

SREBP-2 Responsive miR Operon Regulates Lipid Metabolism

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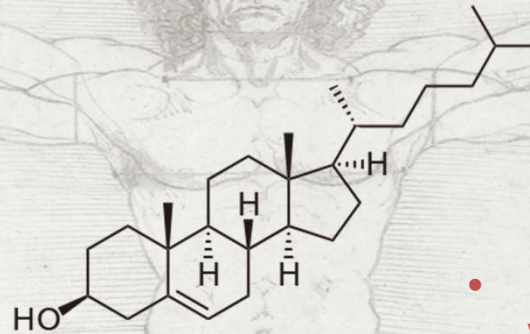
**Division of Animal Science
Chonnam National University**

Cholesterol

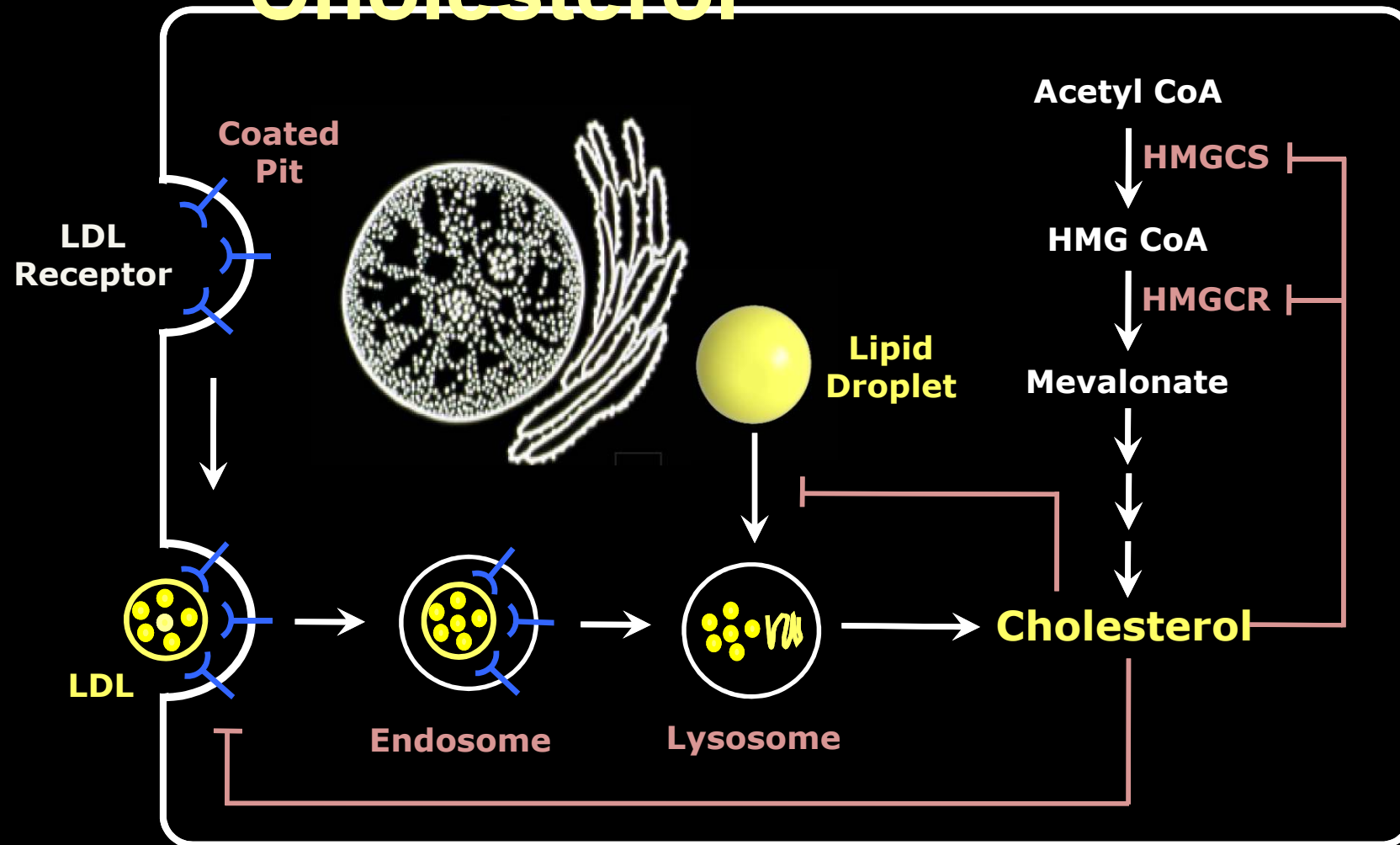
- **Myelin – Brain**
- **Surfactant – Lung**
- **Lipoprotein & Bile acids – Liver**
- **Steroid hormone – Adrenal**

- **Barrier – Skin**
- **Vitamin D – Bone**
- **Sex hormone – Gonads**
- **Storage – Fat**

