

## Supplementary Materials: ARMCX3 Mediates Susceptibility to Hepatic Tumorigenesis Promoted by Dietary Lipotoxicity

Serena Mirra, Aleix Gavaldà-Navarro, Yasmina Manso, Mónica Higuera, Román Serrat, María Teresa Salcedo, Ferran Burgaya, José María Balibrea, Eva Santamaría, Iker Uriarte, Carmen Berasain, Matias A. Avila, Beatriz Mínguez, Eduardo Soriano and Francesc Villarroya

**Table S1.** Clinical characteristics of 24 patients of bariatric surgery used in the study.

Demographics		
Gender, n (%)	Male	45.8%
Age, median (range)		43.69 (58–20)
Race/Ethnicity, n (%)	Caucasian	70.8%
	Hispanic	29.2%
Histology		
NASH CRN	1/8	16.6%
	2/8	8.33%
	3/8	12.5%
	4/8	33.33%
	5/8	4.16%
	6/8	4.16%
	7/8	8.33%
	8/8	4.16%
Fibrosis	F0	15%
	F1	48%
	F2	37%
Laboratory values		
Bilirubin mg/dL, median (range)		0.65 (0.69–0.61)
Albumin g/L, median (range)		3.86 (4.34–2.9)
Diabetes		16.6%
Dyslipidemia		29.2%
Hypertension		41.7%

**Table S2.** Clinical characteristics of the 19 control patients.

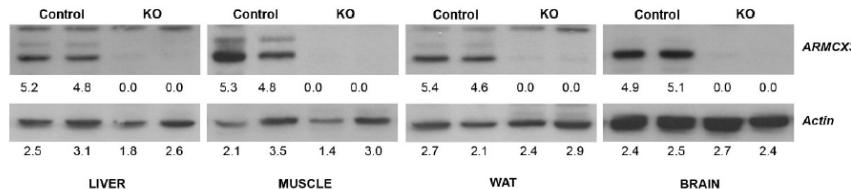
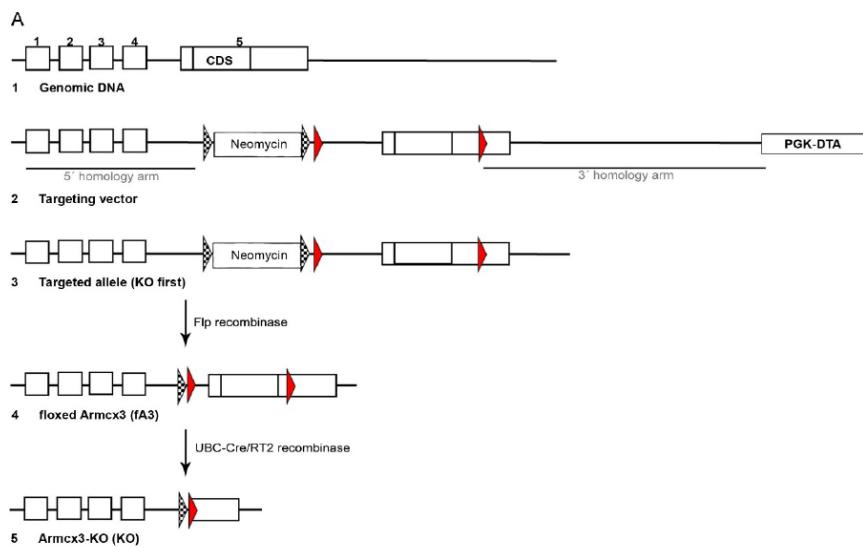
Demographics.		
Gender, n (%)	Male	85%
Age, median (range)		62.9 (76–47)
Race/Ethnicity, n (%)	Caucasian	92%
	Hispanic	8%
Laboratory values		
Bilirubin mg/dL, median (range)		0.43 (0.71–0.28)
Albumin g/L, median (range)		3 (4.4–2.3)
Diabetes		26%
Dyslipidemia		8%
Hypertension		23%

**Table S3.** Liver function tests in fArmcx3/Cre- (Control) and ARMCX3-KO (KO) mice fed low-fat diet (LFD) or high-fat diet (HFD) for 16 weeks. ALP, alkaline phosphatase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase. Mean  $\pm$  SEM ( $n = 6\text{--}8$ ).

header	Control LFD	Control HFD	KO LFD	KO HFD	ANOVA Control v. KO	ANOVA LFD v. HFD
ALP activity (U/L)	11.1 $\pm$ 1.6	13.0 $\pm$ 1.7	9.9 $\pm$ 0.5	9.6 $\pm$ 0.8	$p = 0.19$	$p = 0.64$
AST activity (U/L)	183 $\pm$ 41	232 $\pm$ 23	190 $\pm$ 37	175 $\pm$ 26	$p = 0.50$	$p = 0.64$
LDH activity (U/L)	914 $\pm$ 232	1093 $\pm$ 205	820 $\pm$ 74	897 $\pm$ 86	$p = 0.52$	$p = 0.57$

