

SUPPLEMENTAL DATA

SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1. Analysis of atherosclerosis in the aorta artery of experimental mouse model. *En face* staining of aortas from male C57BL/6 mice fed a standard diet, male $ApoE^{-/-}$ mice fed a STD and male $ApoE^{-/-}$ mice fed a HFD. Scale bar = 100 μ m. WT= Wild type group; STD= standard type diet; $ApoE^{-/-}$ = $ApoE$ deficient mice; HFD= high fat diet. WT STD 18wks (n=4); $ApoE^{-/-}$ STD 18wks (n=5); $ApoE^{-/-}$ HFD 18wks (n=4).

Supplemental Figure 2. Possible targets stood out after *in silico* analysis for both miR-155-5p and miR-143-3p. Venn diagram that represents the different results obtained for miR-155-5p (A) or miR-143-3p (B) in databases like miRDB, TargetScan and miRWalk. Graphics that show some possible targets for miR-155-5p (C) and miR-143-3p (D).

Supplemental Figure 3. Analysis of miR-155-5p in atherosclerotic diabetic and non-diabetic patients. The ACA patients were separated having into account if they have been diagnosed with diabetes or not. miR-155-5p expression was analysed by qPCR. FL=fibrolipidic plaque; ACA= advanced carotid atherosclerotic plaque. Healthy (n=3); fibrolipidic (n=5); ACA (non-diabetic) (n=8); ACA (diabetic) (n=6).

SUPPLEMENTAL TABLES

Supplemental Table 1. Clinical characteristics of patients bearing advanced carotid atherosclerosis (ACA)

	Patients (n=14)
Age, years	70 ± 7
Gender (male/female), %	71,4% / 28,6%
BMI (Kg/m²)	29,2 ± 6,3
Diabetes mellitus, %	42,9%
Hypertension, %	85,7%
Coronary artery disease, %	100%
Current smoking, %	35,70%

Supplemental Table 2. Primary antibodies used

Antibody	Dilution	Supplier	Reference	Technique
IGF-IIR (H-300)	1:1000	Santa Cruz Biotechnology	sc-25462	WB
				IHC
p-AKT (S473) (193H12)	1:1000	Cell Signalling Technology Inc	#4058	WB
AKT	1:1000	Cell Signalling Technology Inc	#9272	WB
				IHC
eNOS	1:1000	Merck Milipore	#07-520	WB
p85 α (EPR18702)	1:1000	Abcam	Ab191606	WB
Cleaved Caspase 3 (D175) β -Actin	1:1000	Cell Signalling Technology Inc	#9661	WB
	1:5000	Sigma Aldrich	A5441	WB

WB: Western-blot; IHC: Immunohistochemistry.

66 **Supplemental Table 3. Characterization of the mouse experimental model**

	WT STD 8 wks	<i>ApoE</i>^{-/-} STD 8 wks	<i>ApoE</i>^{-/-} HFD 8 wks	WT STD 18 wks	<i>ApoE</i>^{-/-} STD 18 wks	<i>ApoE</i>^{-/-} HFD 18 wks
Weight (g)	25,9±0,3	26,6±0,5	30,6±0,7 (****††††)	28,5±0,3	30,1±0,4 (††)	35,8±1,2 (††††§§§§)
Weight gain (g)	9,8±0,5	12,9±0,6 (***)	15,3±0,5 (****††)	12,8±0,6	15,8±0,6 (†††)	21,0±0,9 (††††§§§§)
Cholesterol (mg/dL)	96,4±6,5	188,9±16,8 (***)	209,8±2,1 (****)	117,5±3,9	201,9±8,3 (††††)	234,0±6,5 (††††§§)
Triglycerides (mg/dL)	49,2±4,9	84,8±9,5 (**)	88,5±6,7 (***)	30,7±3,1	72,8±8,1 (††)	86,4±5,4 (††††)

