UQÀM: Department of Biological Sciences

The role of apolipoprotein D in lipid metabolism and metabolic syndrome

Catherine Mounier PhD

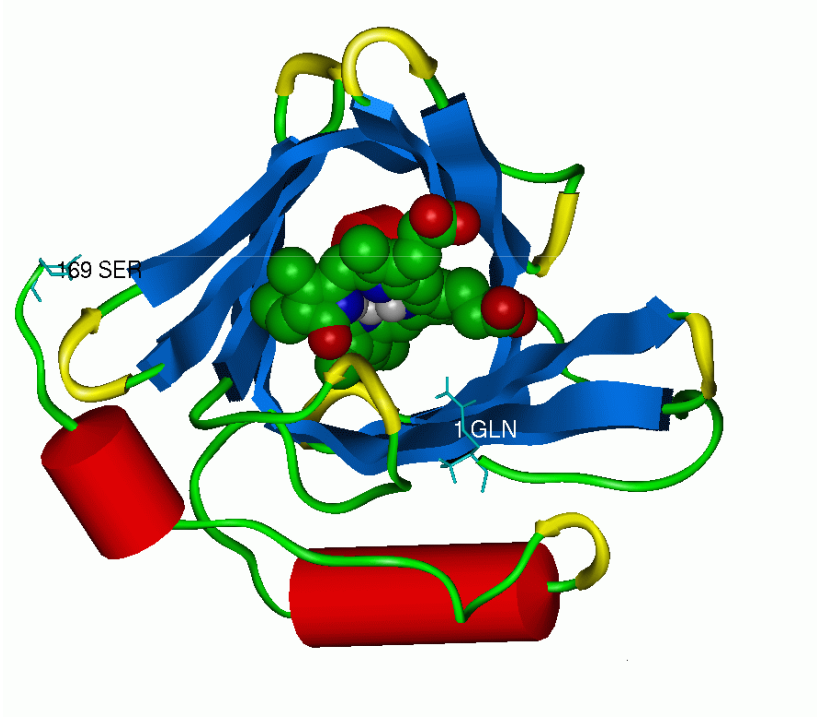


BioMed
UQÀM UQTR INRS

UQÀM Faculté des sciences
Université du Québec à Montréal

Apolipoprotein D

Apolipoprotéine D (apoD)



Secreted protein

Associated with HDL

Secretion stimulated by 25-hydroxycholesterol

Ligands

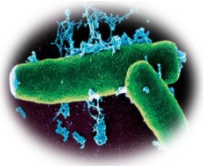
Arachidonic Acid
Heme
Steroids (progesterone, androgen, estrogen)
Cholesterol and CHOL esters

Apolipoprotein D expression











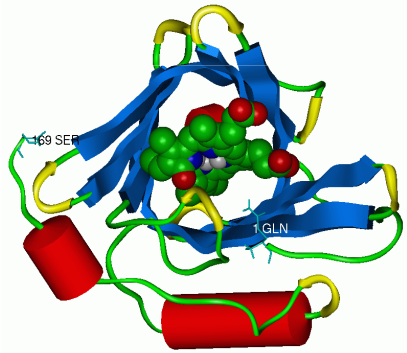


Surrenals
Kidney
Pancreas
Thymus
Central and peripheric nervous systems
Lungs
Ovaries and testis

*Central and peripheric nervous systems
Adipose tissue
Heart
Lungs
Glands
Ovaries and testis

Apolipoprotein D

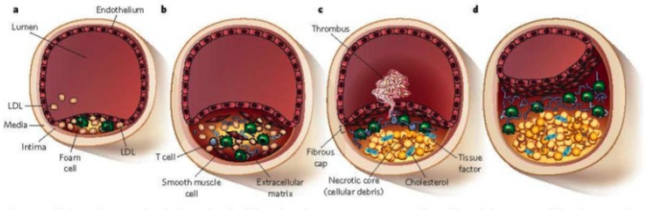
- Involved in growth and cellular differentiation
- Metabolic disorders and energetic homeastasis
- Development
- Cancer
- Protection against stress in drosophila
- Maintance and repair of central nervous system



Apolipoprotein D in metabolism

Low plasma levels of apoD associated with disorders that produce low HDL levels with or without hypertriglyceridemia

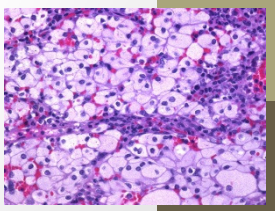
- ✓ *Tangier disease*
- ✓ *Abeta-lipoproteine-mia*
- ✓ *LCAT deficiency*
- ✓ *Hypertrigly-ceride-mia at birth*



