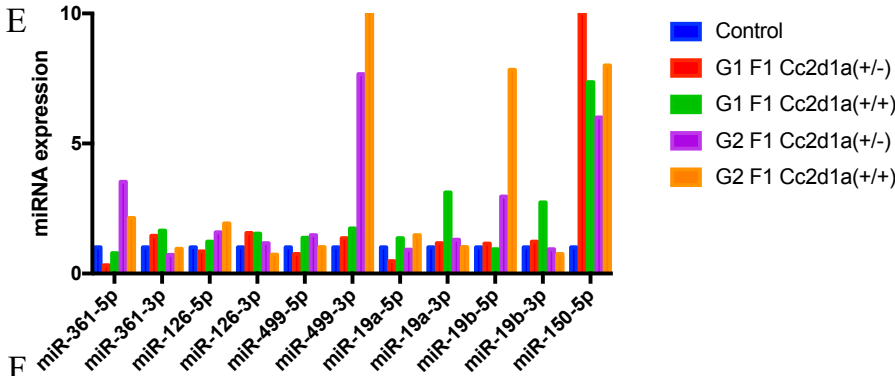
Supplementary Fig.3b

Hippocampus (C) graph (D) Table



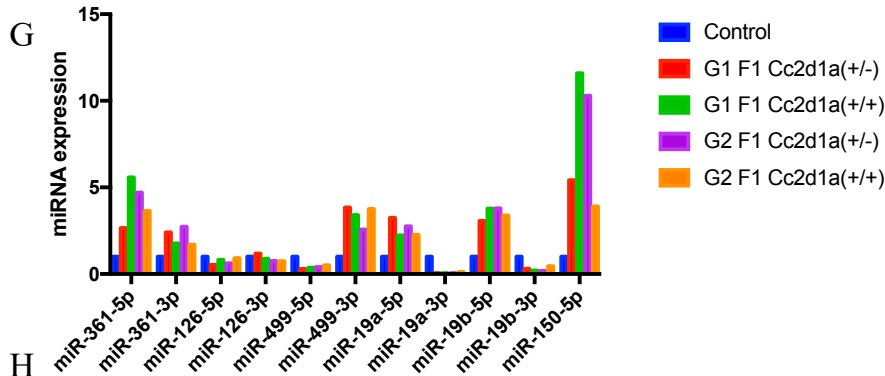
B	Fold Change 500 mg/kg VPA (n=5)	Fold Change Control (n=5)
miR-361-5p	6.026	1
miR-361-3p	2.560	1
miR-126-5p	11.086	1
miR-126-3p	9.297	1
miR-499-5p	0.585	1
miR-499-3p	1.057	1
miR-19a-5p	0.984	1
miR-19a-3p	0.352	1
miR-19b-5p	0.308	1
miR-19b-3p	0.244	1
miR-150-5p	0.118	1

D	Fold Change 500 mg/kg VPA (n=5)	Fold Change Control (n=5)
miR361-5p	1.61	1
miR361-3p	0.74	1
miR-126-5p	0.35	1
miR-126-3p	0.21	1
miR499-5p	3.49	1
miR499-3p	0.86	1
miR-19a-5p	1.06	1
miR-19a-3p	2.16	1
miR-19b-5p	12.94	1
miR-19b-3p	3.01	1
miR150-5p	4.67	1



Supplementary Fig.3c Blood samples (E) graph (F) Table males from the *Cc2d1a* +/- family group compared to the control.

	miR--361-5p	miR-361-3p	miR-126-5p	miR--126-3p	miR-499-5p	miR-499-3p	miR--19a-5p	miR--19a-3p	miR--19b5p	miR--19b-3p	miR-150-5p
Control (n=5)	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
G1 F1 Cc2d1a(+/-) (n=5)	0.32	1.45	0.85	1.56	0.75	1.36	0.48	1.17	1.15	1.23	10.00
G1 F1 Cc2d1a(+/+) (n=5)	0.79	1.65	1.23	1.54	1.38	1.74	1.36	3.12	0.94	2.74	7.36
G2 F1 Cc2d1a(+/-) (n=5)	3.53	0.72	1.59	1.17	1.48	7.67	0.92	1.30	2.96	0.94	6.00
G2F1 Cc2d1a(+/+) (n=5)	2.14	0.95	1.93	0.73	1.02	10.00	1.48	1.02	7.84	0.75	8.00

