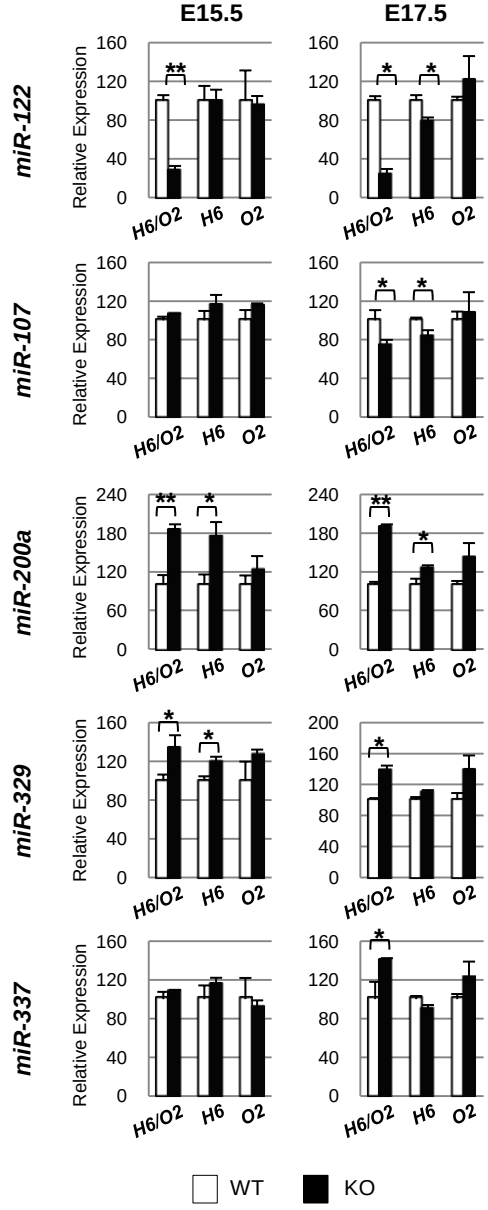
A

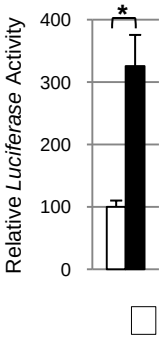
microRNA	H6O2 dKO/WT (Fold change)	p-values
mmu-miR-122a	0.15	9.4E-05
mmu-miR-200a	1.88	6.7E-04
hsa-miR-491-3p	0.88	1.2E-03
mmu-miR-292-5p	1.30	3.0E-03
mmu-miR-744	1.26	3.4E-03
hsa-miR-193a-5p	1.17	4.2E-03
mmu-miR-689	1.28	8.6E-03
mmu-miR-18	1.09	1.3E-02
mmu-miR-107	0.91	1.6E-02
mmu-miR-341	1.26	2.1E-02
mmu-miR-710	0.92	2.2E-02
mmu-miR-329	1.17	2.4E-02
mmu-miR-337	1.12	3.4E-02
hsa-miR-200b*	0.92	3.5E-02
mmu-miR-143	1.32	3.8E-02

