

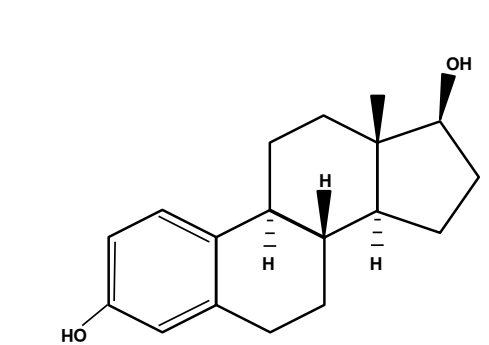
Respective role of nuclear versus membrane ERα in the vasculoprotective effect of estrogens

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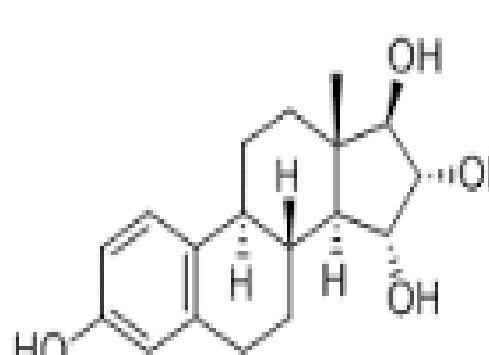
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Background