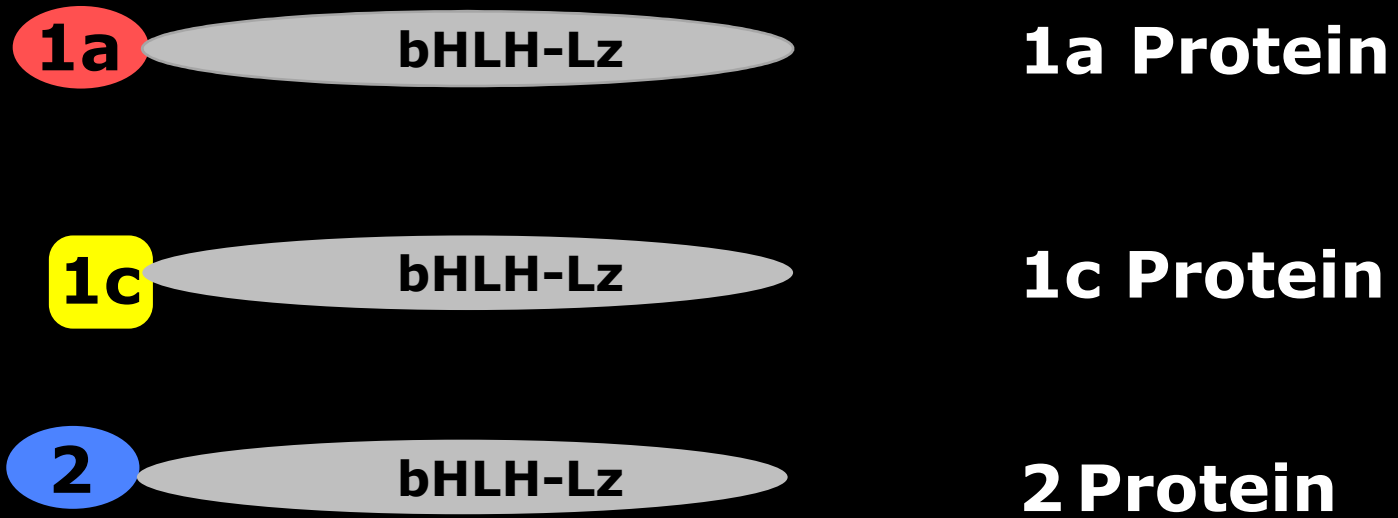
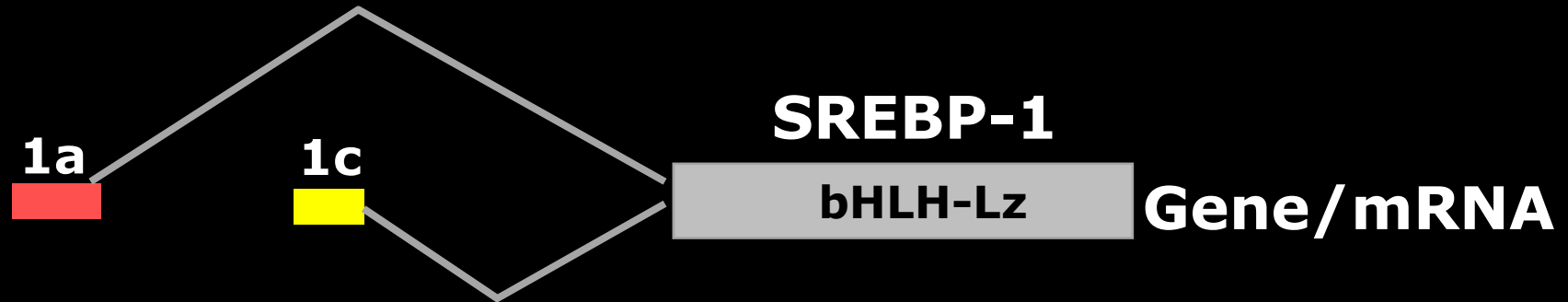
All Cell Membranes

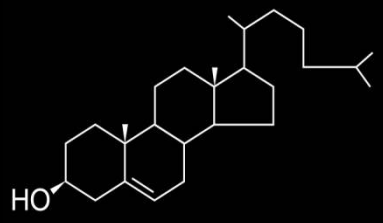
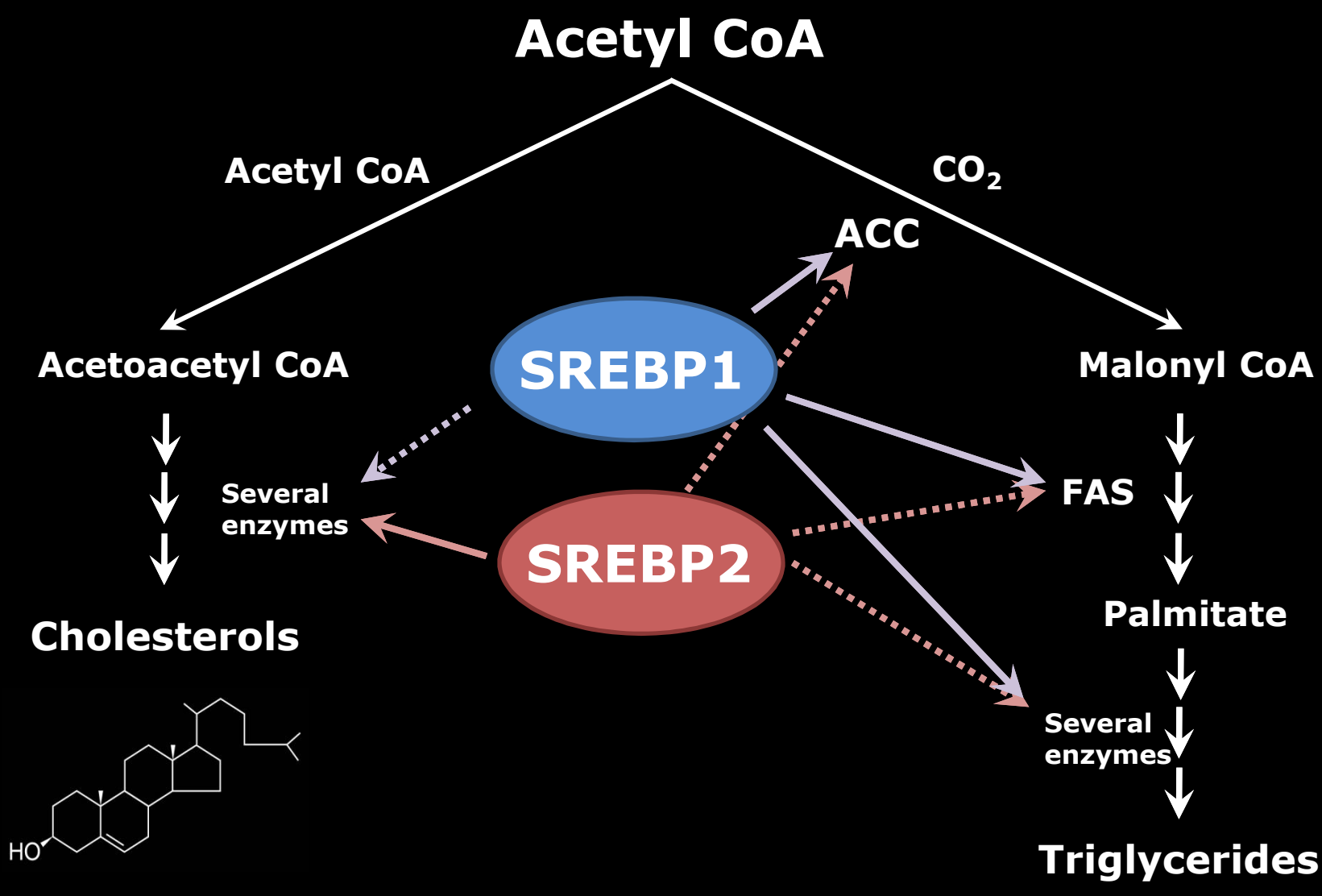