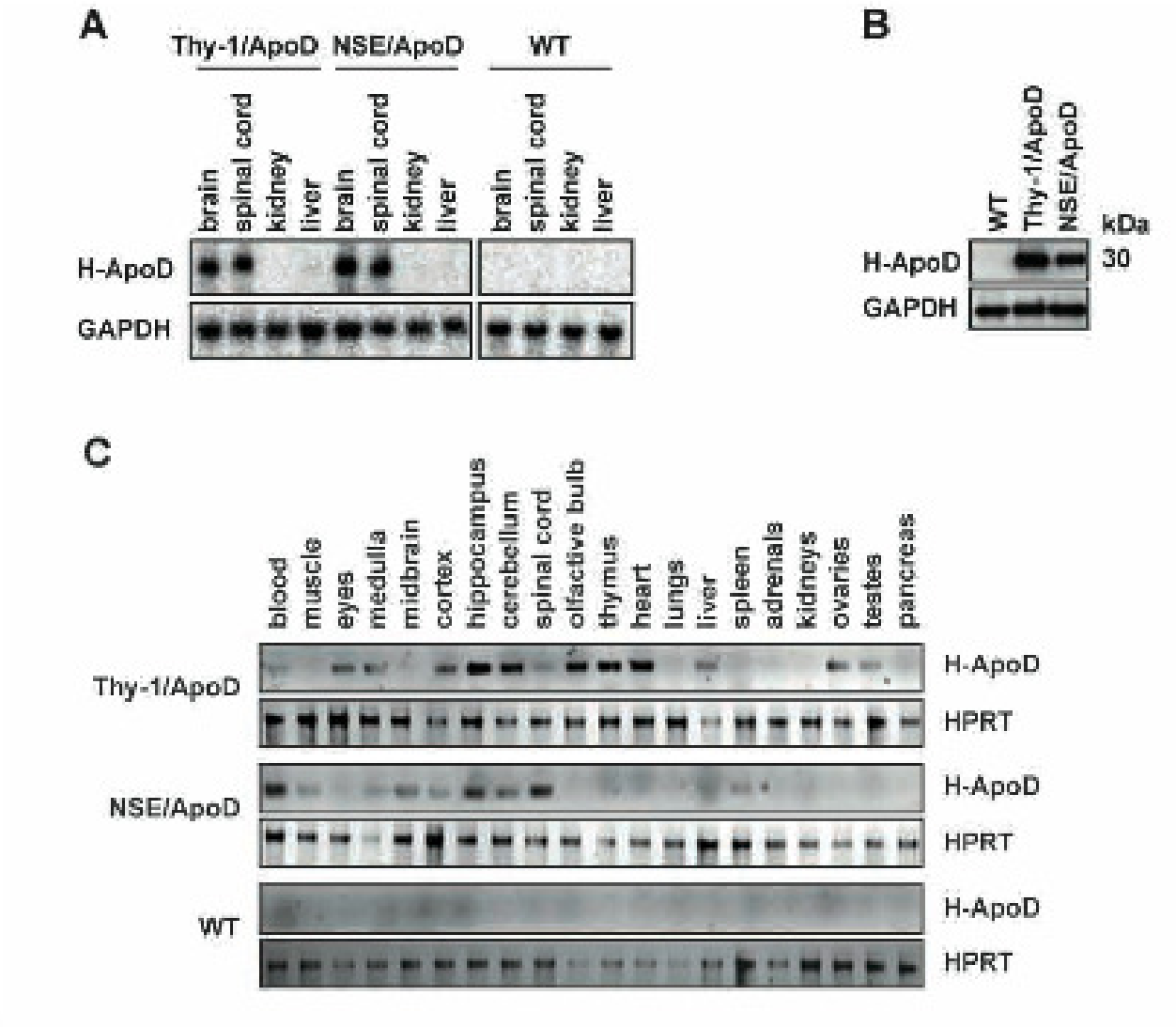
ApoD modulation in non-insulin dependent diabetes mellitus (NIDDM)

Increased expression and defective processing of apoD in Niemann-Pick disease type C mouse (NPC).

Animal model of human NPC, which is a genetic disorder affecting cellular cholesterol transport



Apolipoprotein D Tissue expression



Do Carmo et al, AJP Endo Met 2008

Tg ApoD mice characteristics

Table 2. Morphometric parameters of H-apoD Tg mice and WT littermates.

	WT	Thy-1/ApoD	NSE/ApoD
Body weight (g)	38.95 ± 4.57	44.06 ± 5.42	43.83 ± 4.16
Body lenght (cm)	9.86 ± 0.40	10.11 ± 0.36	10.00 ± 0.18
Body mass index (g/cm2)	0.40 ± 0.03	0.43 ± 0.05	0.44 ± 0.04
Weights of tissue (g/g of body weight, x 100)			
Brain	1.07 ± 0.08	0.97 ± 0.08	0.96 ± 0.07
Liver	4.03 ± 0.58	5.24 ± 0.68 **	4.91 ± 0.73 *
Inguinal fat	4.87 ± 1.54	4.40 ± 0.68	5.19 ± 0.90
Mesenteric fat	5.26 ± 1.01	4.77 ± 0.83	5.37 ± 0.95
Epididymal fat	0.88 ± 0.26	0.82 ± 0.23	0.68 ± 0.31

Data are means ± SE of 12 mice per group. * $p<0.05$, ** $p<0.01$ vs WT mice.