**Table S4.** Liver function tests in fArmcx3/Cre- (Control) and ARMCX3-KO (KO) mice treated with DEN and fed low-fat diet (LFD) or high-fat diet (HFD) for 24 weeks. ALP, alkaline phosphatase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase. Mean  $\pm$  SEM ( $n = 9\text{--}13$ ).

header	Control LFD	Control HFD	KO LFD	KO HFD	ANOVA Control v. KO	ANOVA LFD v. HFD
ALP activity (U/L)	12.3 $\pm$ 1.1	12.8 $\pm$ 3.5	10.7 $\pm$ 0.8	10.9 $\pm$ 0.8	$p = 0.39$	$p = 0.85$
AST activity (U/L)	189 $\pm$ 13	262 $\pm$ 29	202 $\pm$ 24	267 $\pm$ 41	$p = 0.75$	$p = 0.02$
LDH activity (U/L)	897 $\pm$ 95	903 $\pm$ 151	664 $\pm$ 93	1016 $\pm$ 141	$p = 0.62$	$p = 0.15$



**Figure S1.**

Comentari [M1]: Please add a header

Comentari [M2]: Should it be vs.?

Comentari [M3]: Please check if it is right.

Comentari [M4]: Please add a header

Comentari [M5]: Please add a figure legend.

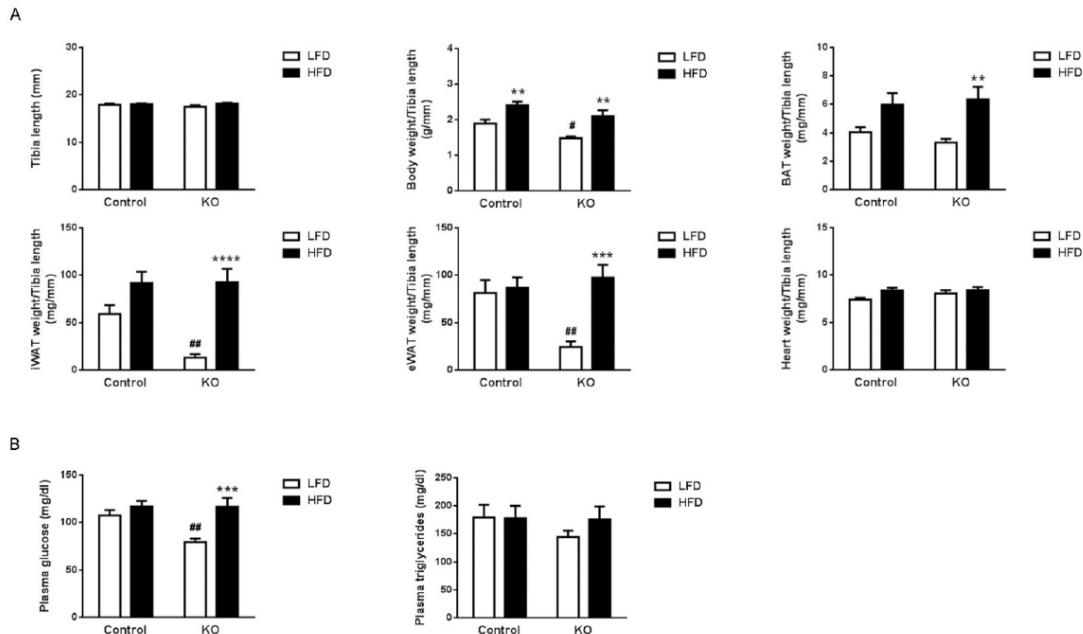
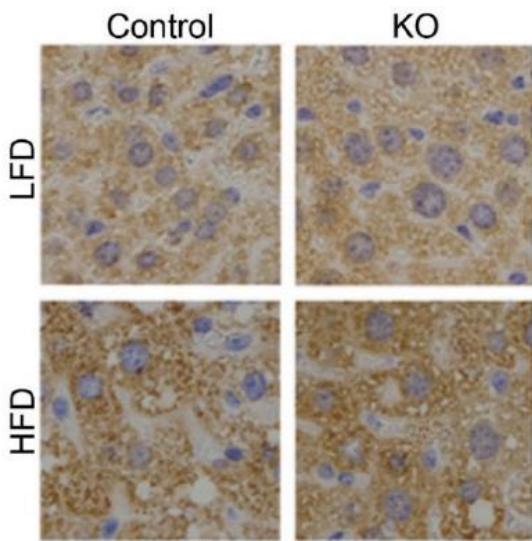
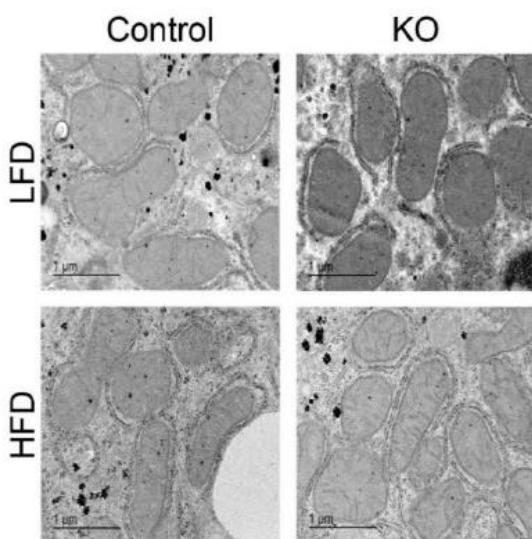