Three Sources of Cholesterol

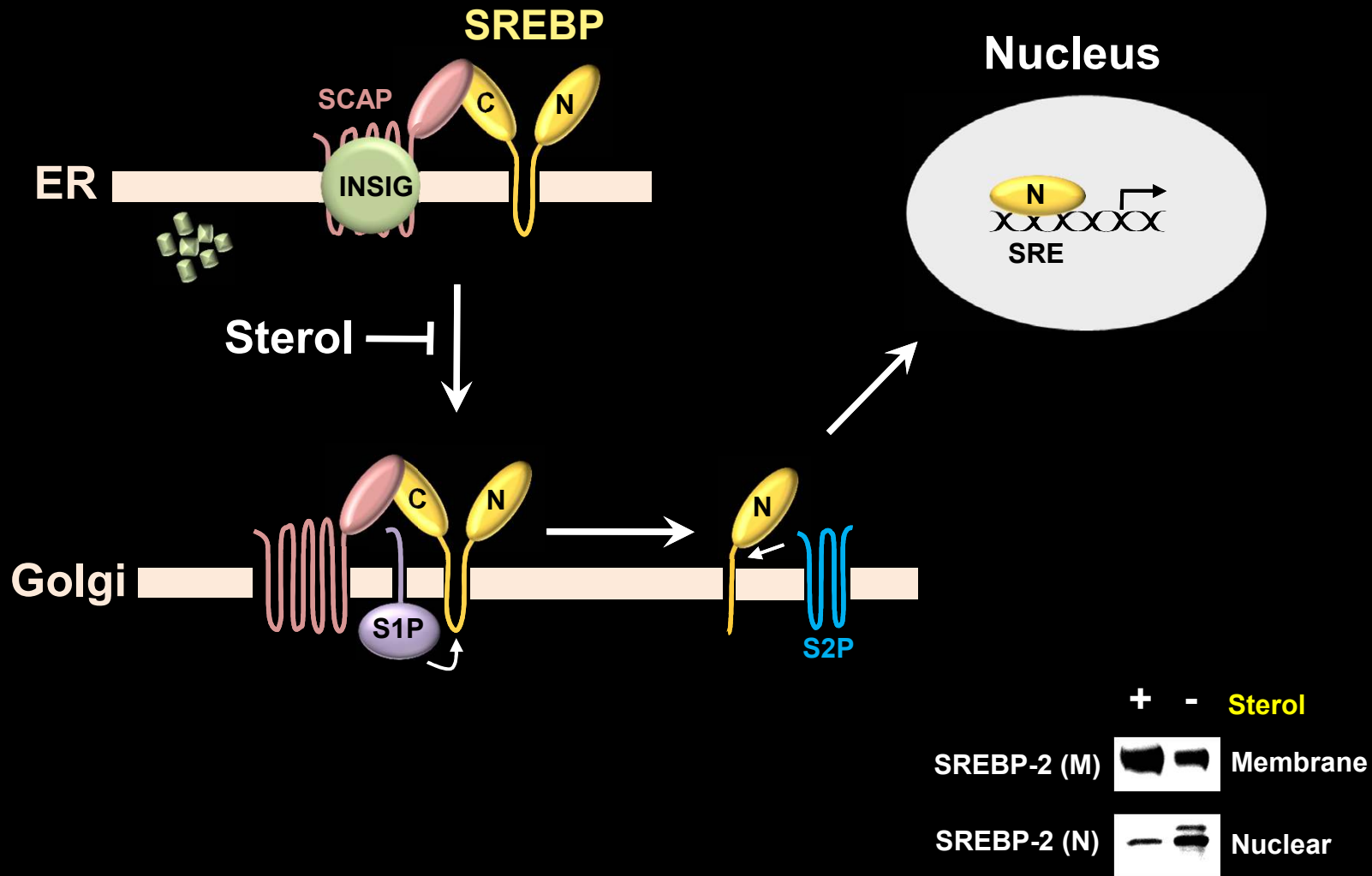


Sterol Regulatory Element Binding Proteins (SREBPs)