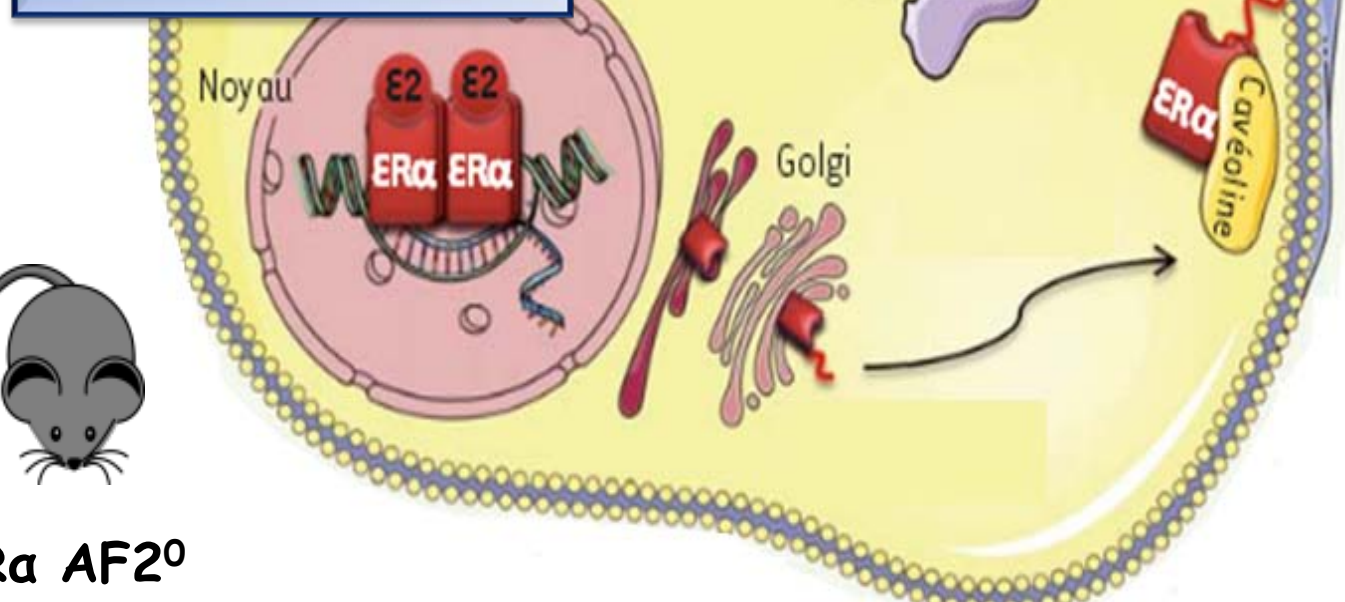
E2: 17β-Estradiol



E4: Estetrol

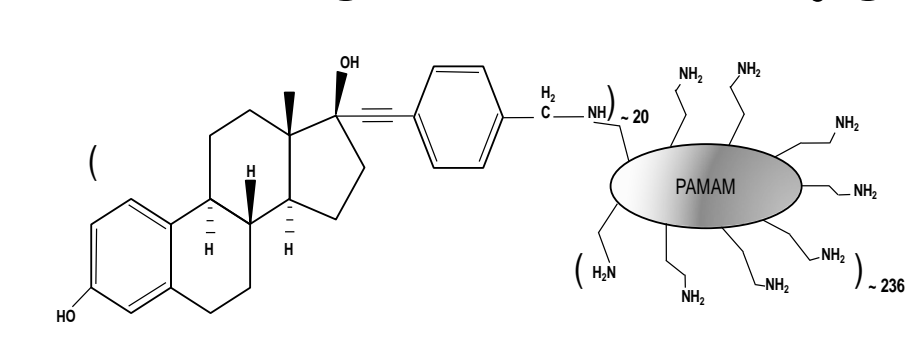


Genomic Effect