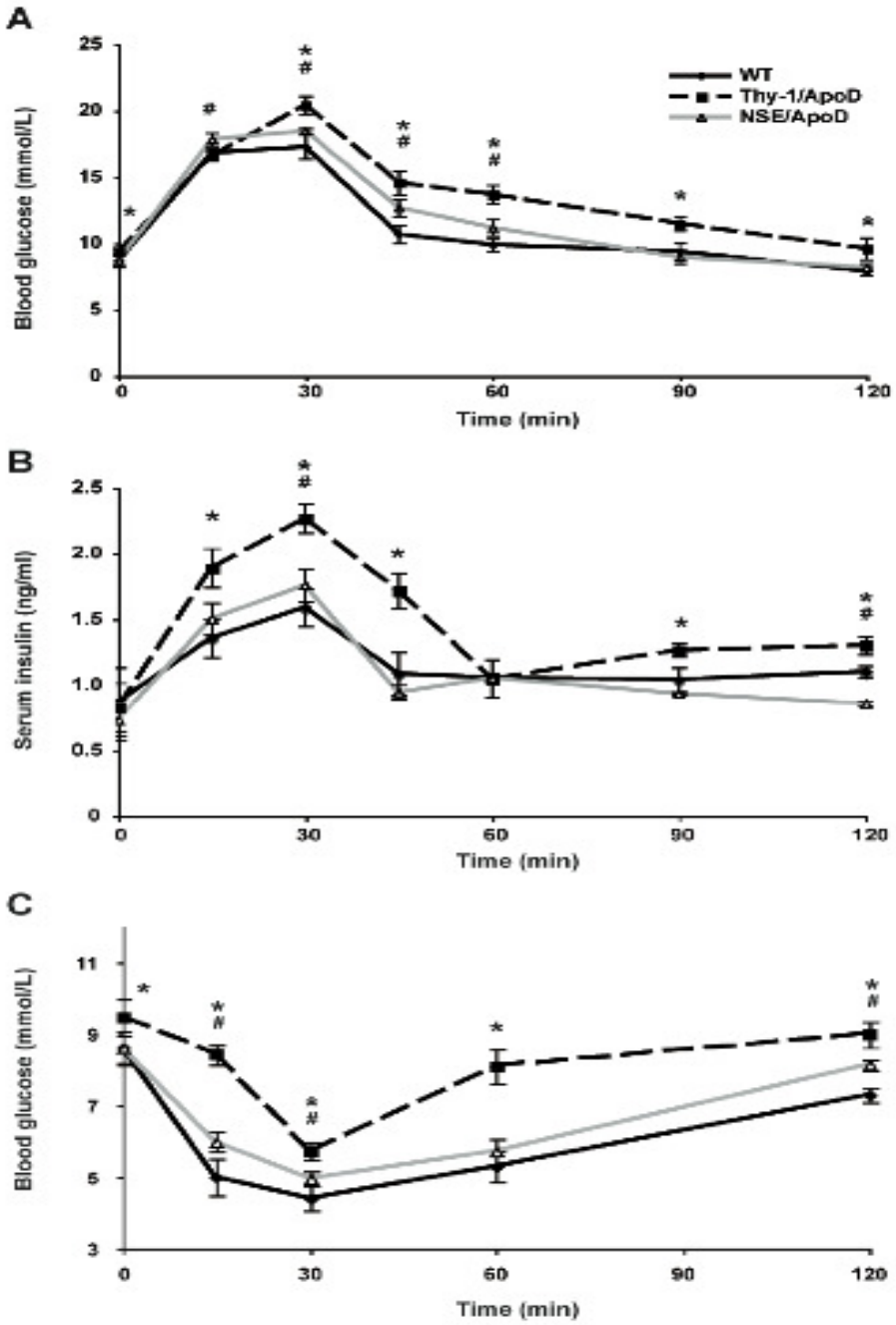
Table 3. Serum parameters in H-apoD Tg mice and WT littermates.

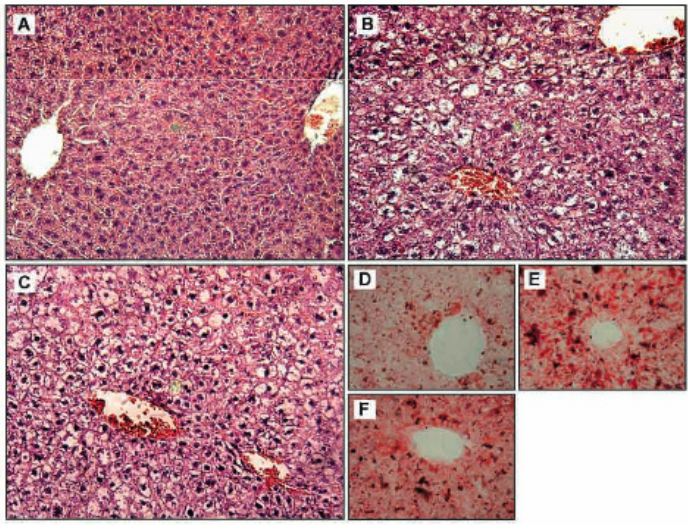
	WT	Thy-1/ApoD	NSE/ApoD
Total protein (g/L)	52.20 ± 4.09	52.33 ± 5.16	55.40 ± 11.61
Albumin (g/L)	27.40 ±7.50	27.83 ± 6.71	30.20 ± 8.47
Glucose (mmol/L)	10.90 ± 0.75	12.52 ± 3.44	11.28 ± 2.95
Insulin (ng/ml)	1.44 ± 0.37	3.15 ± 0.56 ***	2.32 ± 0.37 *
BUN urea (mmol/L)	8.28 ± 1.01	7.98 ± 1.79	7.62 ± 1.09
Creatinine (µmol/L)	13.33 ± 0.58	15.33 ± 5.13	17.67 ± 2.52 **
Total bilirubin (µmol/L)	2.92 ± 0.94	2.82 ± 1.48	3.56 ± 1.36
ALT (U/L)	39.00 ± 1.00	38.00 ± 2.65	72.00 ± 26.29 *
AST (U/L)	86.00 ± 20.88	78.67 ± 2.08	173.67 ± 65.26 *
Alkaline phosphatase (U/L)	82.40 ± 14.96	120.80 ± 62.50	73.00 ± 29.51
Creatine kinase (U/L)	85.33 ± 47.51	102.67 ± 27.01	94.00 ± 49.12
Cholesterol (mmol/L)	2.98 ± 0.36	3.13 ± 0.63	4.25 ± 1.98
HDL (mmol/L)	2.42 ± 0.31	2.60 ± 0.63	3.07 ± 1.57
Triglycerides (mmol/L)	1.15 ± 0.31	1.71 ± 0.89	1.14 ± 0.50

Data are means ± SE of 6 mice per group. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ vs WT mice.