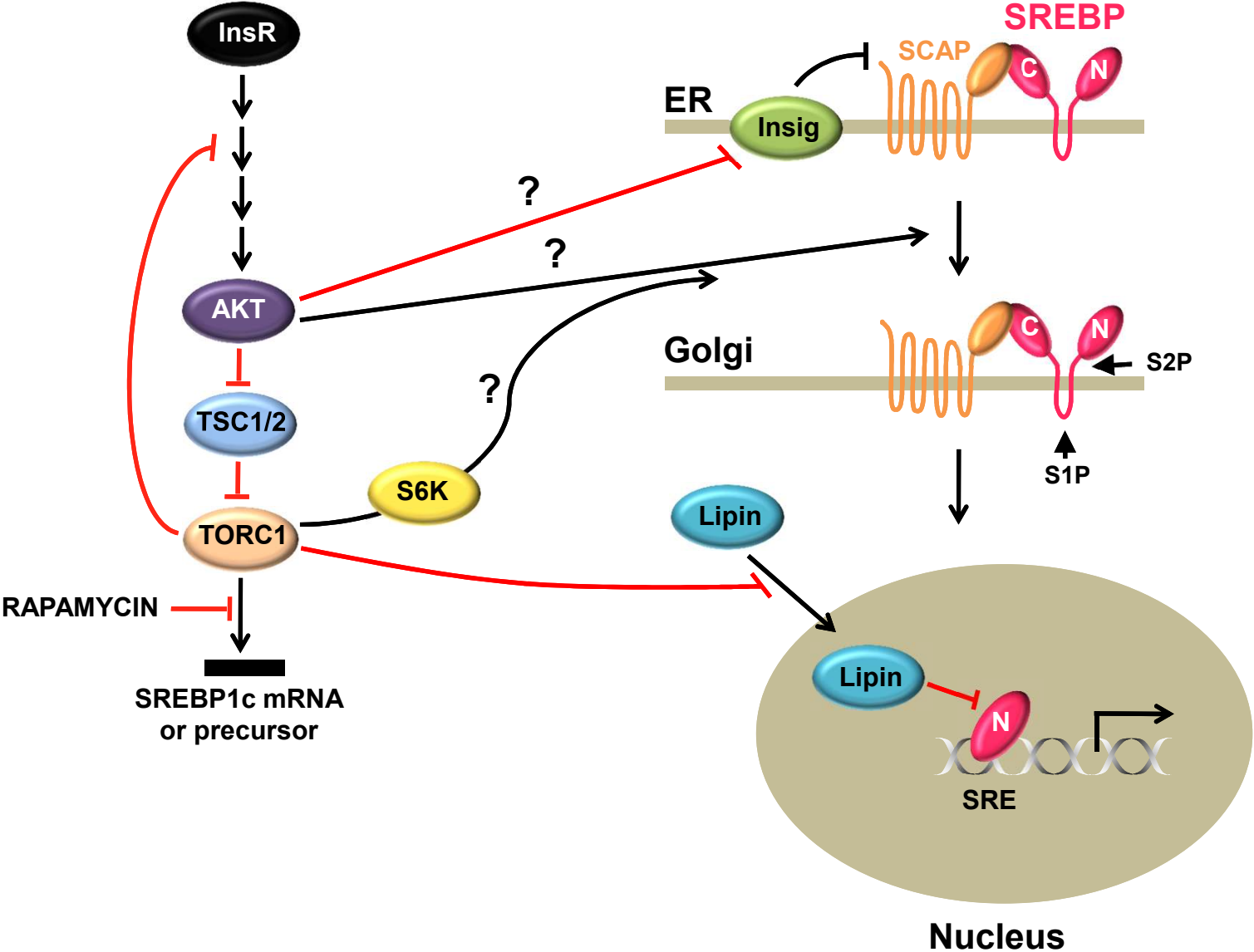




SREBPs Processing



SREBPS Maturation



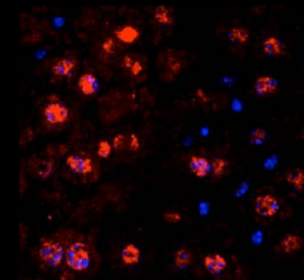
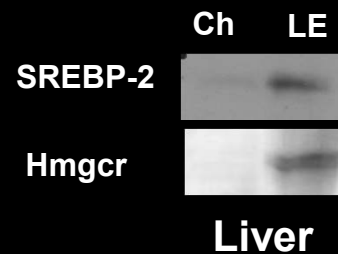
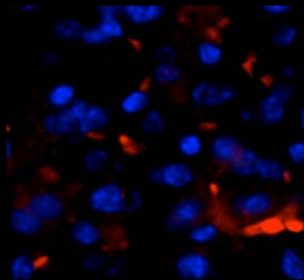
Normal chow diet
+
1% Cholesterol (Ch)



Normal chow diet
+
Lovastatin/Ezetimibe (LE)

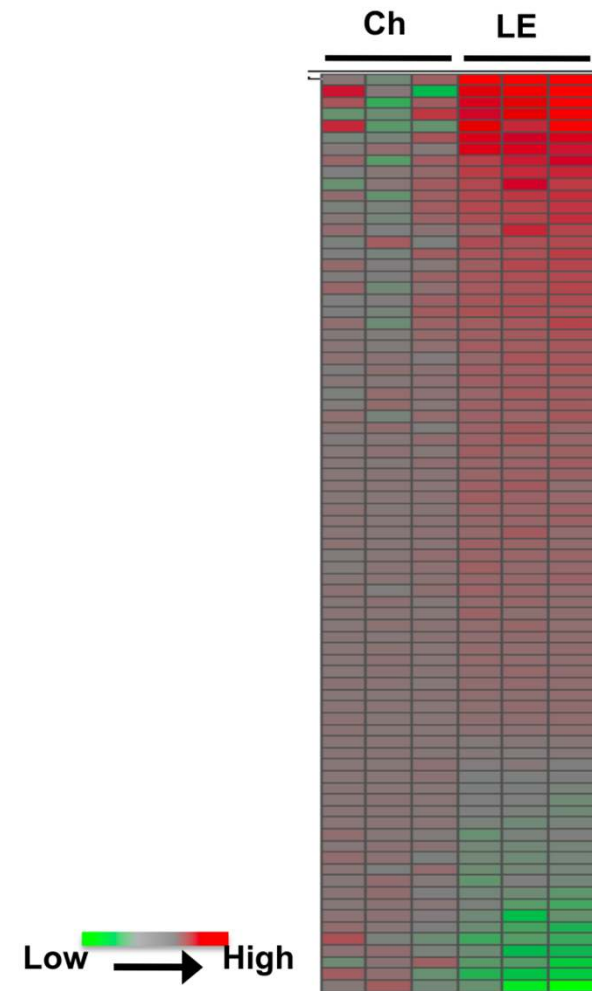


Lovastatin inhibits cholesterol synthesis
Ezetimibe inhibits cholesterol uptake
SREBP-2 and target genes ↑

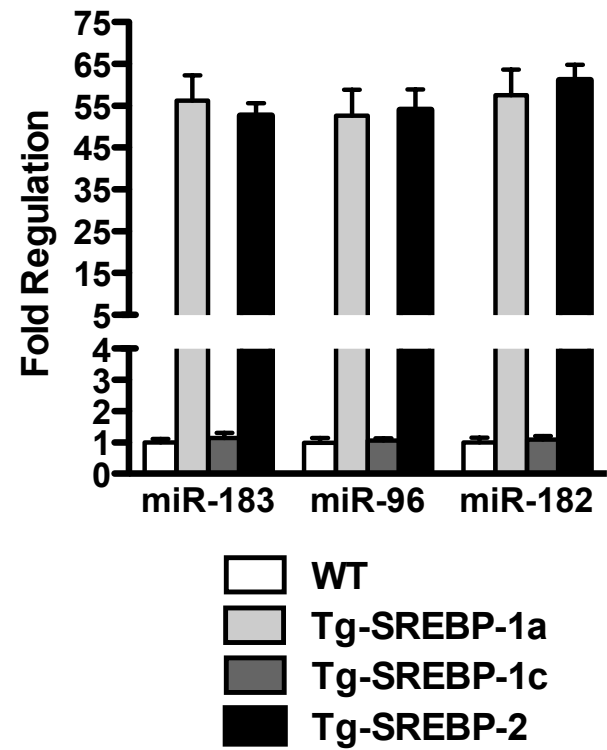
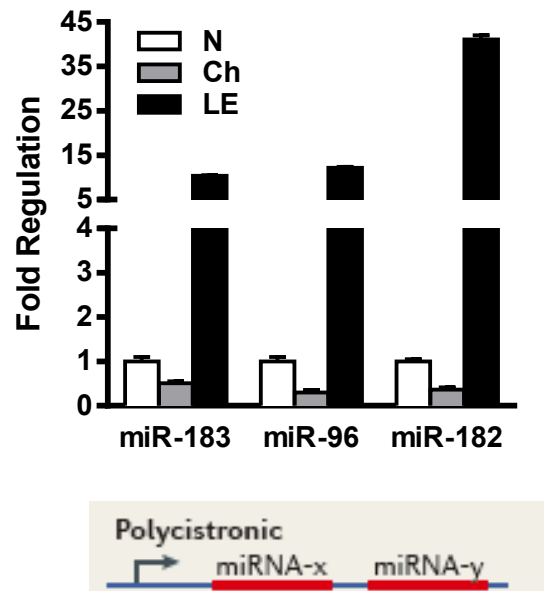