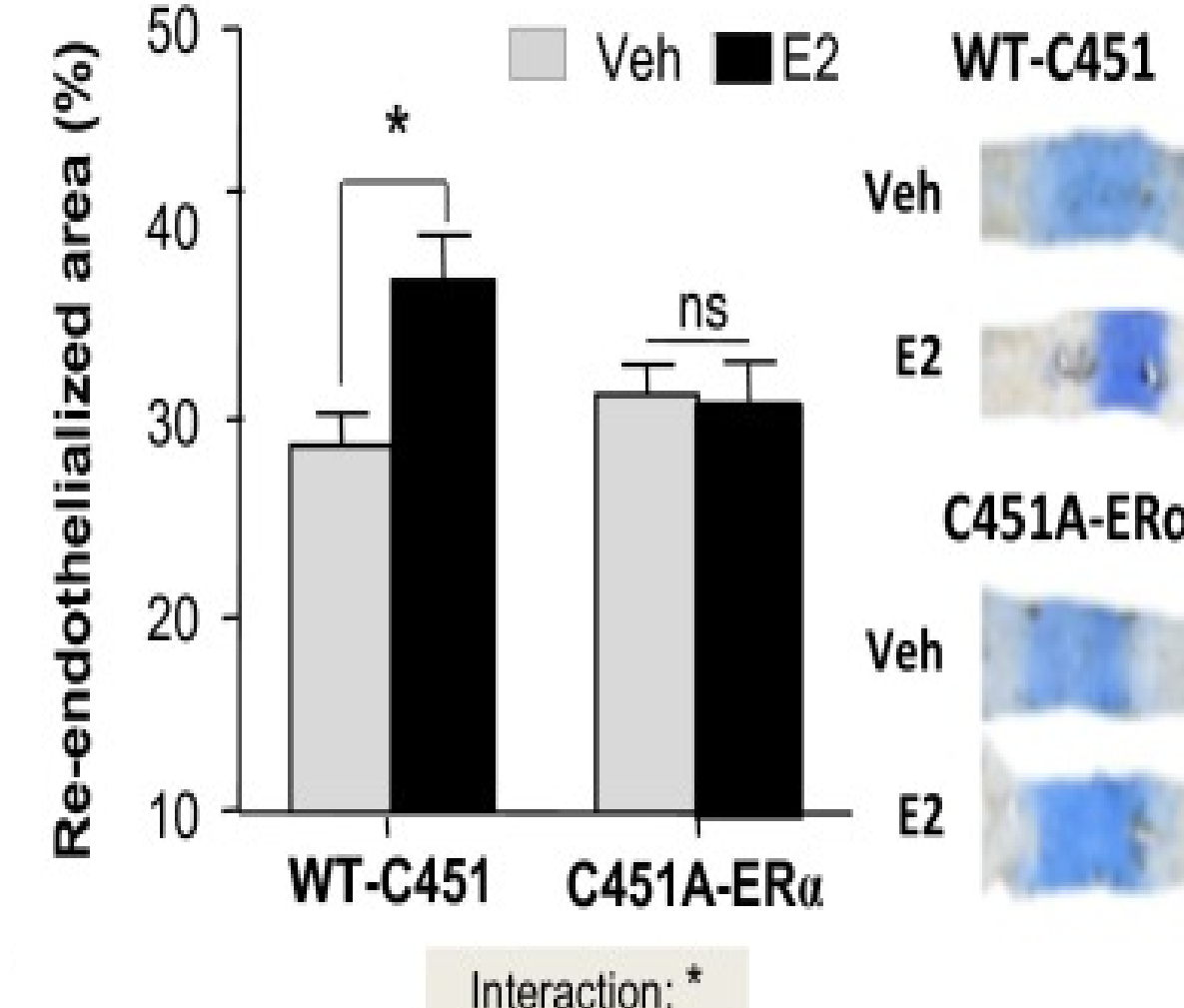
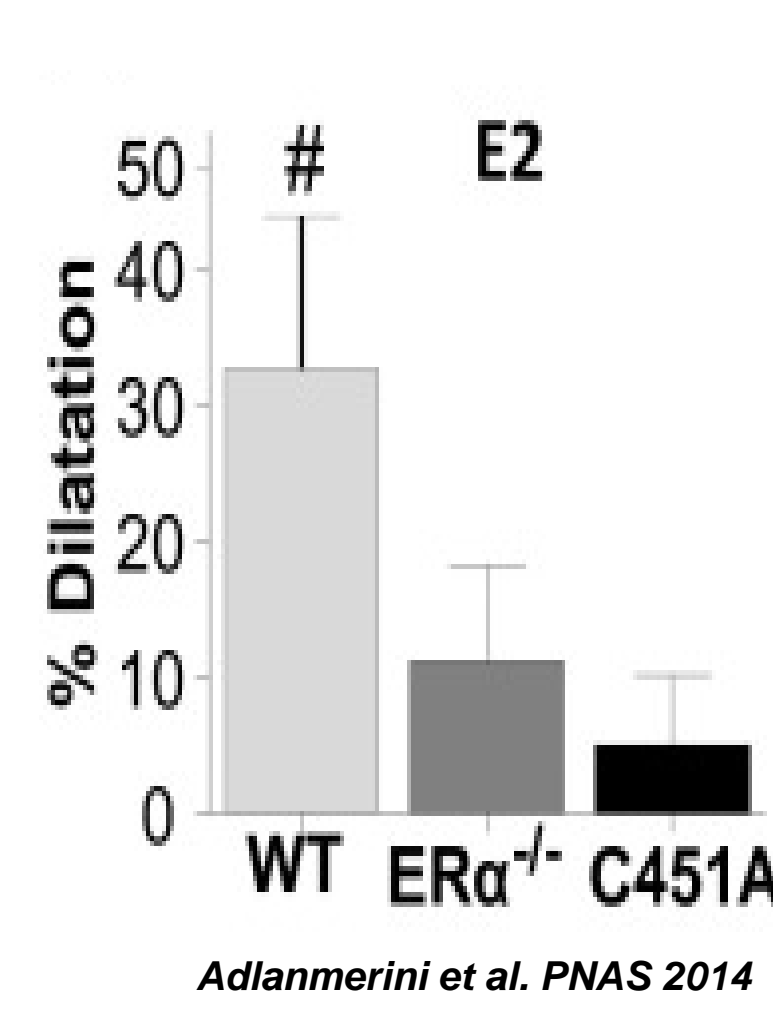
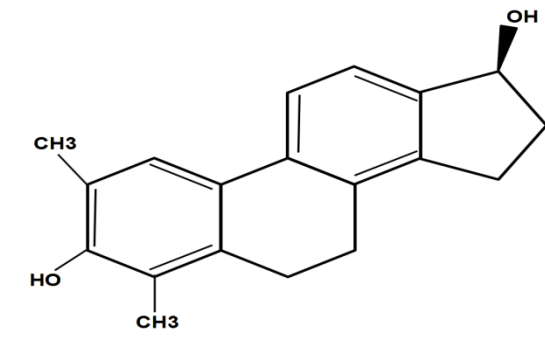