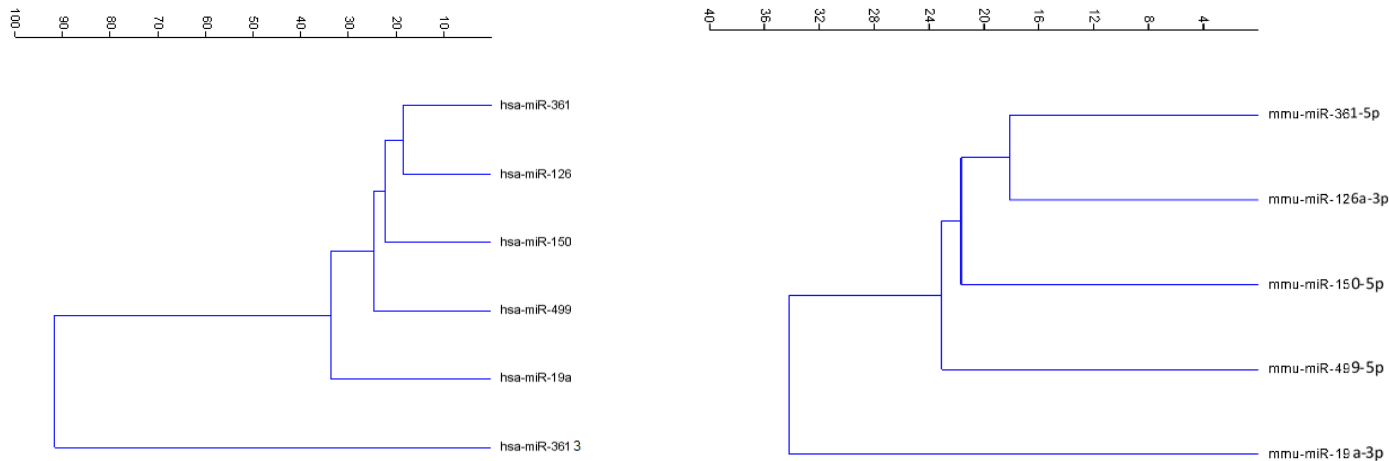
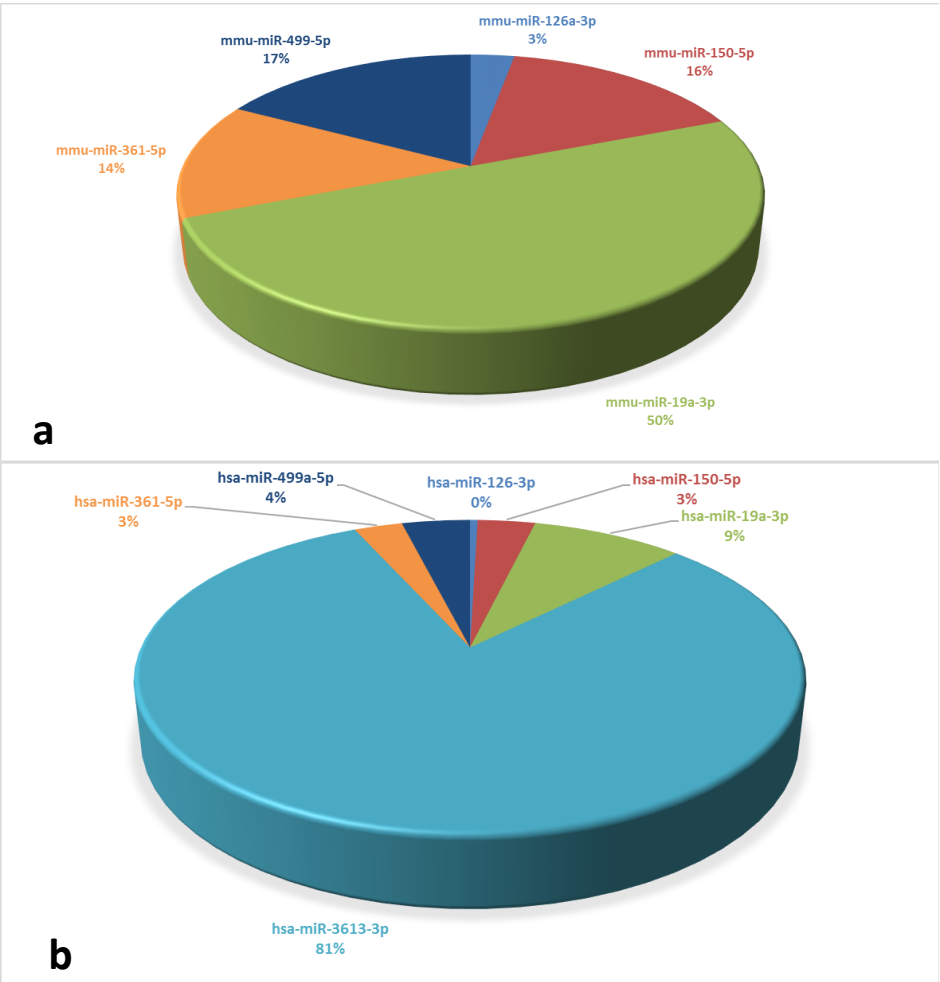


Supplementary Fig.3c Blood samples (G) graph (H) Table males from the *Cc2d1a* +/- family group compared to the control.