miRNA profiles LE vs Ch

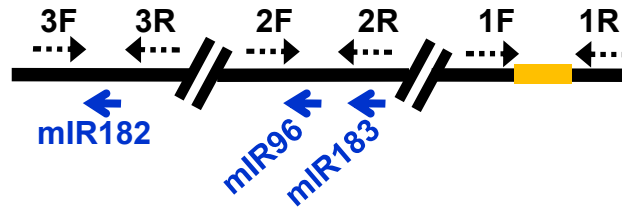
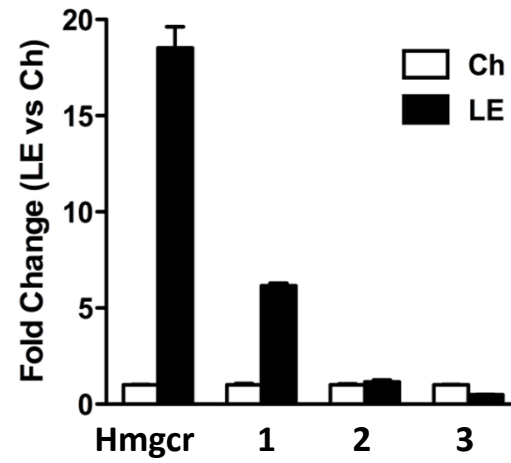
miRNA	Fold change
mmu-miR-182	81.6
mmu-miR-470*	28.3
mmu-miR-34b-3p	17.7
mmu-miR-741	12.5
mmu-miR-877	7.2
mmu-miR-20b	6.2
mmu-miR-297a*	5.7
mmu-miR-19a	4.3
mmu-miR-875-5p	3.6
mmu-miR-33*	3.2
mmu-miR-188-5p	3.2
mmu-miR-467a*	3.0
mmu-miR-195	2.9
mmu-miR-877*	2.9
mmu-miR-126-5p	2.8
mmu-miR-130b	2.7
mmu-miR-101a	2.3
mmu-miR-339-3p	2.1
mmu-miR-301b	2.1
mmu-miR-331-3p	2.1
mmu-miR-135a*	2.1
mmu-miR-185	2.1
mmu-miR-676	.50
mmu-miR-15a	.28
mmu-miR-339-5p	.26
mmu-miR-425	.23
mmu-miR-221	.20
mmu-miR-215	.19
mmu-miR-210	.10
mmu-miR-455	.04



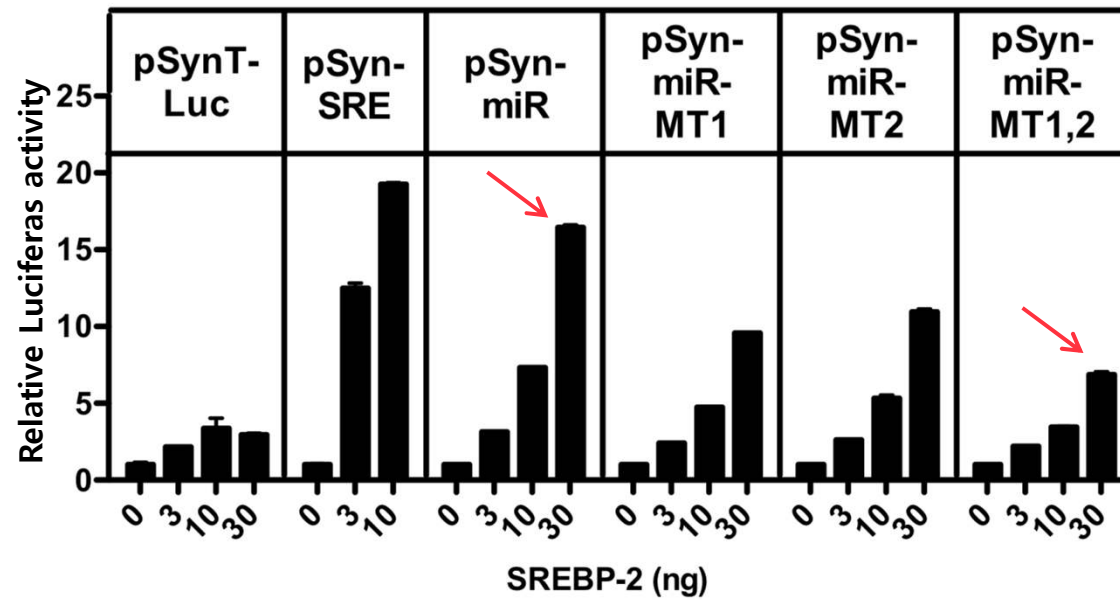
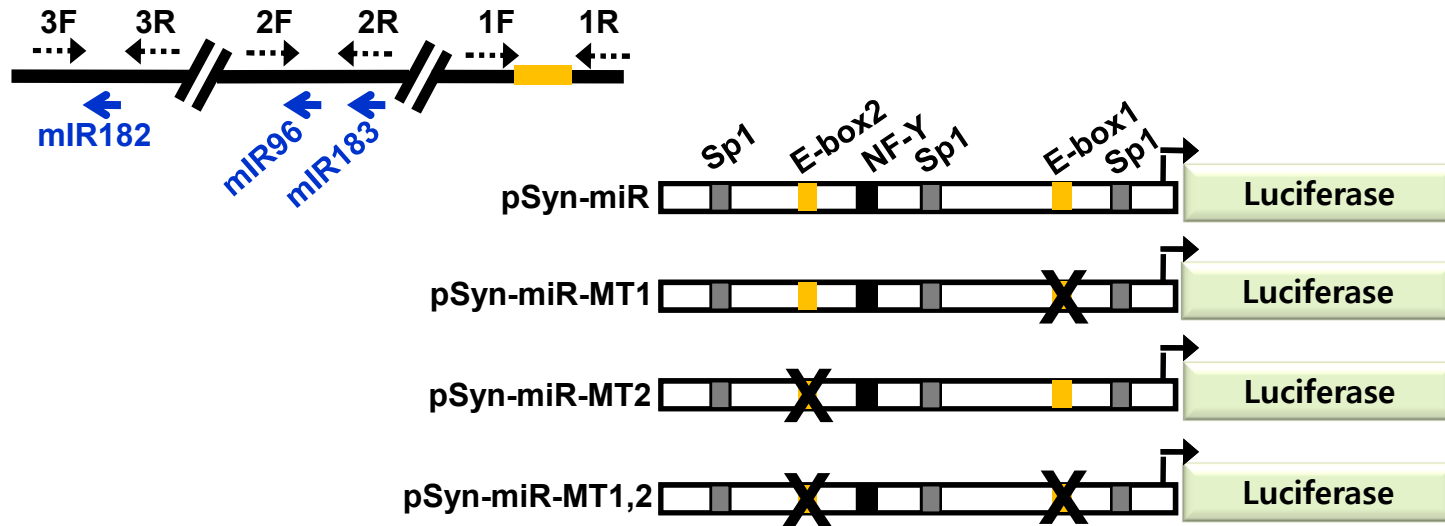
miR-182-96-183 cluster