Do Carmo et al, AJP Endo Met 2008

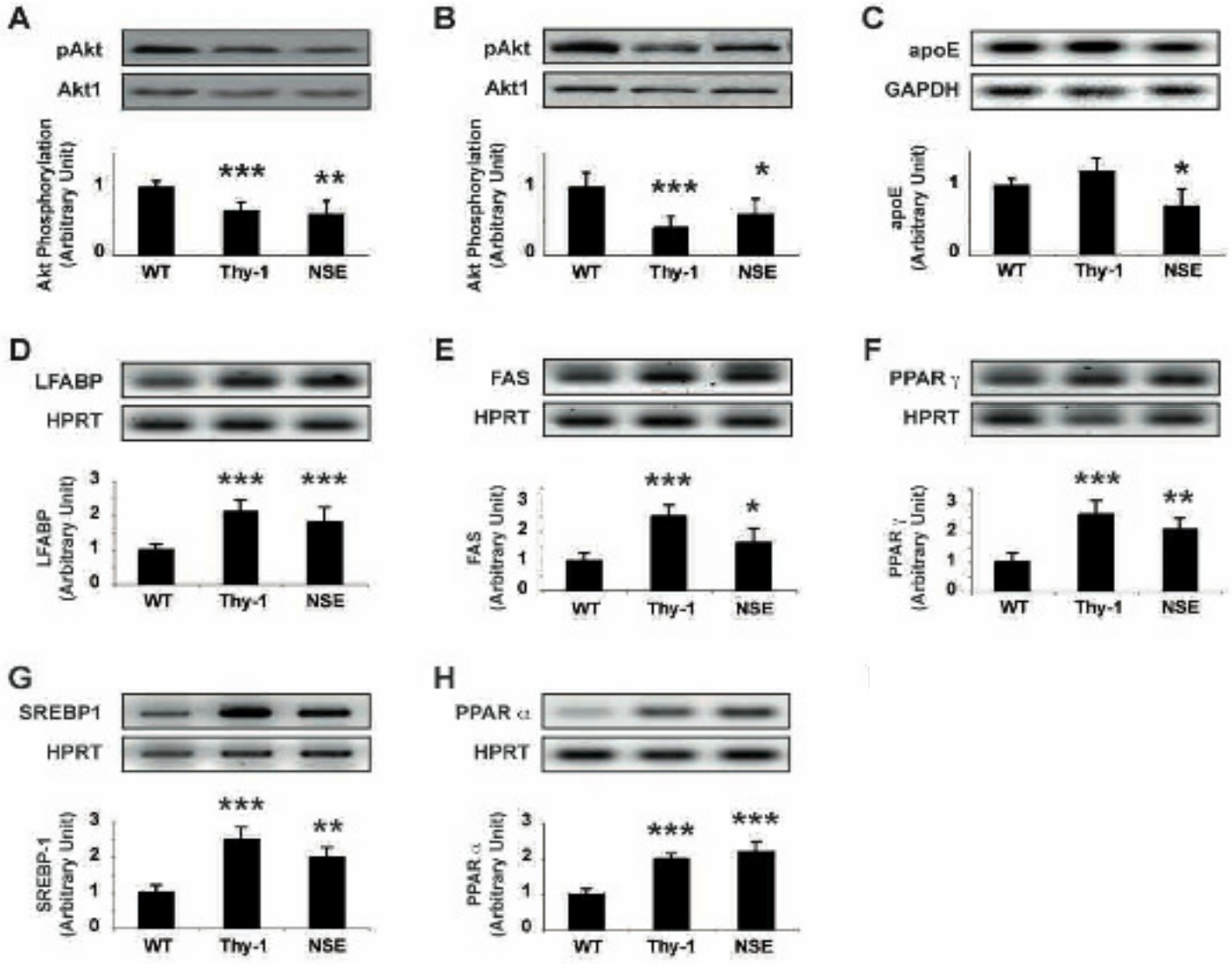
TgApoD mice and hepatic steatosis





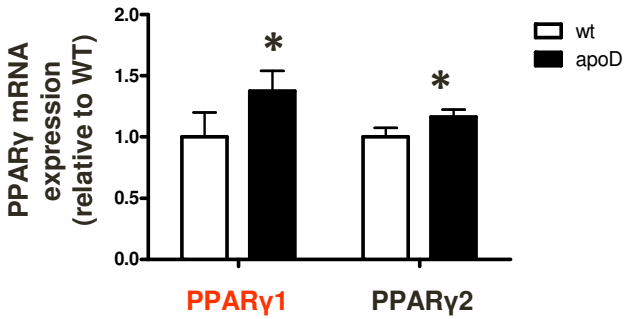
Do Carmo et al, AJP Endo Met 2008

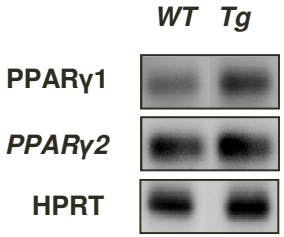
TgApoD mice characterization

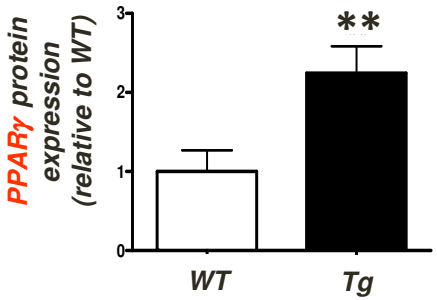


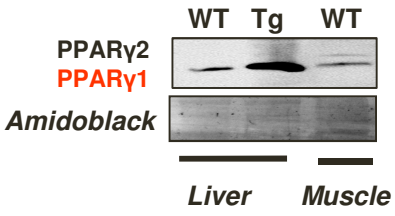