B

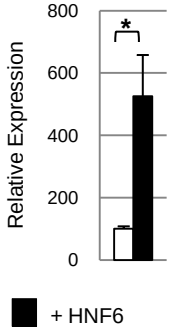


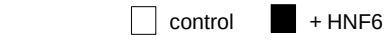
A

B ***miR-122 promoter (– 300 to +327)-Luc***

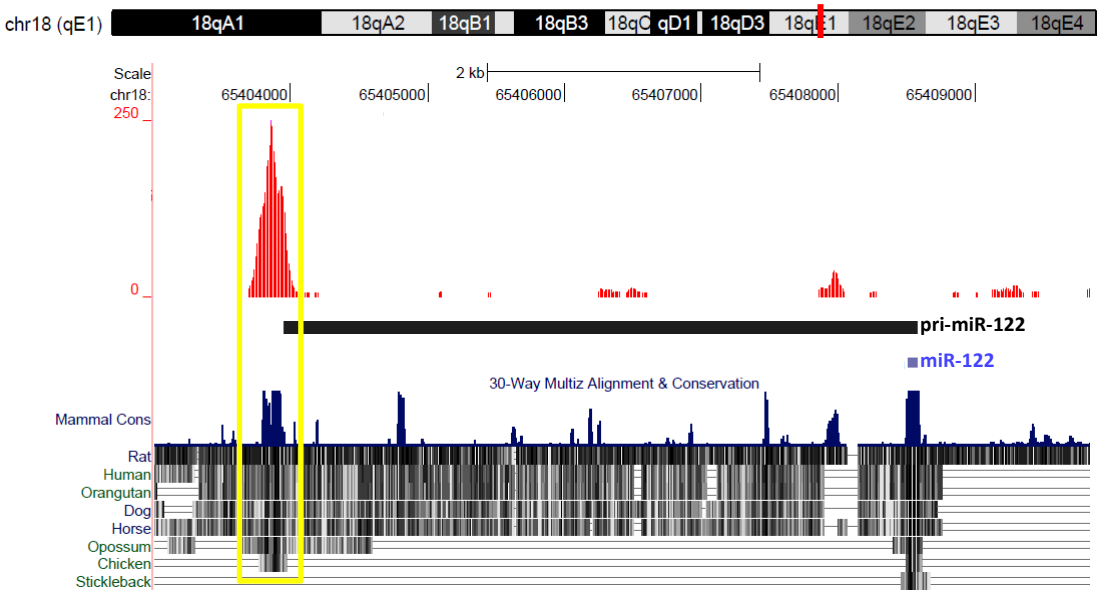


C ***Endogenous miR-122***

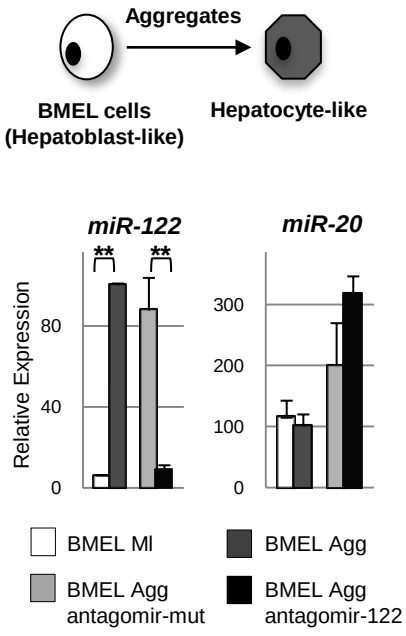




D



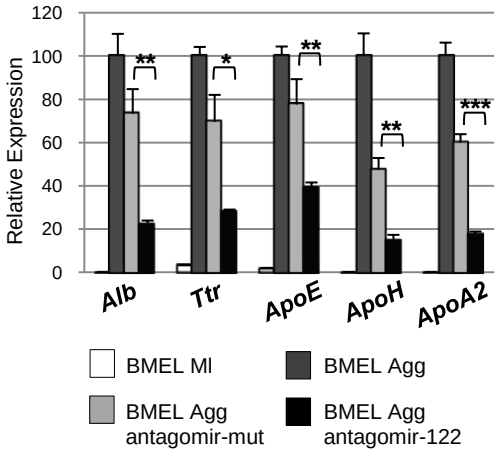
A



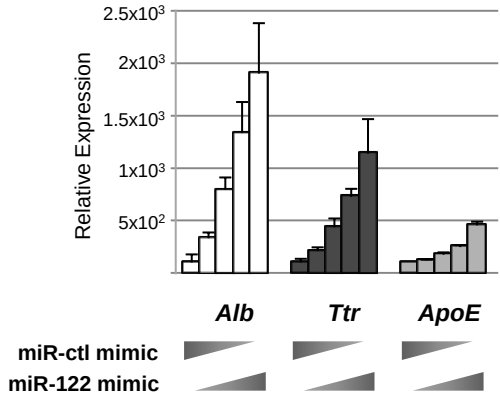
B

BMEL Agg antagomir-122/ antagomir-mut (Fold change)	Gene Symbol	Gene Title
0.51	Apoe	*apolipoprotein E*
0.53	Apoa2	*apolipoprotein A-II*
0.54	Alb	*albumin*
0.55	Apoh	*apolipoprotein H*
0.59	Itih2	*inter-alpha trypsin inhibitor, heavy chain 2*
0.64	Afm	*afamin*
0.64	Fgb	*fibrinogen. B beta polypeptide*
0.65	Itih4	*inter alpha-trypsin inhibitor, heavy chain 4*
0.66	Apoc1	*apolipoprotein C-I*
0.67	Pzp	*pregnancy zone protein*
0.71	Afp	*alpha fetoprotein*
0.71	Tff3	*trefoil factor 3, intestinal*
0.71	Apoa1	*apolipoprotein A-I*
0.71	Acat1	*acetyl-Coenzyme A acetyltransferase 1*
0.71	H19	*H19 fetal liver mRNA*
0.71	Gkn2	*gastrokine 2*
0.72	Fga	*fibrinogen, alpha polypeptide*
0.73	Ttr	*transthyretin*
0.73	Kng1	*kininogen 1*
0.73	Rdh7	*retinol dehydrogenase 7*
0.74	Gc	*group specific component*
0.74	Tff1	*trefoil factor 1 /// similar to pS2m*
0.77	Spp2	*secreted phosphoprotein 2*
0.78	Trf	*transferrin*