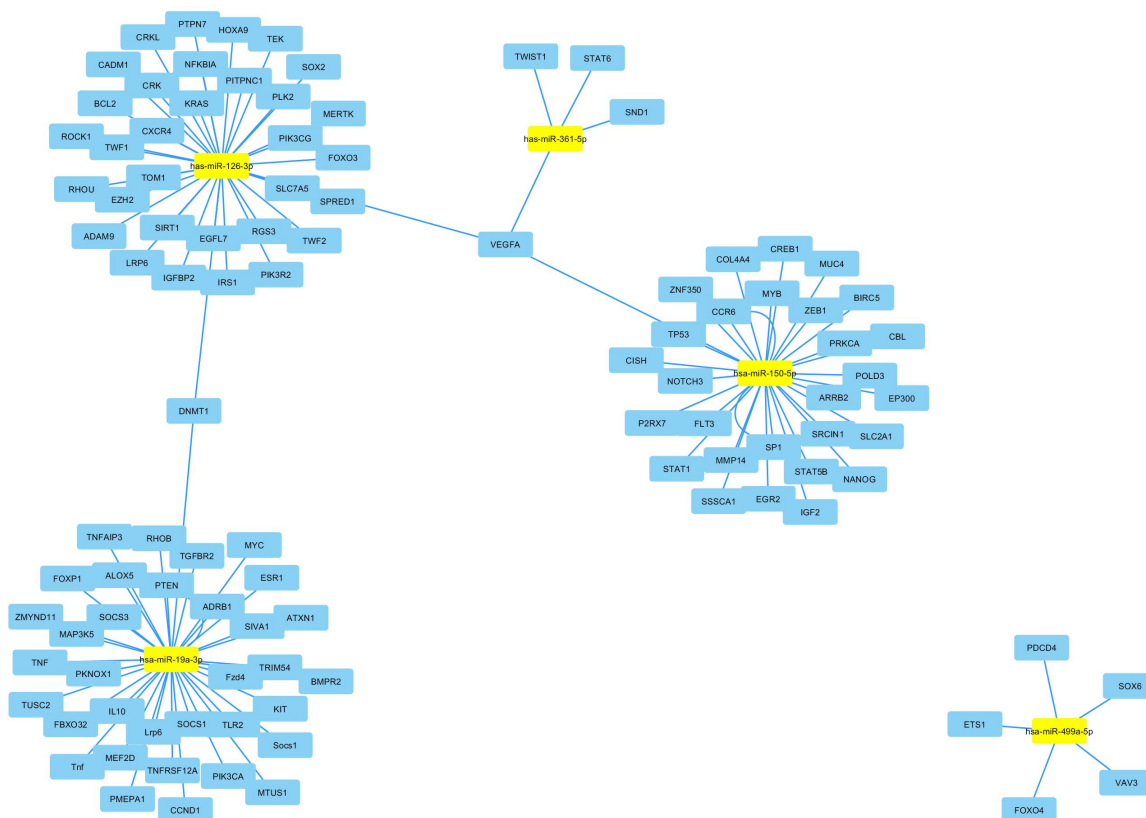
	miR--361-5p	miR-361-3p	miR-126-5p	miR--126-3p	miR-499-5p	miR-499-3p	miR--19a-5p	miR--19a-3p	miR--19b5p	miR--19b-3p	miR-150-5p
Control (n=5)	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
G1 F1 Cc2d1a(+/-) (n=5)	2.66	2.41	0.53	1.18	0.29	3.84	3.24	0.05	3.07	0.31	5.42
G1 F1 Cc2d1a(+/+) (n=5)	5.58	1.77	0.82	0.88	0.37	3.41	2.23	0.05	3.78	0.20	11.59
G2 F1 Cc2d1a(+/-) (n=5)	4.70	2.73	0.62	0.75	0.41	2.57	2.76	0.05	3.80	0.18	10.29
G2F1 Cc2d1a(+/+) (n=5)	3.64	1.69	0.92	0.74	0.50	3.76	2.27	0.12	3.38	0.45	3.91

Supplementary Fig. 4
Pie chart reflecting the relative percentages of newly identified miRNA target genes.

Predicted miRNA target genes in (a), *Mus musculus*, including miR-19a-3p, miR-361-5p, miR-150-5p, miR-126-3p, and miR-499a-5p and (b) *Homo sapiens*, including miR-19a-3p, miR-361-5p, miR-3613-3p, miR-150-5p, miR-126-3p, and miR-499a-5p. Mouse target genes for miR-3613-3p are unknown. Each group of predicted target genes of these miRNAs with conserved sites was selected from the most recently updated list from TargetScan7.2.