Do Carmo et al, AJP Endo Met 2008

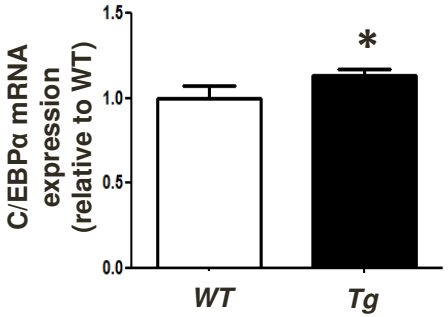
TgApoD mice characterization

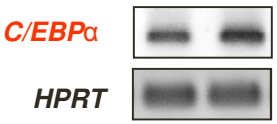


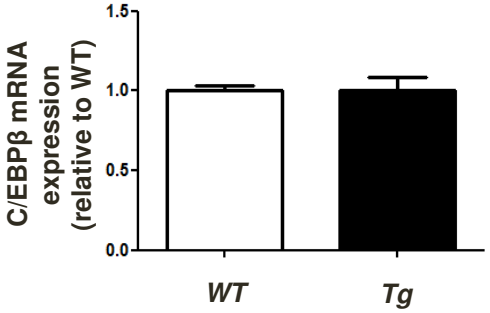


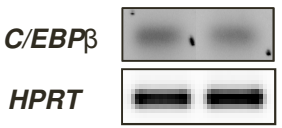






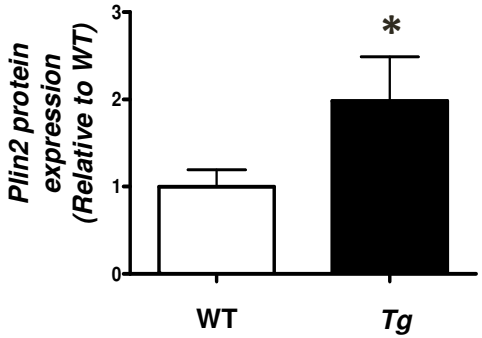


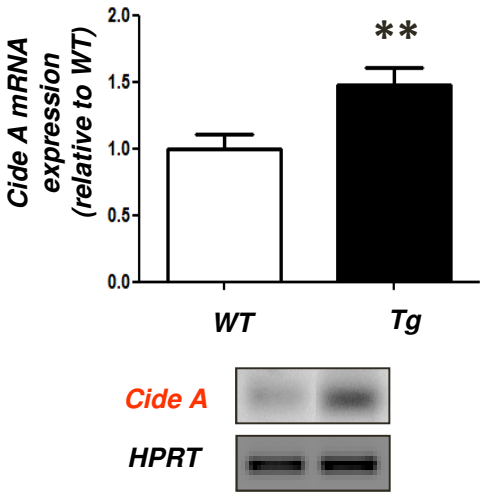


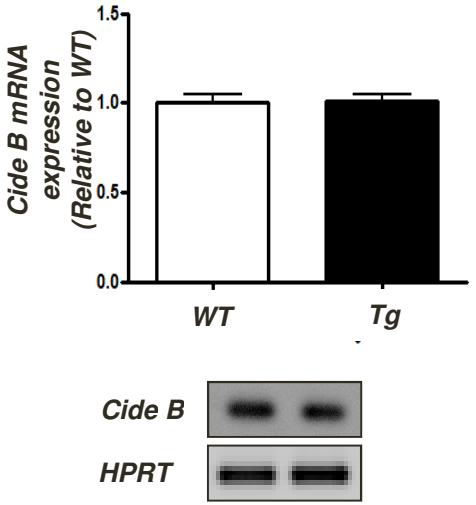