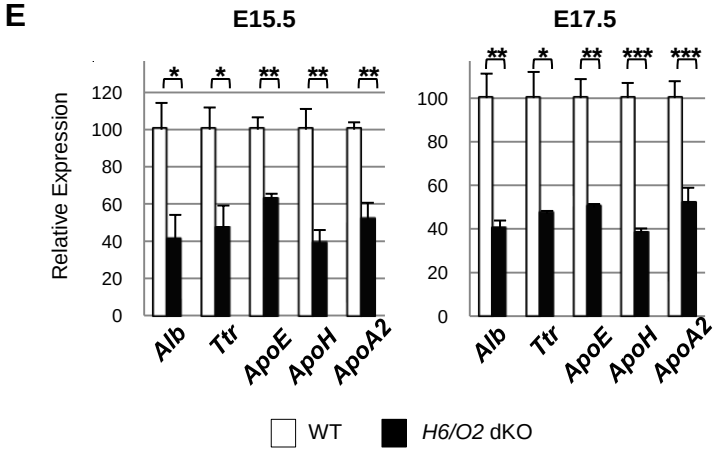
C

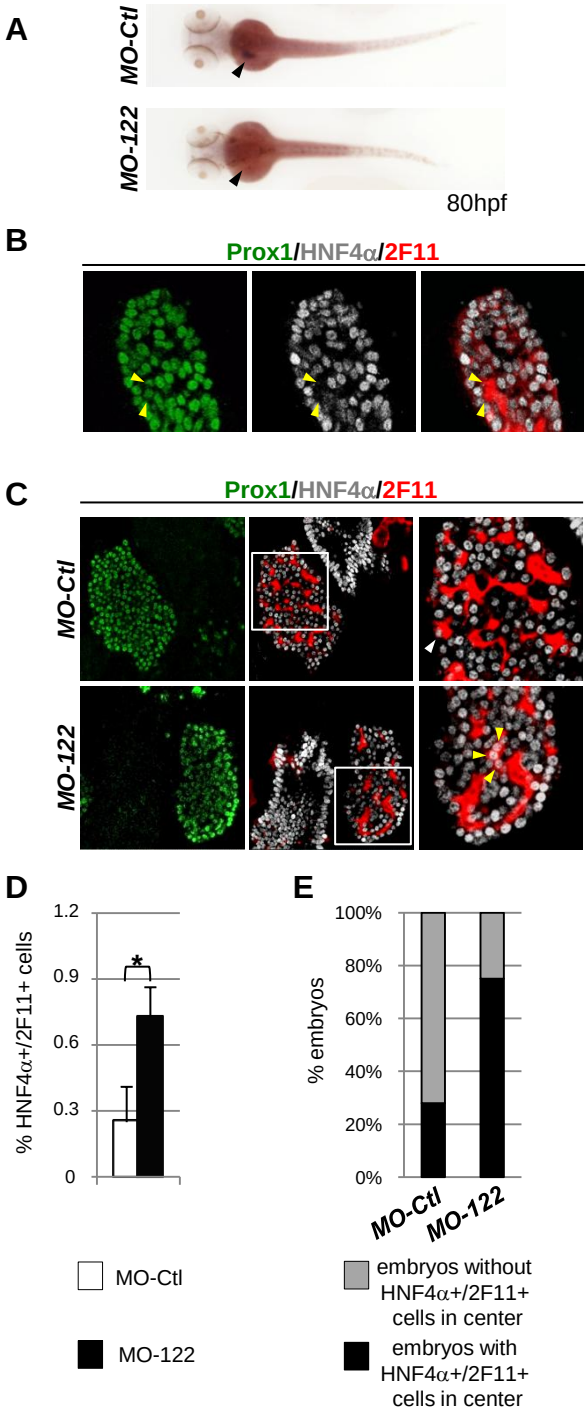


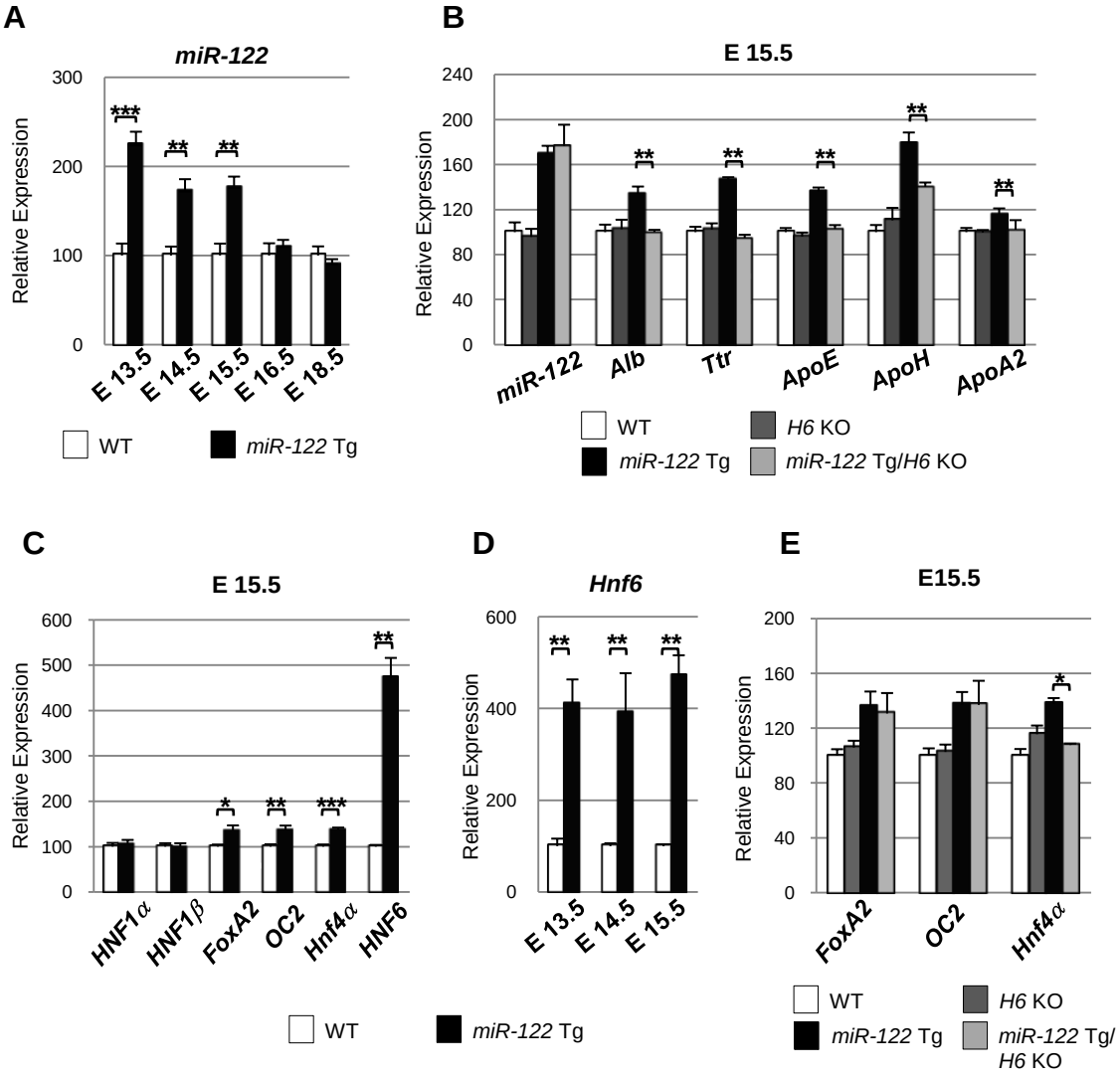
D

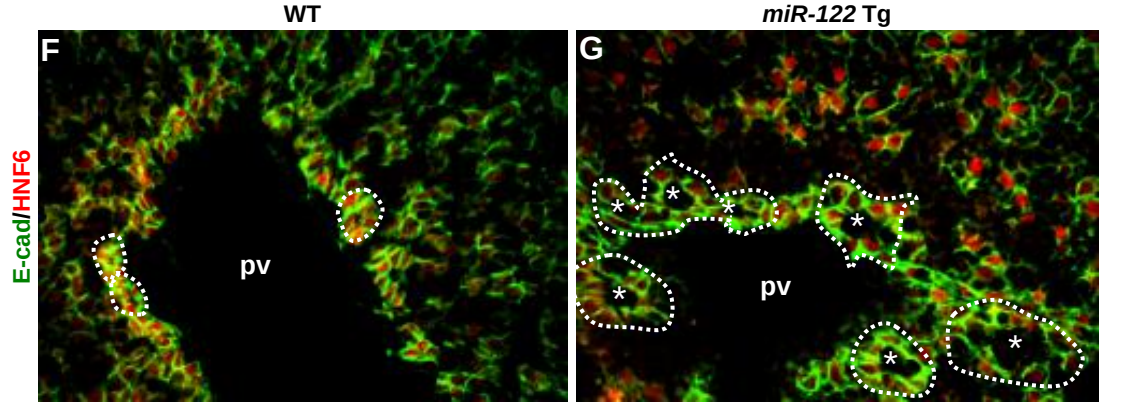


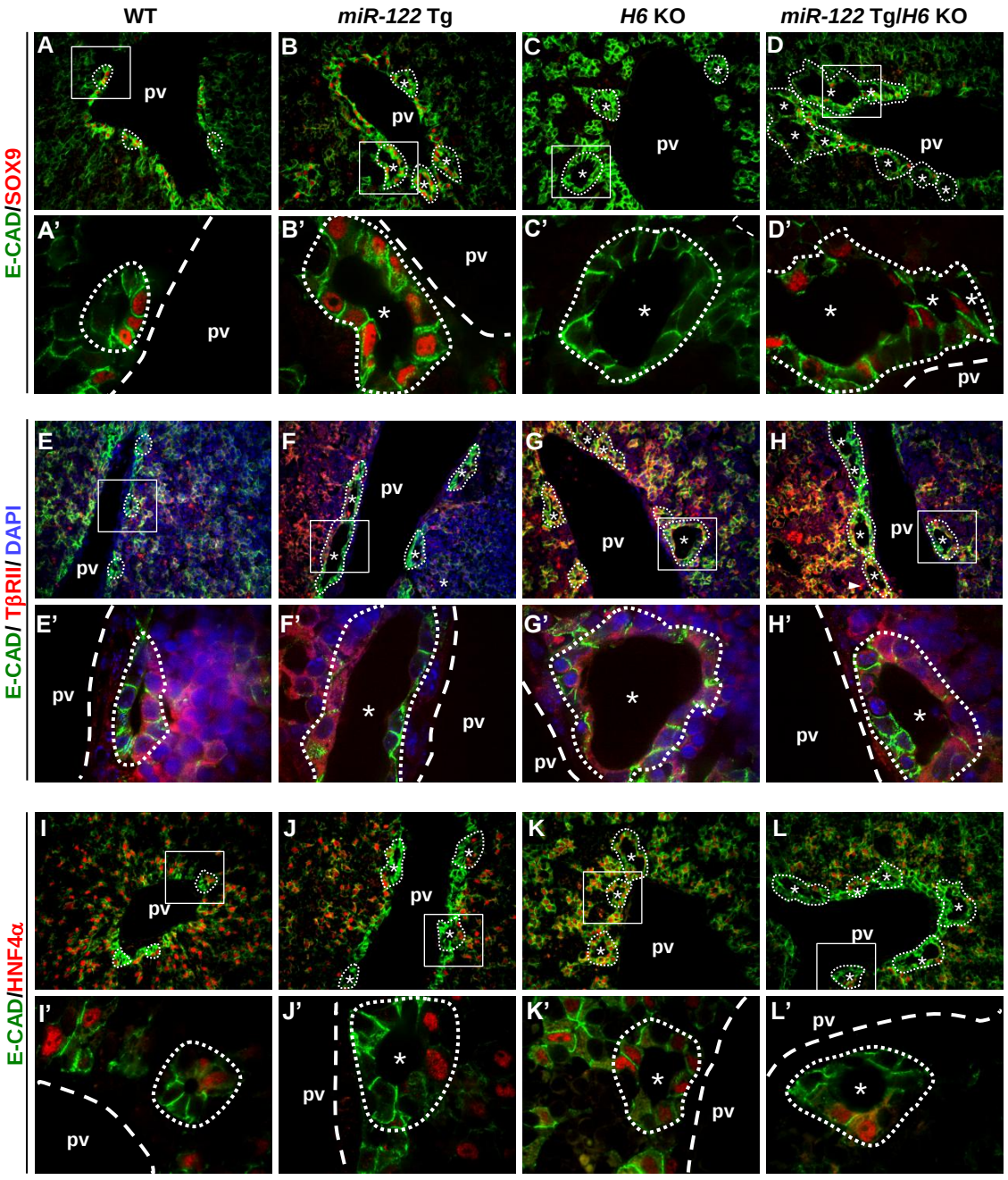
E



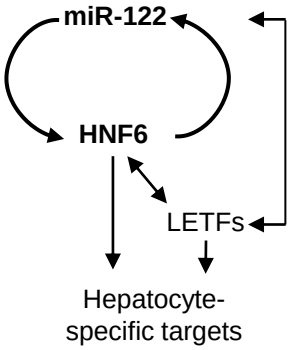

A
MO-Ctl
MO-122
80hpf
B
Prox1/HNF4α/2F11
C