Membrane Initiated steroid Signaling (MISS)

EDC : Estrogen dendrimer conjugated



PaPE : Pathway Preferential Estrogens

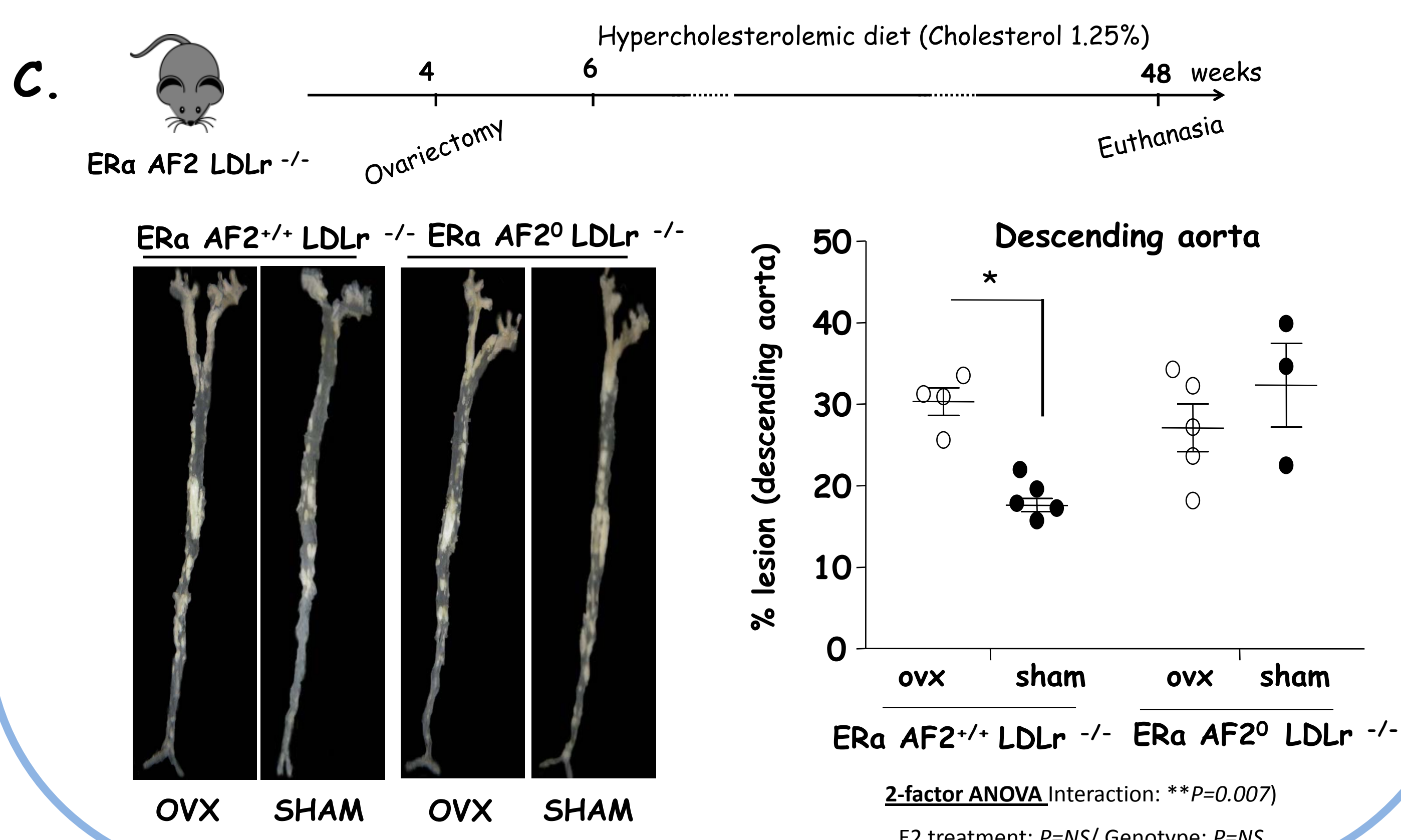
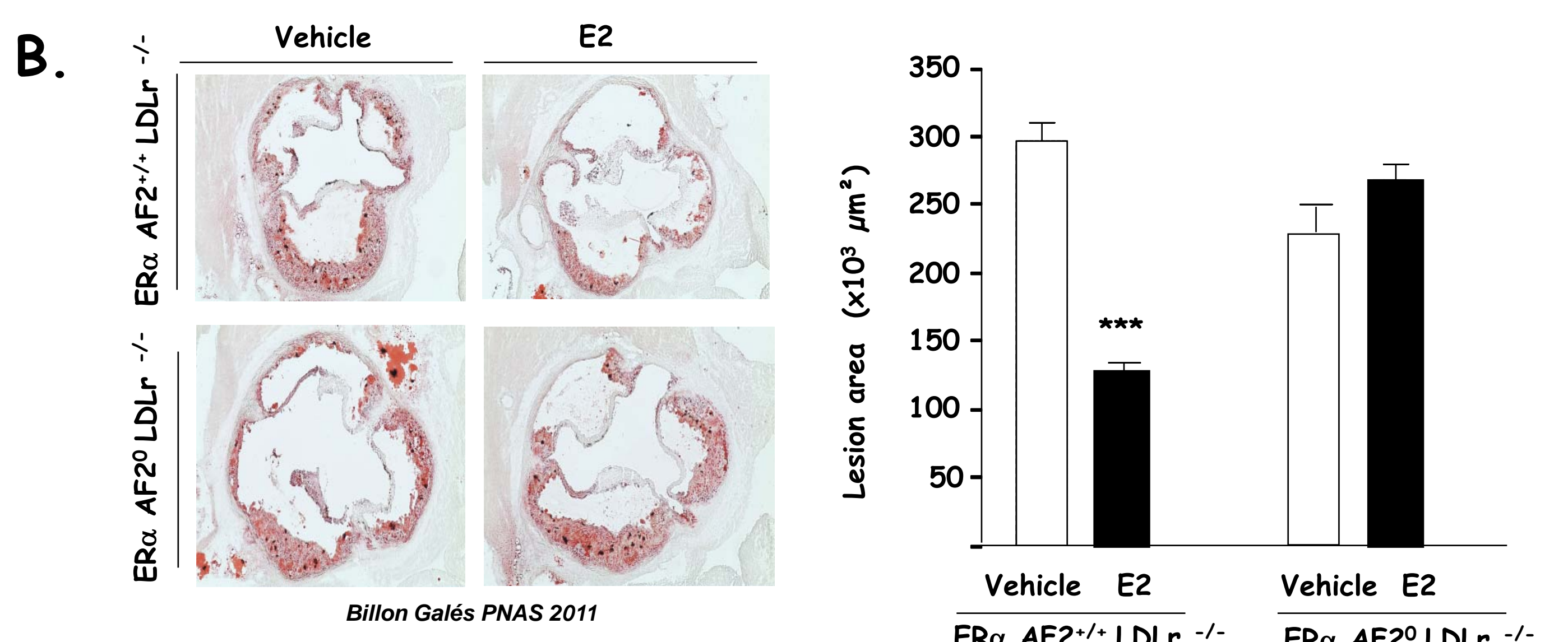
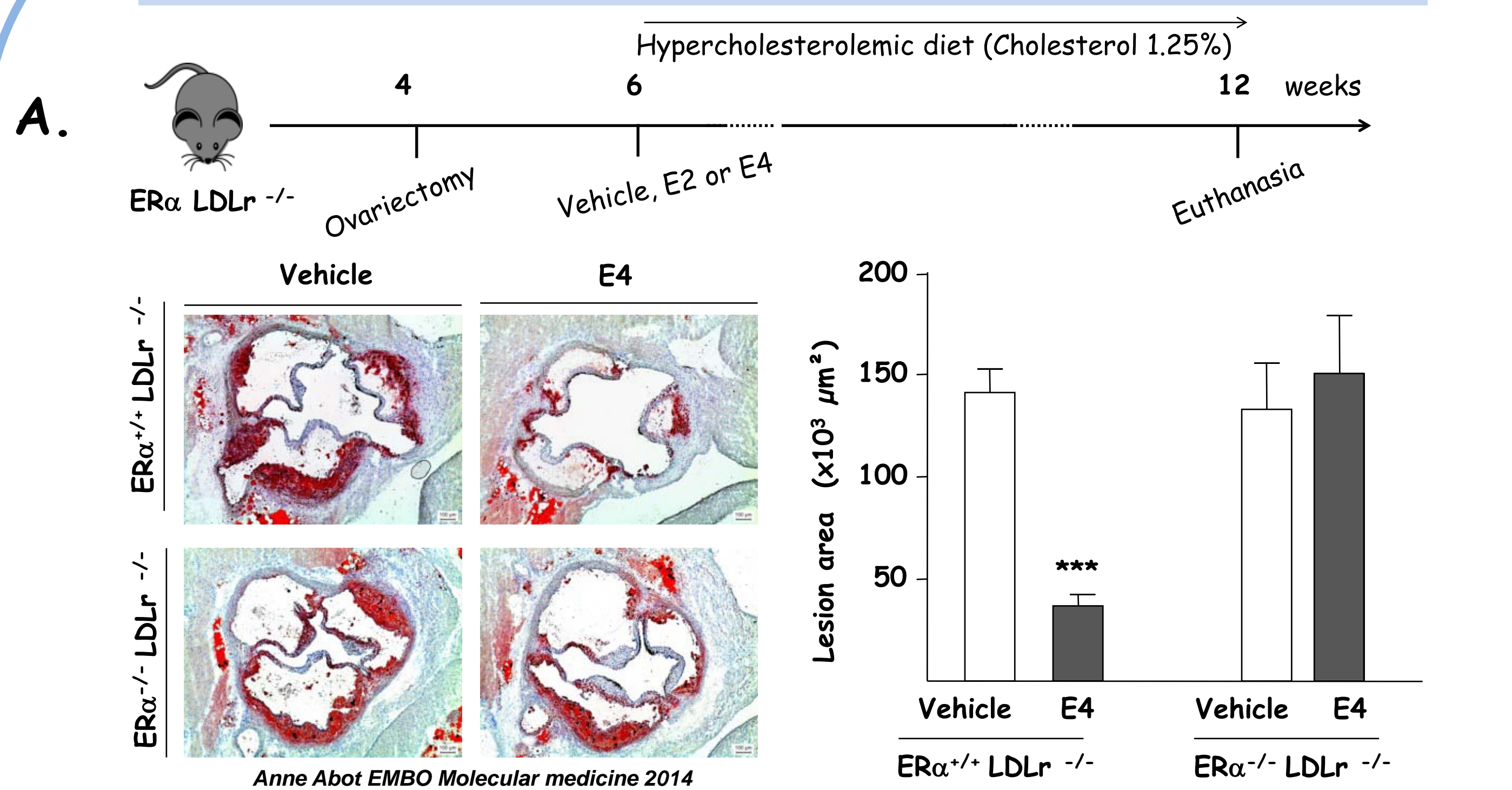