Supplementary Fig. 4c Hierarchical clustering dendrogram displaying the similarity between the genes targeted by each of six *Homo sapiens* miRNAs: miR-19a-3p, miR-361-5p, miR-3613-3p, miR-150-5p, miR-126-3p, and miR-499a-5p (left), and each of five *Mus musculus* predicted target microRNAs: miR-19a-3p, miR-361-5p, miR-150-5p, miR-126-3p, and miR-499a-5p (right). For both groups, the distinction between the miRNAs is based on the suggested target genes. The horizontal axis represents the distance between miRNA clusters. This demonstrates that each group of miRNAs in one cluster exhibits more common targeted genes or is very close together. As an example, mmu-miR-361-5p and mmu-miR-126-3p show more similarity, while hsa-miR-3613 appears to present more target genes than any of the other microRNAs. Predicted target genes with conserved sites were downloaded from TargetScan7.2.



Supplementary Fig. 4d- Visualization of miRNA-target interaction using miRTarBase network where yellow squares refer to miRNAs, while blue ones refer to their target genes. With this program, for five out of six miRs multiples target genes are found, but any target for miR-3613-3p.

Sequences of the “Six-microRNAs” which was found downregulated in all autistic children

miRNAs	Sequence
miR-19a-3p	GUGCAAUAUCUAUGCAAACUGA
miR-361-5p	UUAUCAGAAUCUCCAGGGGUAC
miR-3613-3p	UGUUGUACUUUUUUUUUUGUUC
miR-150-5p	UCUCCCAACCCUUGUACCAGUG
miR-126-3p	UCGUACCGUGAGUAAUAAUGCG
miR-499a-5p	UUAAGACUUGCAGUGAUGUUU

Supplementary Table 3 Numbers of animals under study after valproic acid

treatment (founder F0) and their progenies (F: Female, M: Male). At 14 days post birth, all offspring (8-12 pups from each litter) were injected (intraperitoneally) with sodium salt VPA at 300 to 700 mg/ml or with saline buffer as a control. Only 10 males were used for the behavioral tests and 5 for the miRNA evaluation.

[illegible]

Supplementary Table 4 Samples and list of miRNAs Samples and sequences of the microRNAs used in the mouse models.

Group Name	Behavioural Test	miRNA expression samples	Names of miRNAs	Sequences of miRNAs
F0 300 VPA	10 males from each group Novel object Social interaction Tail suspension Marble burying	5 males from each group Sperm Blood Hippocampus	mmu-miR-150-5p	UCUCCCAACCCUUGUACCAGUG
F0 400 VPA			mmu-miR-150-3p	CUGGUACAGGCCUGGGGGAUAG
F0 500 VPA			mmu-miR-126a-3p	UCGUACCGUGAGUAAUAAUGCG
F1 500 VPA			mmu-miR-126a-5p	CAUUAUUACUUUUGGUACGCG
Saline Control			mmu-miR-361-5p	UUAUCAGAAUCUCCAGGGGUAC
Control			mmu-miR-361-3p	UCCCCCAGGUGUGAUUCUGAUUUGU
Group1 <i>Cc2d1a</i> (+/+)			mmu-miR-499-5p	UUAAGACUUGCAGUGAUGUUU
Group1 <i>Cc2d1a</i> (+/-)			mmu-miR-499-3p	GAACAUCACAGCAAGUCUGUGCU
Group2 <i>Cc2d1a</i> (+/+)			mmu-miR-19a-3p	UGUGCAAAUCUAUGCAAAACUGA
Group2 <i>Cc2d1a</i> (+/-)			mmu-miR-19a-5p	UAGUUUUGCAUAGUUGCACUAC
Human Sperm (Father of two patients)	1 man	Sperm	mmu-miR-19b-3p	UGUGCAAAUCCAUGCAAAACUGA
Human Sperm Control	3 men	Sperm	mmu-miR-19b-1-5p	AGUUUUGCAGGUUUGCAUCCAGC

Supplementary Table 5 miRNAs gene target

Some of the candidate genes indicated to be involved in autism by in silico analysis share common microRNAs that target their transcripts and are mostly expressed at the early stage of development.

Gene	microRNA		Est in early embryos	
	Mouse	Human	Mouse	Human
<i>Nlgn1</i>		miR-495	+	+
<i>Pten</i>	miR-495 miR-19a miR-19b	miR-495 miR-19a	+	+
<i>Gabrb3</i>		miR-499	-	+
<i>Slc6a4</i>			-	-
<i>Fmr1</i>	miR-495 miR-19a miR-19b miR-499	miR-19a miR-19b miR-499	+	+
<i>Foxp2</i>	miR-19a miR-19b miR-499	miR-19a miR-19b miR-499	-	-
<i>Cadps2</i>	miR-495	miR-495 miR-499		+
<i>Cc2d1a</i>	miR-19a miR-19b		+	+