Prox1/HNF4α/2F11
MO-Ctl
MO-122
D
% HNF4α+/2F11+ cells
1.2
0.9
0.6
0.3
0
*
MO-Ctl
MO-122
E
% embryos
100%
80%
60%
40%
20%
0%
MO-Ctl
MO-122
embryos without HNF4α+/2F11+ cells in center
embryos with HNF4α+/2F11+ cells in center


A
miR-122
Relative Expression
300
200
100
0
***
**
**
E 13.5
E 14.5
E 15.5
E 16.5
E 18.5
WT
miR-122 Tg
B
E 15.5
Relative Expression
240
200
160
120
80
40
0
**
**
**
**
**
miR-122
Alb
Ttr
ApoE
ApoH
ApoA2
WT
H6 KO
miR-122 Tg
miR-122 Tg/H6 KO
C
E 15.5
Relative Expression
600
500
400
300
200
100
0
*
**
***
**
HNF1α
HNF1β
FoxA2
OC2
Hnf4α
HNF6
WT
miR-122 Tg
D
Hnf6
Relative Expression
600
400
200
0
**
**
**
E 13.5
E 14.5
E 15.5
E
E15.5
Relative Expression
200
160
120
80
40
0
*
FoxA2
OC2
Hnf4α
WT
H6 KO
miR-122 Tg
miR-122 Tg/ H6 KO


WT
miR-122 Tg
E-cad/HNF6
F
G
pv
pv


WT
miR-122 Tg
H6 KO
miR-122 Tg/H6 KO
E-CAD/SOX9
E-CAD/ TβRII/ DAPI
E-CAD/HNF4α
A
A'
B
B'
C
C'
D
D'
E
E'
F
F'
G
G'
H
H'
I
I'
J
J'
K
K'
L
L'
pv