ERα AF2⁰
Billon Galés et al. PNAS 2011

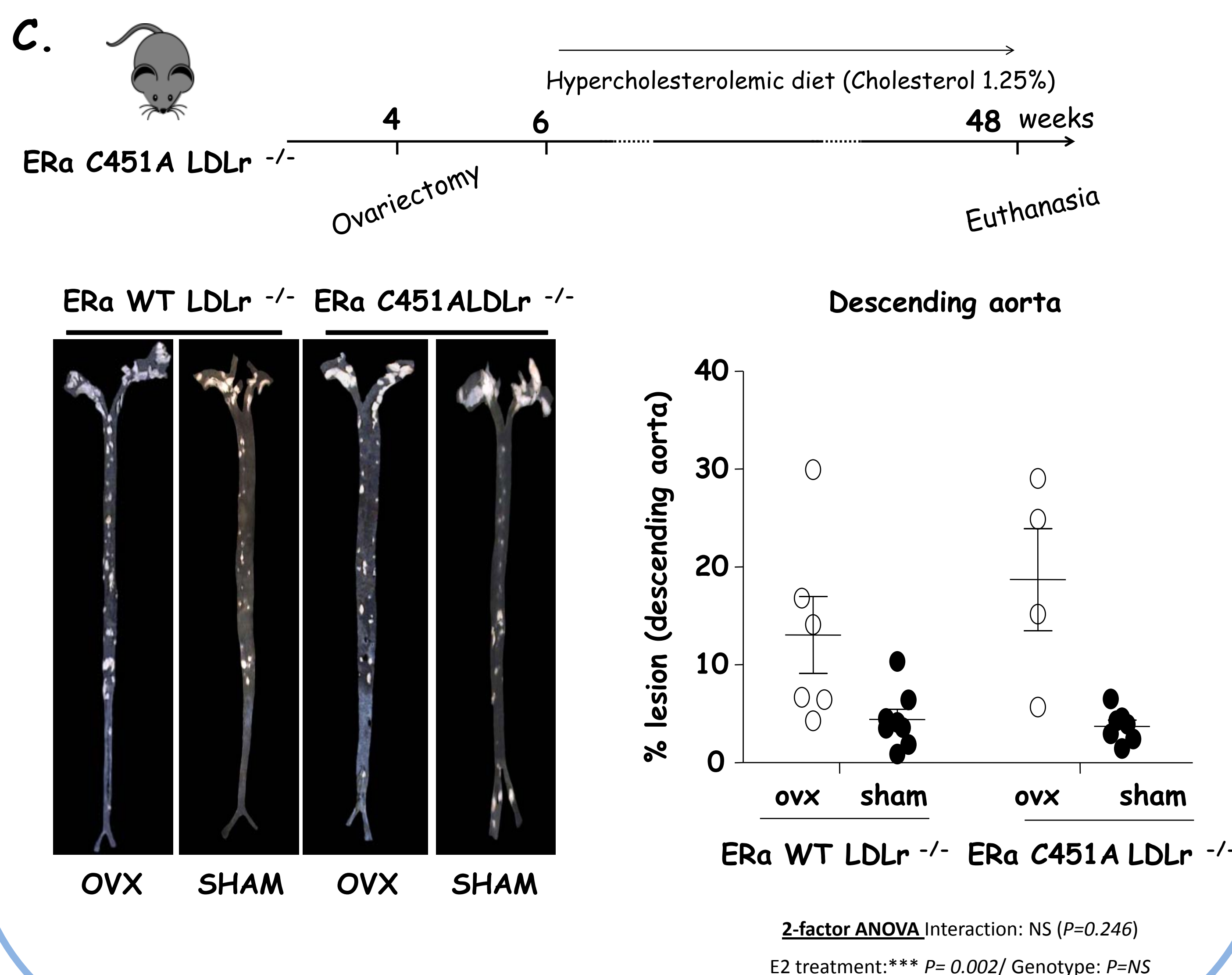