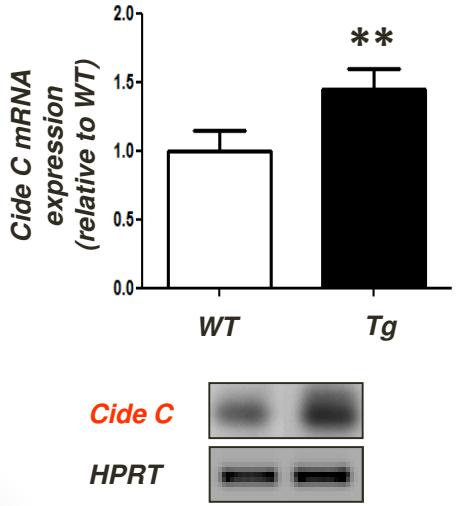
Labrie et al. 2014 BBA-lipids submitted

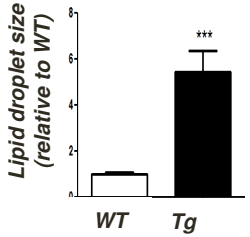
TgApoD mice Lipid droplets formation

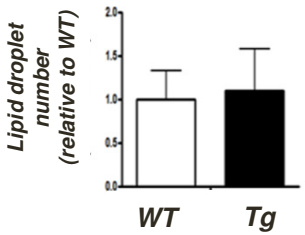


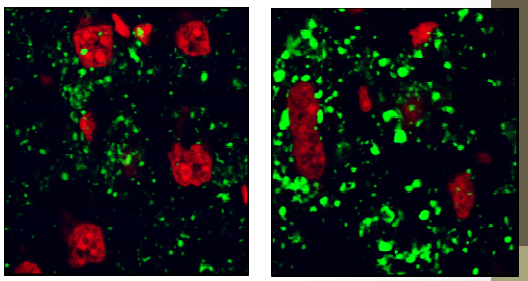






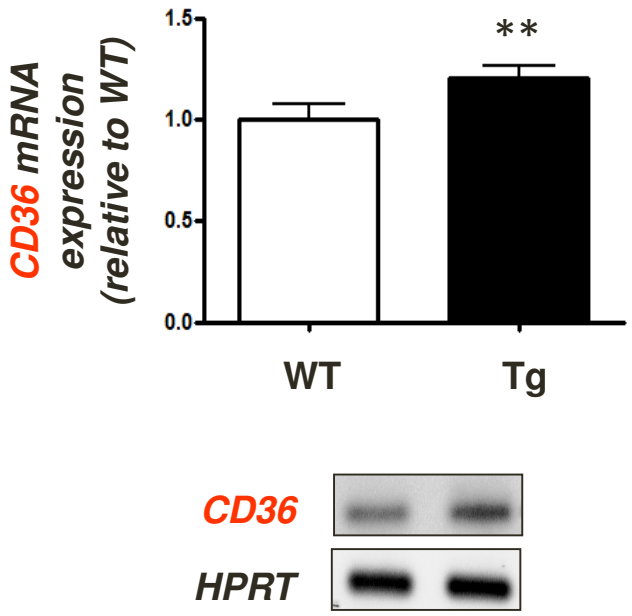


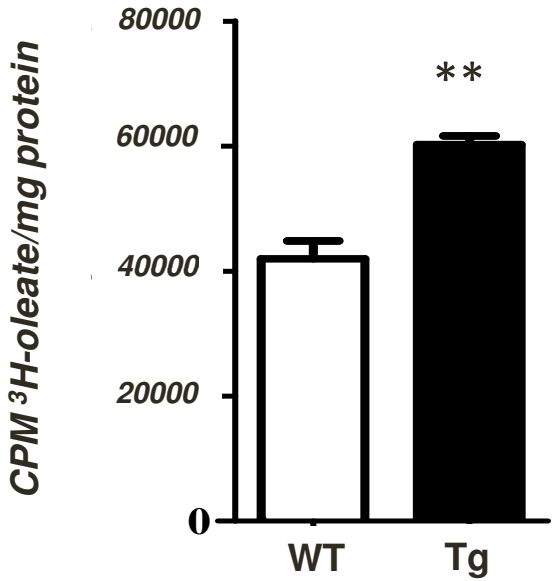