SREBP-2 regulatory region



Promoter region of miR-182-96-183 cluster

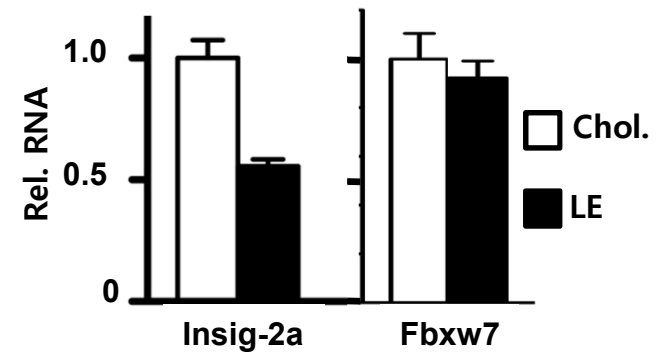
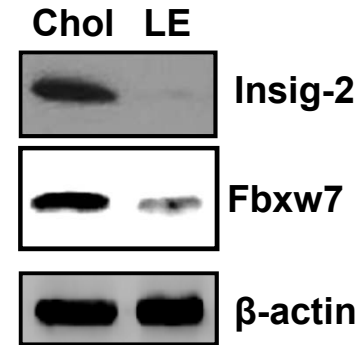
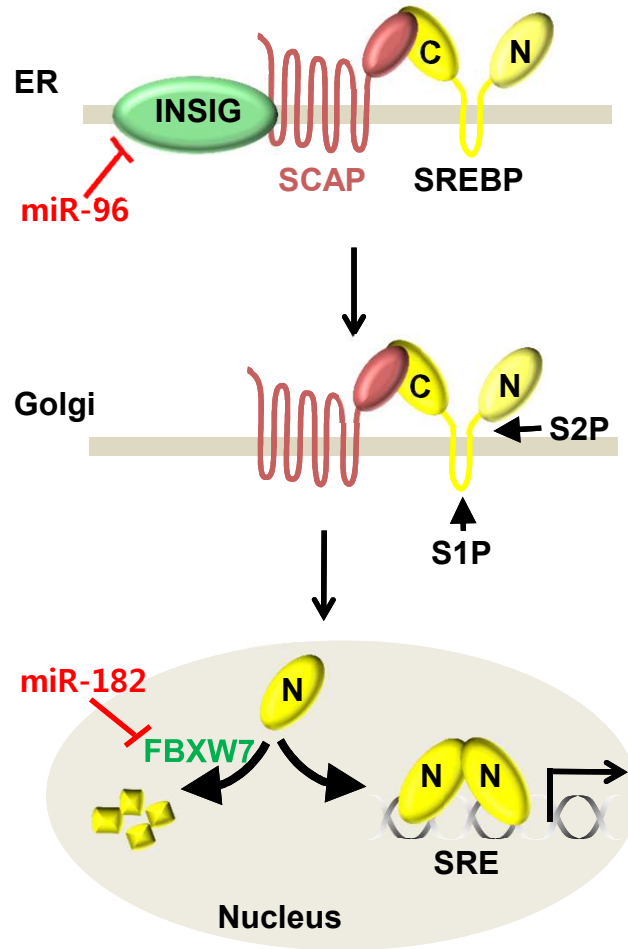


SREBP-2

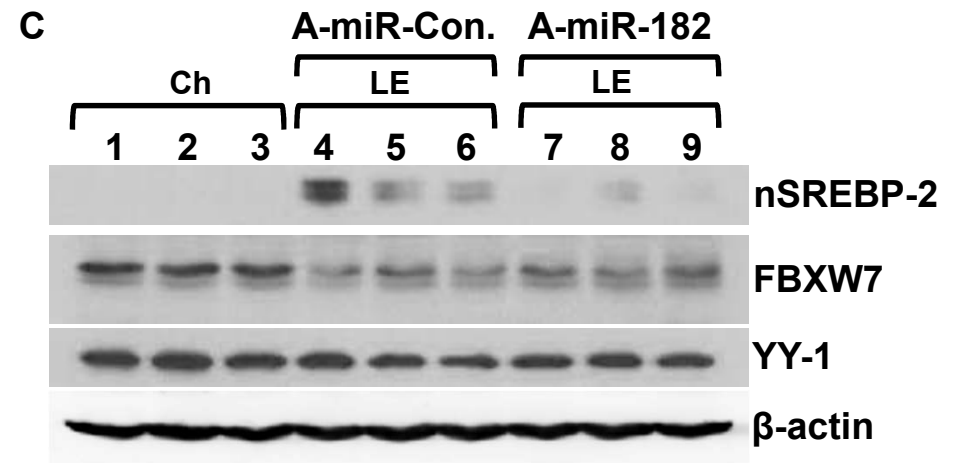
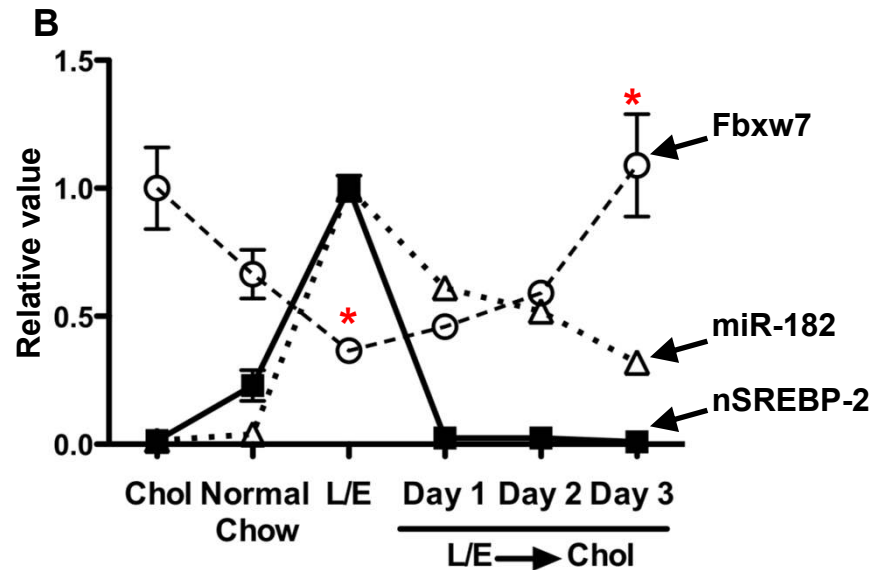
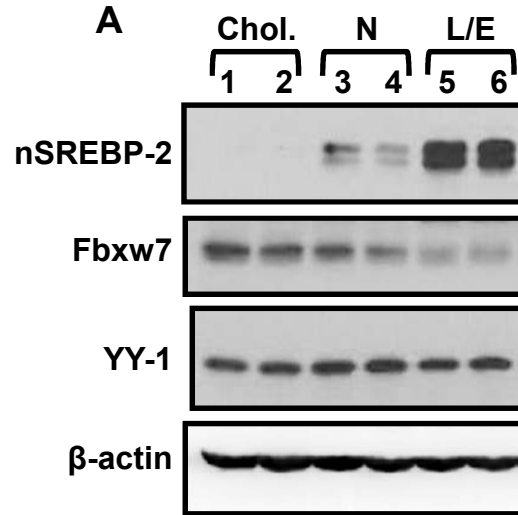