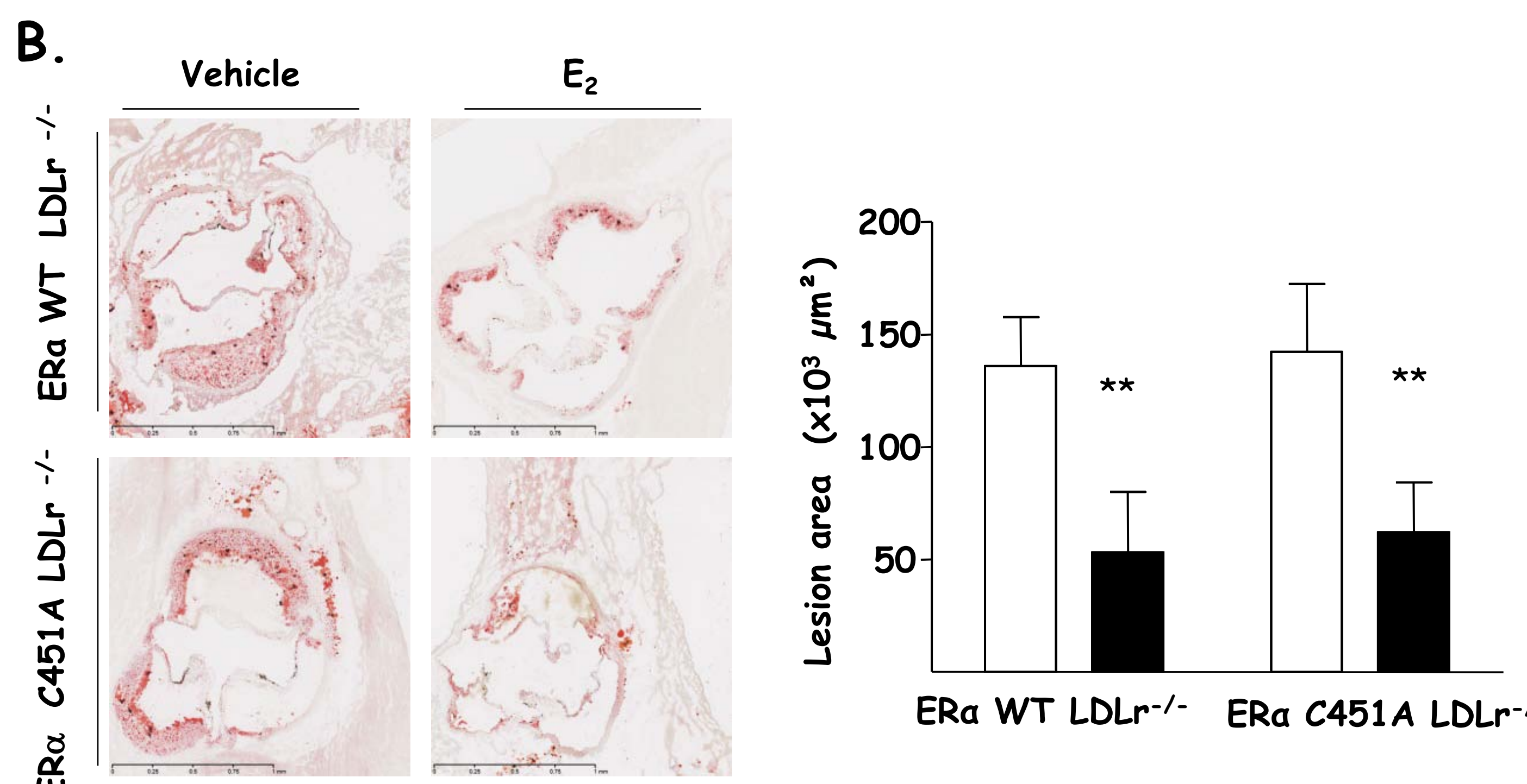
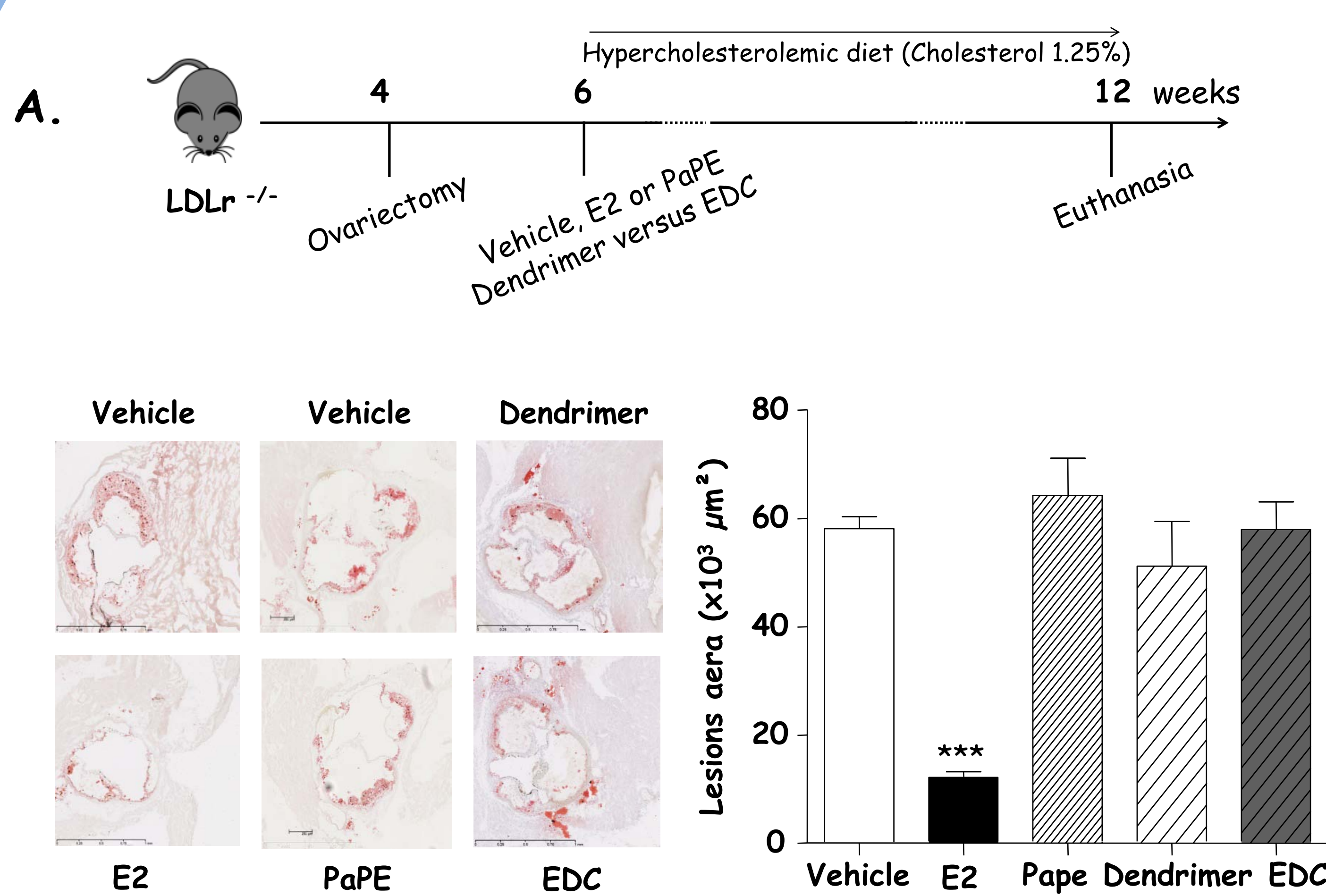
Madak-Erdogan et al. Sci Signal 2016