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68 This table collects the weight (g), weight gain (g), cholesterol (mg/dL) and triglycerides (mg/dL)
69 of the six mouse groups: WT fed with STD, and *ApoE*^{-/-} fed with STD and HFD at 8 and 18 weeks.
70 Statistical significance between the different groups was assessed with a two-tailed Student's t-
71 test., **p<0.01 vs. WT STD weeks, ***p<0.001 vs. WT STD weeks, ****p<0.0001 vs. WT STD
72 weeks. ††p<0.01 vs. *ApoE*^{-/-} STD 8 weeks; ††††p<0.0001 vs. *ApoE*^{-/-} STD 8 weeks; ††p<0.01 vs.
73 WT STD 18 wks; ††††p<0.001 vs *ApoE*^{-/-}STD 18 weeks

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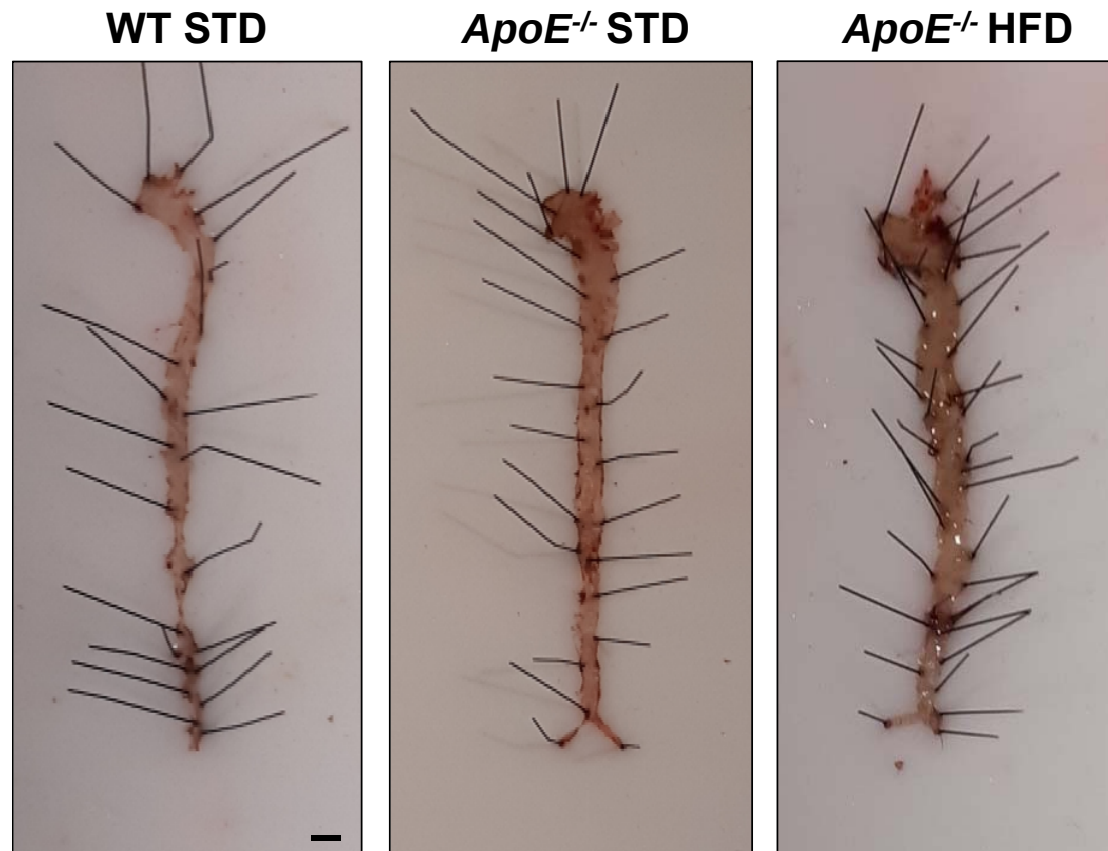
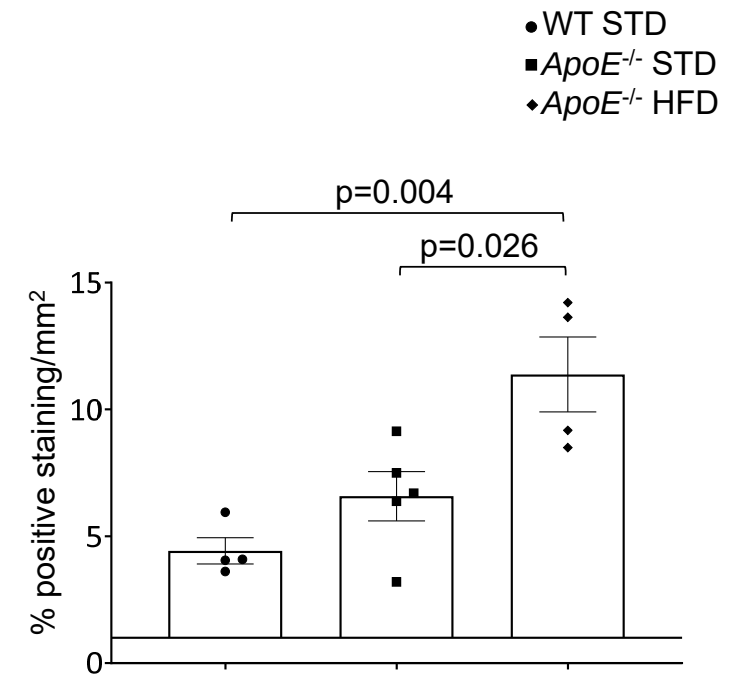