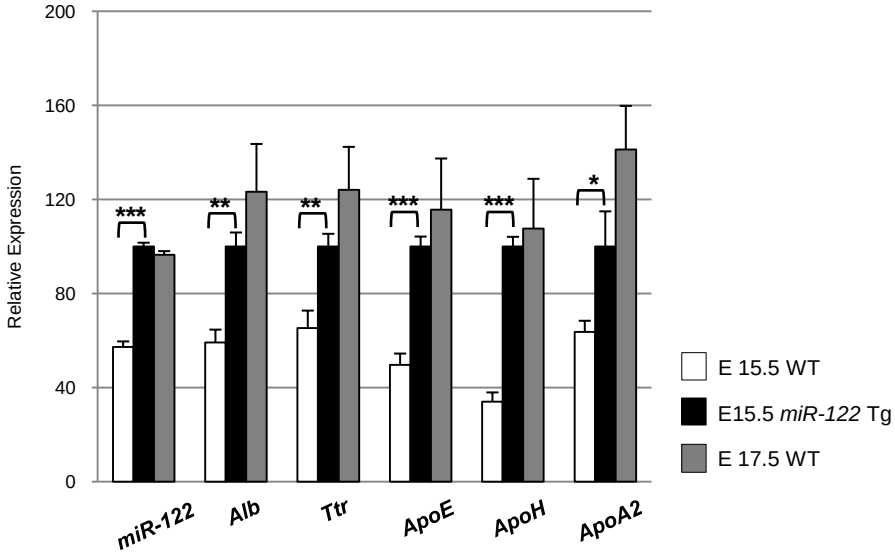
Laudadio-Fig. 7



Laudadio- Supplementary Fig. 1

BMEL Agg antagomir-122/ antagomir-mut (Fold change)	Gene Symbol	Gene Title
3.19	**Saa3**	*serum amyloid A 3*
2.93	**Lcn2**	*lipocalin 2*
2.83	**Clca4**	*chloride channel calcium activated 4*
1.83	**Cebpd**	*CCAAT/enhancer binding protein (C/EBP), delta*
1.60	**Tnfaip2**	*tumor necrosis factor, alpha-induced protein 2*
1.57	**Ccl20**	*chemokine (C-C motif) ligand 20*
1.52	**Idi1**	*isopentenyl-diphosphate delta isomerase*
1.52	**Mmp13**	*matrix metallopeptidase 13*
1.49	**Klhl2**	*kelch-like 2, Mayven (Drosophila)*
1.44	**Vnn3**	*vanin 3*
1.44	**Spink4**	*serine peptidase inhibitor, Kazal type 4*
1.41	**Zc3h12a**	*zinc finger CCCH type containing 12A*
1.39	**Oxct1**	*3-oxoacid CoA transferase 1*
1.37	**Nfkbiz**	*nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta*
1.37	**Nfkbia**	*nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor.,alpha*
1.32	**Hk2**	*hexokinase 2*
1.27	**Cdkn1a**	*cyclin-dependent kinase inhibitor 1A (P21)*
1.27	**Acat2**	*acetyl-Coenzyme A acetyltransferase 2*
1.27	**Pmaip1**	*phorbol-12-myristate-13-acetate-induced protein 1*
1.25	**Ctsc**	*cathepsin C*
1.21	**Dmbt1**	*deleted in malignant brain tumors 1*
1.19	**Abcc3**	*ATP-binding cassette, sub-family C (CFTR/MRP), member 3*
0.51	**Apoe**	*apolipoprotein E*
0.53	**Apoa2**	*apolipoprotein A-II*
0.54	**Alb**	*albumin*
0.55	**Apoh**	*apolipoprotein H*
0.59	**Itih2**	*inter-alpha trypsin inhibitor, heavy chain 2*
0.64	**Afm**	*afamin*
0.64	**Fgb**	*fibrinogen. B beta polypeptide*
0.65	**Itih4**	*inter alpha-trypsin inhibitor, heavy chain 4*
0.66	**Apoc1**	*apolipoprotein C-I*
0.67	**Pzp**	*pregnancy zone protein*
0.71	**Afp**	*alpha fetoprotein*
0.71	**Tff3**	*trefoil factor 3, intestinal*
0.71	**Apoa1**	*apolipoprotein A-I*
0.71	**Acat1**	*acetyl-Coenzyme A acetyltransferase 1*
0.71	**H19**	*H19 fetal liver mRNA*
0.71	**Gkn2**	*gastrokine 2*
0.72	**Fga**	*fibrinogen, alpha polypeptide*
0.73	**Ttr**	*transthyretin*
0.73	**Kng1**	*kininogen 1*
0.73	**Rdh7**	*retinol dehydrogenase 7*
0.74	**Gc**	*group specific component*
0.74	**Tff1**	*trefoil factor 1 /// similar to pS2m*
0.77	**Spp2**	*secreted phosphoprotein 2*
0.78	**Trf**	*transferrin*
0.78	**Gstm1**	*glutathione S-transferase, mu 1*
0.78	**F10**	*coagulation factor X*

Laudadio- Supplementary Fig. 2



Laudadio- Supplementary Fig. 3