miR-183/96/182

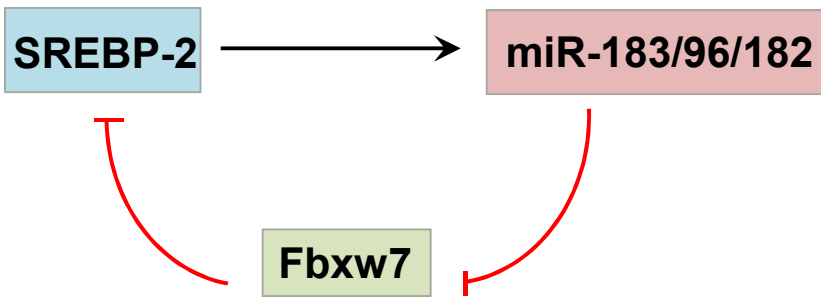
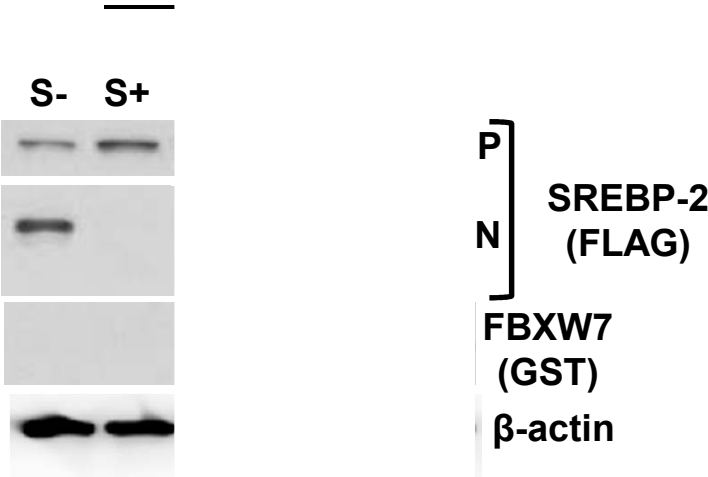
SREBP processing



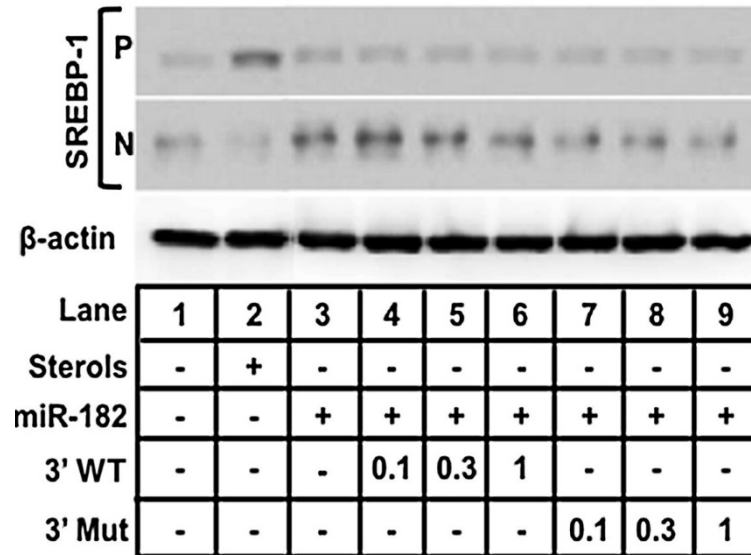
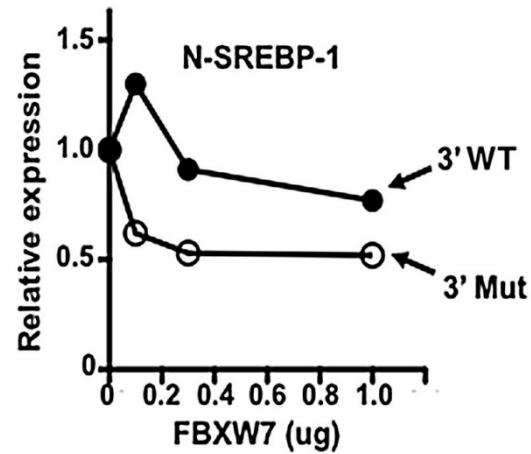
Coordinate and reciprocal regulation of nSREBP-2 with miR-182 or Fbxw7