Figure S2.

**Comentari [M6]:** Please add a figure legend.

**A****B****Figure S3.**

**Comentari [M7]:** Please add a figure legend.

<b>Query ID</b>	<a href="#">NP_808817.1</a>
<b>Description</b>	armadillo repeat-containing X-linked protein 3 [Homo sapiens]
<b>Molecule type</b>	amino acid
<b>Query Length</b>	379
<b>Subject ID</b>	<a href="#">NP_082146.2</a>
<b>Description</b>	armadillo repeat-containing X-linked protein 3 [Mus musculus]
<b>Molecule type</b>	amino acid
<b>Subject Length</b>	379
<b>Program</b>	BLASTP 2.9.0+ ▾ <a href="#">Citation</a>

Range 1: 1 to 379 <a href="#">GenPept</a> <a href="#">Graphics</a>				
Score	Expect	Method	Identities	Positives
652 bits(1682)	0.0	Compositional matrix adjust.	366/379(97%)	371/379(97%)
				0/379(0%)
Query 1	MGYARKVGVIVTAGLVIGAGACYCIYRLTRGRKQNKEKMAEGGSGDVDDAGDCSGARYNDW		60	
Sbjct 1	MGYARKVGVIVTAGLVIGAGACYCIYRLTRGRKQNKEKMAEGGSGDVDDAGDCSGARYNDW		60	
Query 61	sdddddsNESKSIVWYPPWarigteagtrararararararraraVOKRASPNSDDTVLSP		120	
Sbjct 61	SDDDDDSNEKSIVWYPPWarigTEA7RARARARARARRAVQKRASPNSDDTVLSP		120	
Query 121	QELOQVVLCLVEMSEKPYILEAALIALGNNAAYAFNRDIIRDLGLGLPIVAKILNTRDPIVK		180	
Sbjct 121	QELOQVVLCLVEMSEKPYILEAALIALGNNAAYAFNRDIIRDLGLGLPIVAKILNTRDPIVK		180	
Query 181	EKALIVLNILSVNAENQRRLKVYMMQVCDDTITSRLNSSVQLAGLRLLTNMVTNEYQHM		240	
Sbjct 181	EKALIVLNILSVNAENQRRLKVYMMQVCDDTITSRLNSSVQLAGLRLLTNMVTNEYQHM		240	
Query 241	LANSISDFRRLFSAGNEETKLqlvkllln1AENPAMTRELLRAQVPSSLGSLFNKKENKE		300	
Sbjct 241	LANSISDFRRLFSAGNEETKLqlvkllln1AENPAMTRELLRAQVPSSLGSLFNKKENKE		300	
Query 301	VILKLLVIFENINDNFKEEENEPTQNQFGEGLSFLFFLKEFQVCADKVLGIESHHDFLVKV		360	
Sbjct 301	VILKLLVIFENINDNFKEEENEPTQNQFGEGLSFLFFLKEFQVCADKVLGIESHHDFLVKV		360	
Query 361	KVGKFMAKLAEHMFPKSQE	379		
Sbjct 361	KVGKF+AKL E MFPKSQE	379		

Figure S4.