Labrie et al. 2014 BBA-lipids submitted

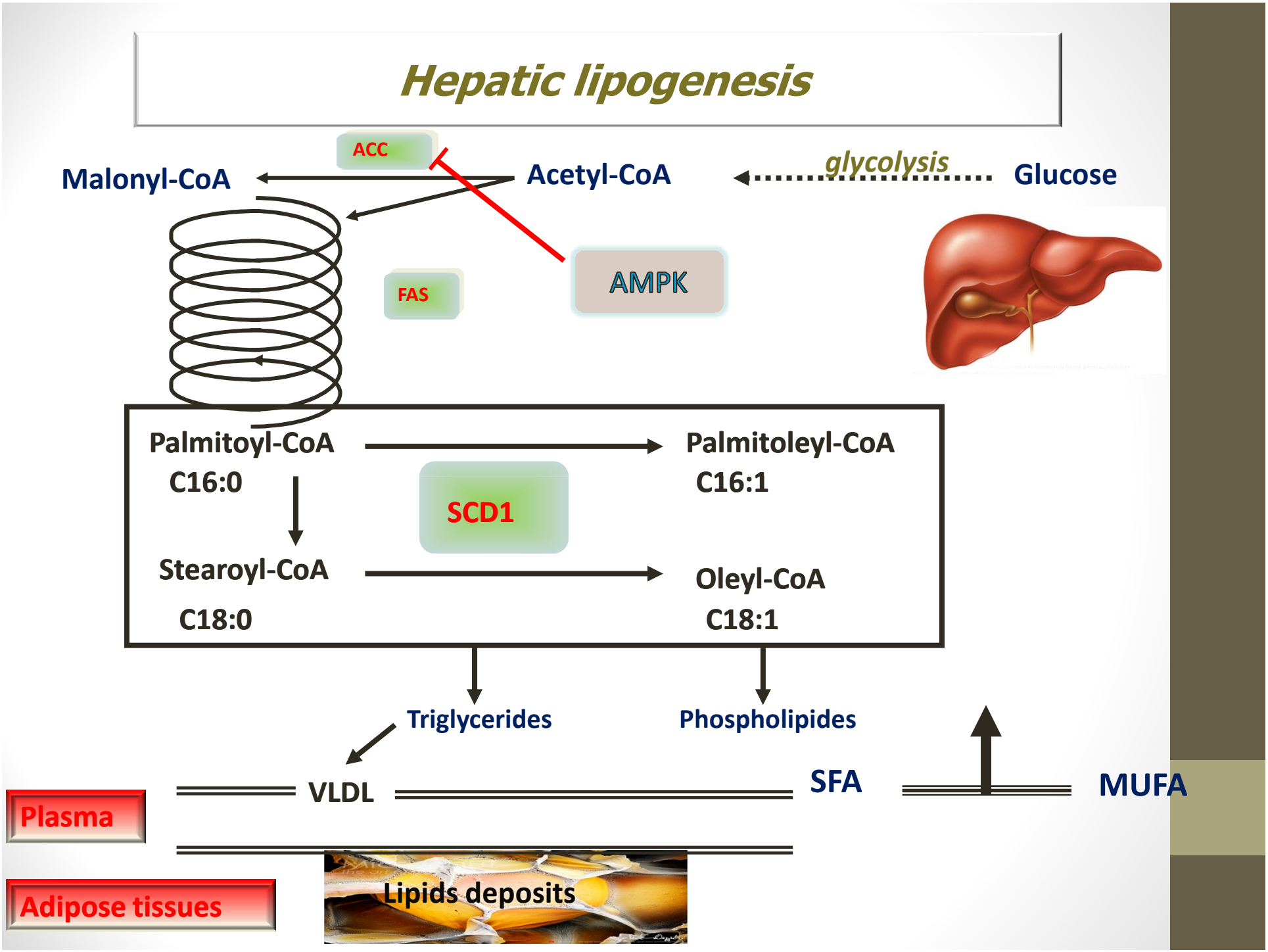
TgApoD mice and Fatty acid uptake



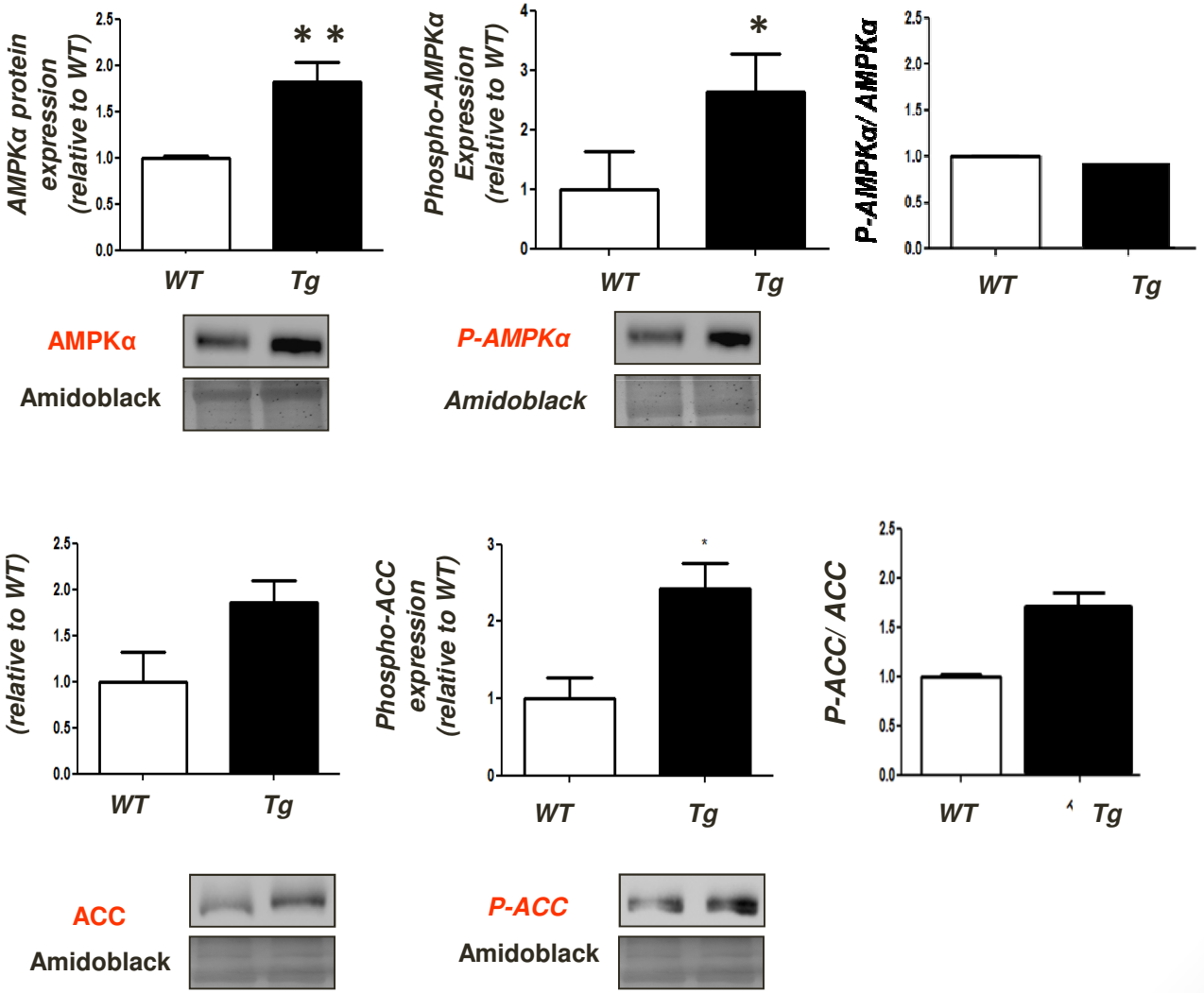


Labrie et al. 2014 BBA-lipids submitted

Hepatic lipogenesis

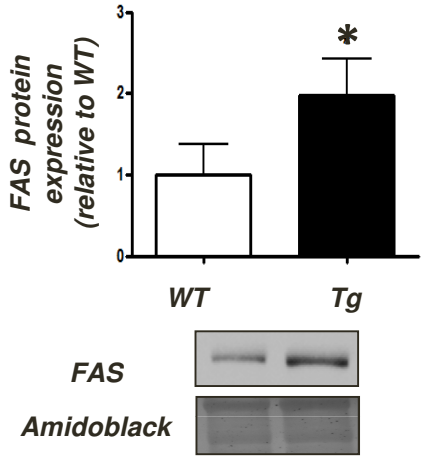


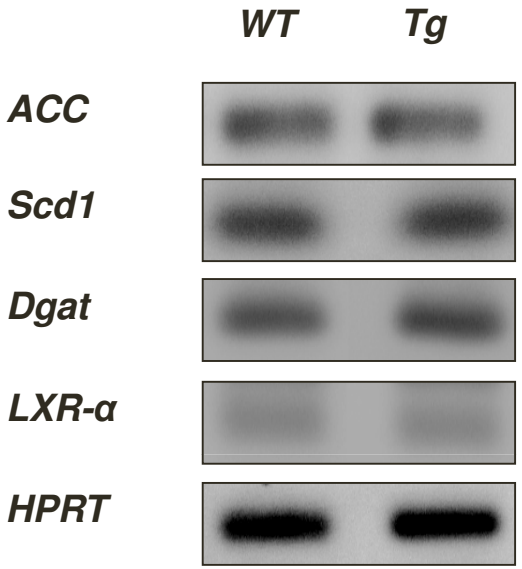
TgApoD mice and lipogenesis