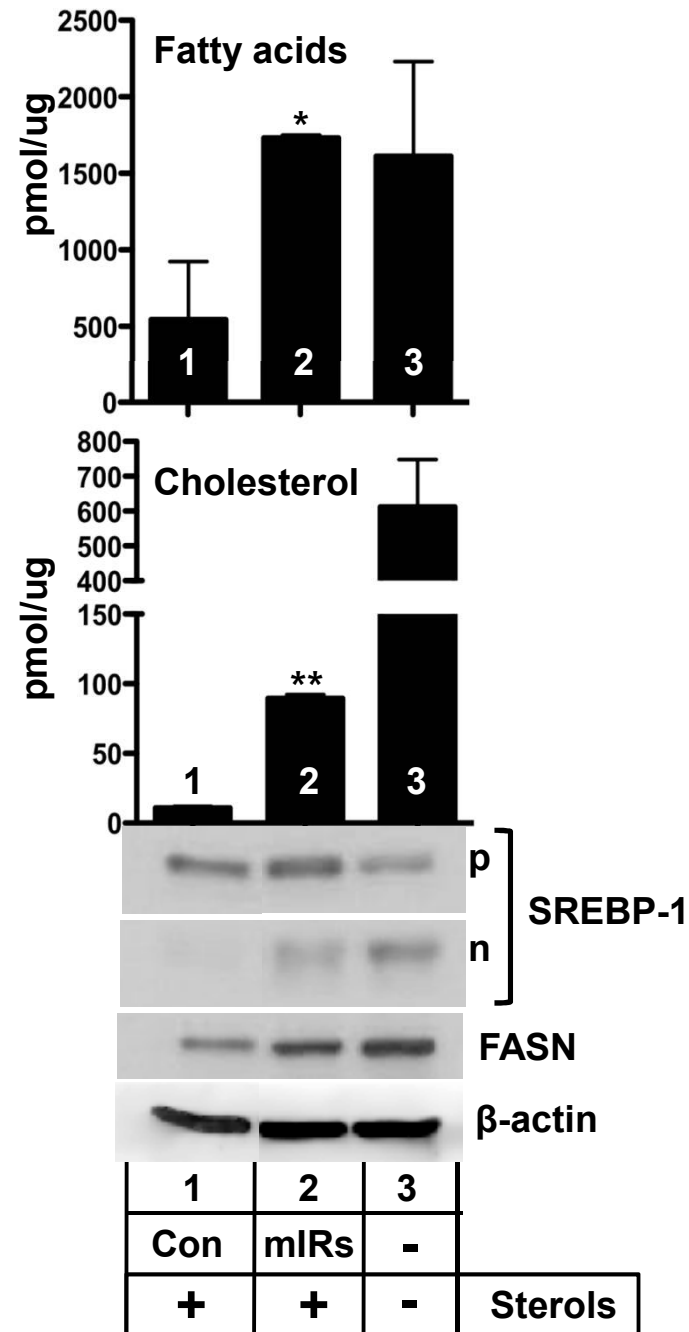
FBXW7 overexpression rescues nSREBP-2 accumulation by miR-182



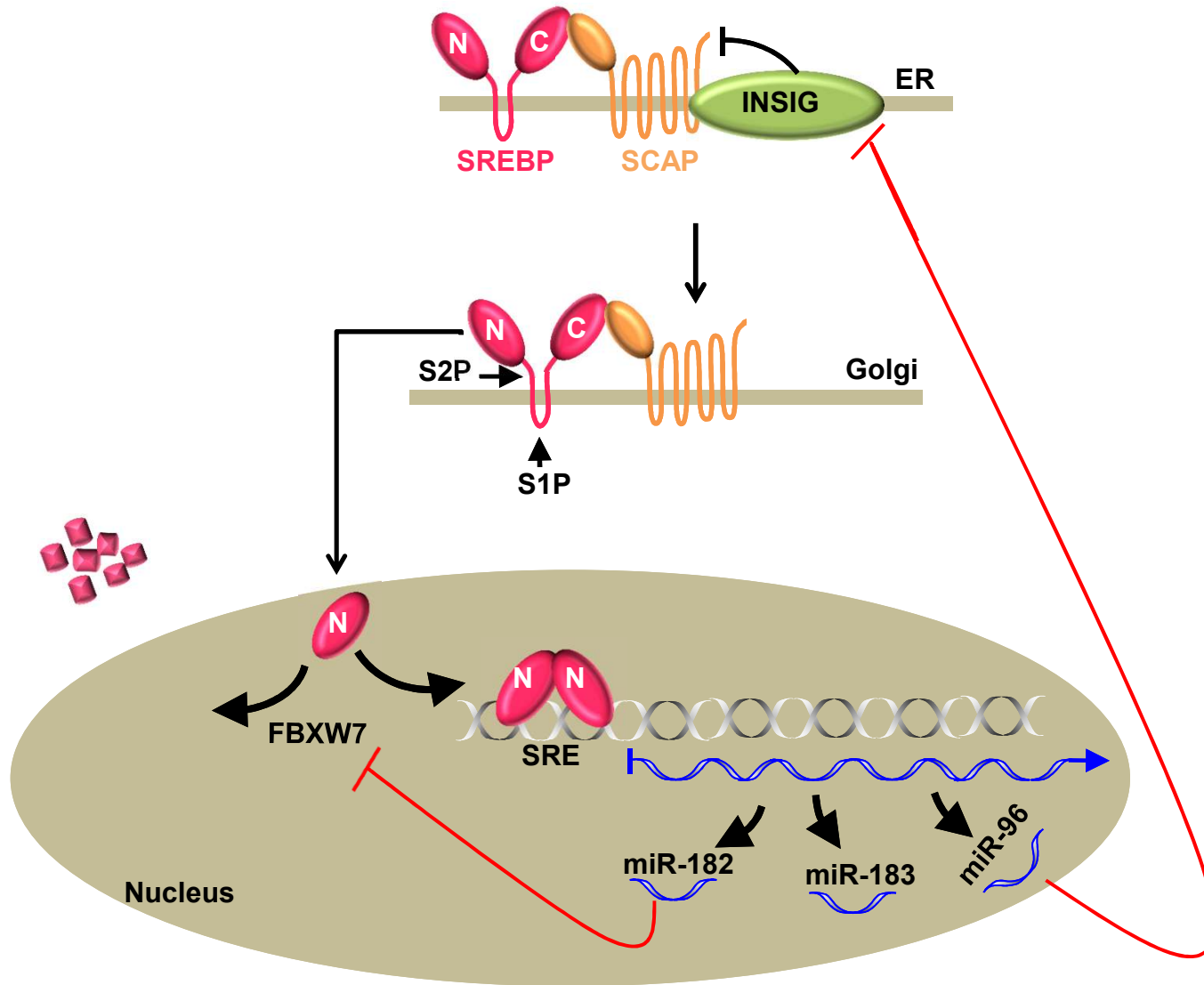
Effect of ectopic FBXW7 on nSREBPs is sensitive to miR-182-binding sites in the FBXW7 3'UTR



miR regulation of SREBP levels induces lipid biosynthesis



An SREBP-2 regulated miR operon regulates lipid metabolism



ACKNOWLEDGEMENTS



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