**Comentari [M8]:** Please add a figure legend.

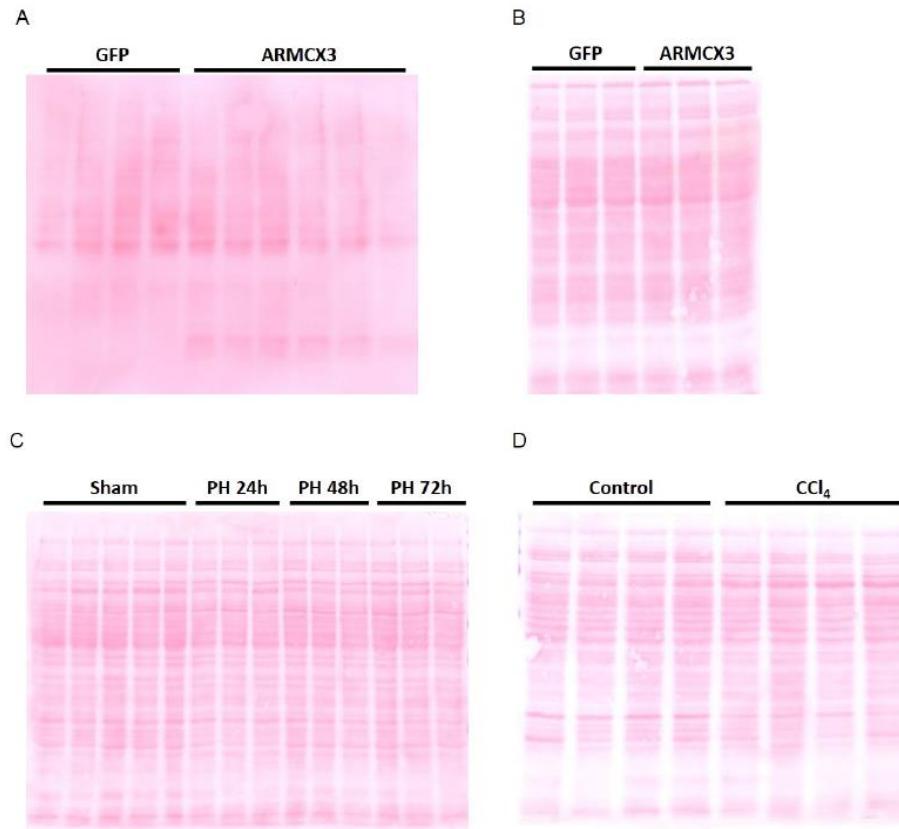
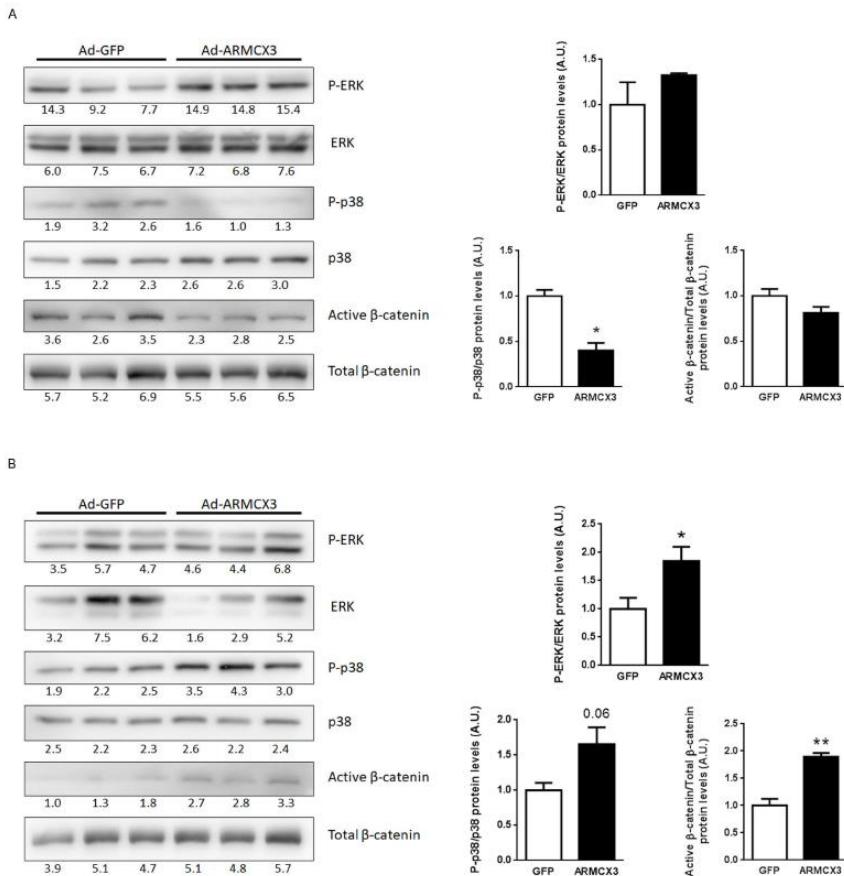


Figure S5.

**Comentari [M9]:** Please add a figure legend.

**Figure S6.**

**Comentari [M10]:** Please add a figure legend. Please add the reference of Figure S6 in the main text.