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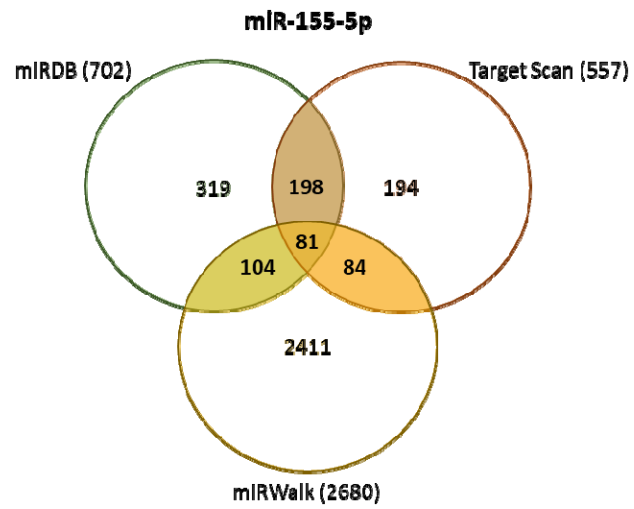
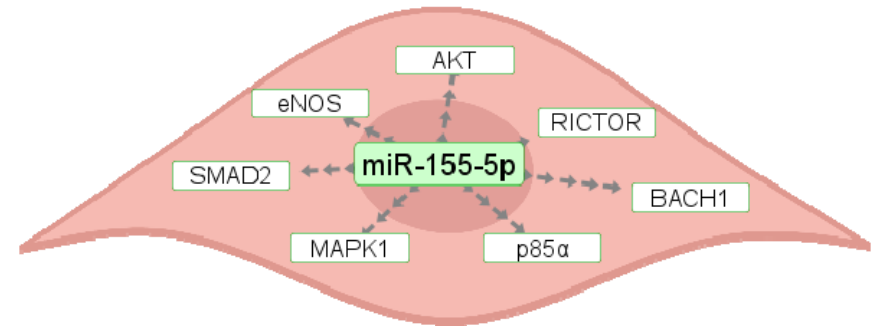
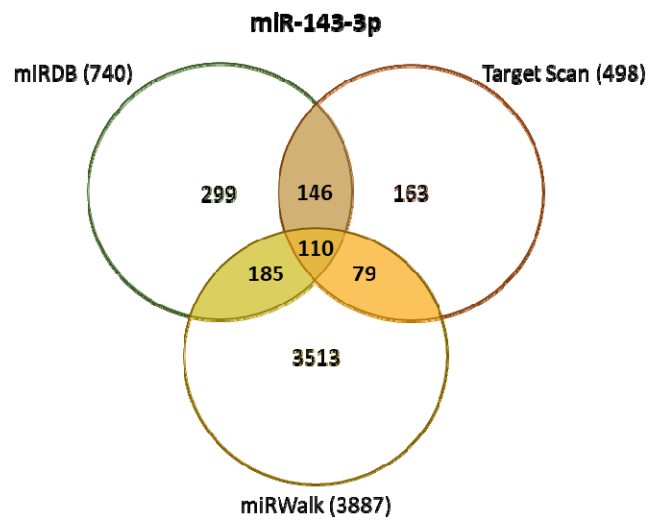
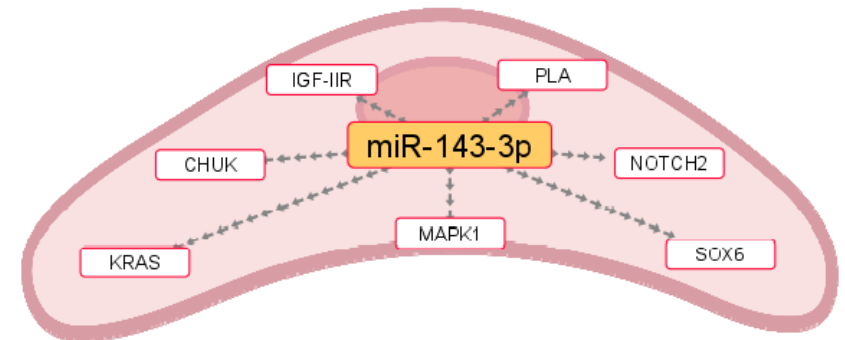
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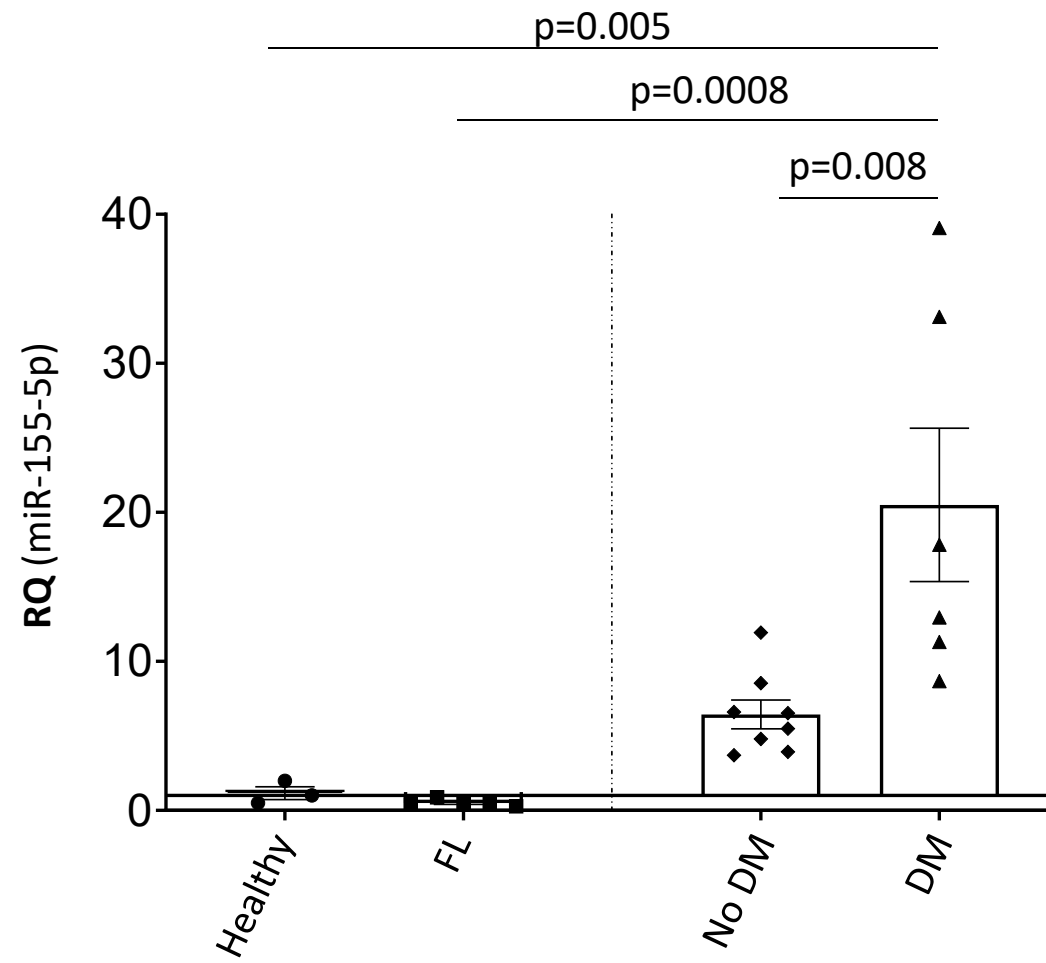
Supplemental Table 4. miRNAs studied in experimental atherosclerosis model and human atherosclerosis samples.