ERα C451A
Adlanmerini et al. PNAS 2014

Nuclear ERα is necessary and sufficient to prevent atherosclerosis



ERα MISS is not necessary to prevent atherosclerosis



Conclusion

	Genetically modified mouse model = Loss-of function		Pharmacological approaches = Gain of function	
	Nuclear ERα	ERαMISS	Nuclear ERα	ERαMISS
ERα Function	Nuclear ERα	ERαMISS	Nuclear ERα	ERαMISS
Genotype	ERα AF2 ⁰	ERα C451A	ERαWT	
Treatment	Estradiol (E2)		Estetrol (E4)	EDC
Acceleration of endothelial healing	YES ⁽¹⁾	NO ⁽²⁾	NO ⁽³⁾	YES ^(2,4)
Increase of NO production	YES ⁽¹⁾	NO ⁽²⁾	NO ⁽³⁾	YES ⁽²⁾
Prevention of atheroma at aortic sinus	NO ⁽¹⁾	YES	YES ⁽³⁾	NO
Prevention of atheroma on descending aorta	NO	YES	-	-

¹ Billon-Galés et al. Proc Natl Acad Sci U S A. 2011;108:13311-13316
² Adlanmerini et al. Proc Natl Acad Sci U S A. 2014;111:E283-290
³ Abot et al. EMBO molecular medicine. 2014;6:1328-1346
⁴ Chambliss et al. The Journal of clinical investigation. 2010;120:2319-2330