	8 weeks-fed mouse model		18 weeks-fed mouse model		Human samples	
miRNAs	Change	p value	Change	p value	Change	p value
Let-7c-5p	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	Upregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.035	Upregulation (ACA vs. Healthy)	0.230
	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999	Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. STD)	0.030	Upregulation (ACA Vs. FL)	0.332
Let-7d-5p	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.616	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.081	Upregulation (ACA Vs. Healthy)	0.753
	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999	Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.027	Upregulation (ACA Vs. FL)	0.641
Let-7g-5p	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.570		
	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999		
Let-7i-5p	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	Upregulation (ACA Vs. Healthy)	>0.999
	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.450	Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. STD)	0.021	Downregulation (ACA Vs. FL)	>0.999
miR-15b-5p	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.561	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999		
	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.640	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999		
miR-22-3p	Upregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999		
	Upregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.355	Upregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.697		
miR-26b-5p	Downregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.728	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	None (ACA Vs. Healthy)	>0.999
	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999	Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.056	None (ACA Vs. FL)	>0.999
miR-27b-3p	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999		
	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999	Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999		
miR-34a-5p	Downregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.459	Downregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999		
	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999	None (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999		
miR-145-5p			Downregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.274		
			Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.248		
miR-146b-5p	Downregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	Upregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.255		
	Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999	Upregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.784		
miR-149-5p	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	Upregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.015	Upregulation (ACA Vs. Healthy)	0.317
	Upregulation (<i>ApoE</i> ^{-/-} HFD Vs. STD)	0.043	Upregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.057	Undetermined data for FL	
miR-218-5p			Upregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.243		
			Upregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.976		
miR-223-3p	None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999	Downregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.600		
	Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.022	Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.460		
miR-301a-3p			None (<i>ApoE</i> ^{-/-} STD Vs. WT)	>0.999		
			Downregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	0.625		
miR-375-3p			Upregulation (<i>ApoE</i> ^{-/-} STD Vs. WT)	0.079		
			Upregulation (<i>ApoE</i> ^{-/-} HFD Vs. WT)	>0.999		

A**B****Supplemental Figure 1**

A**B****C****D**

Supplemental Figure 2



Supplemental Figure 3