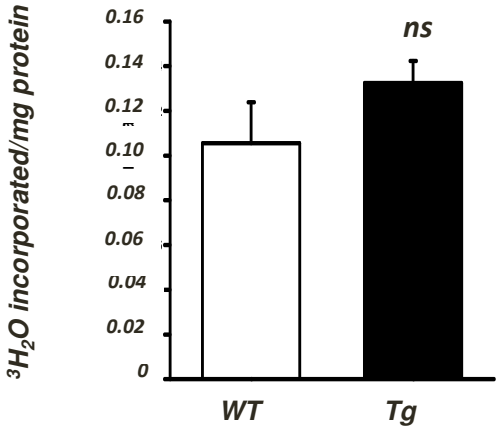


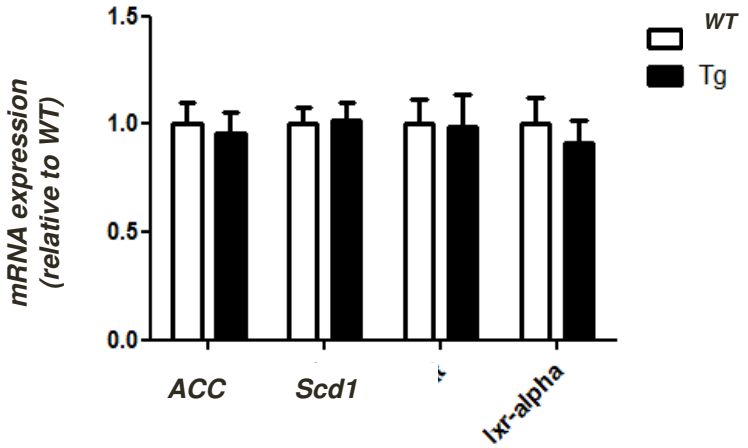
Labrie et al. 2014 BBA-lipids submitted

TgApoD mice and lipogenesis





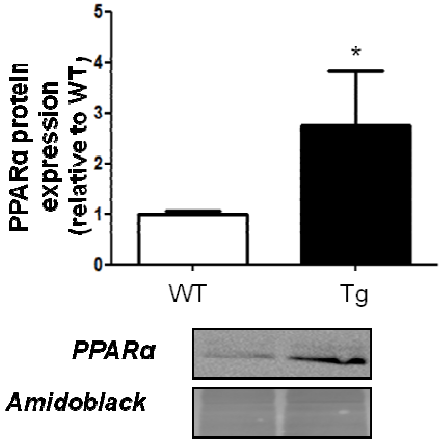




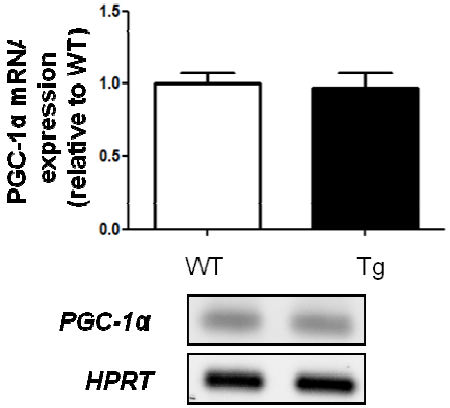
Labrie et al. 2014 BBA-lipids submitted

TgApoD mice and β-oxydation

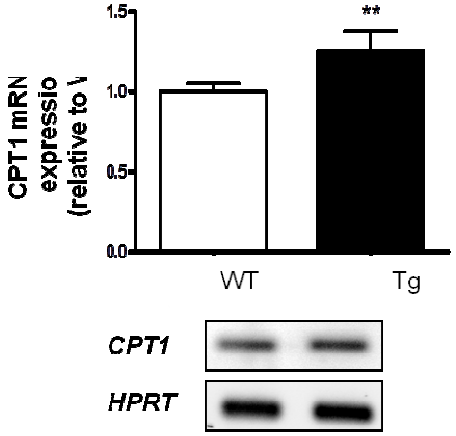
C

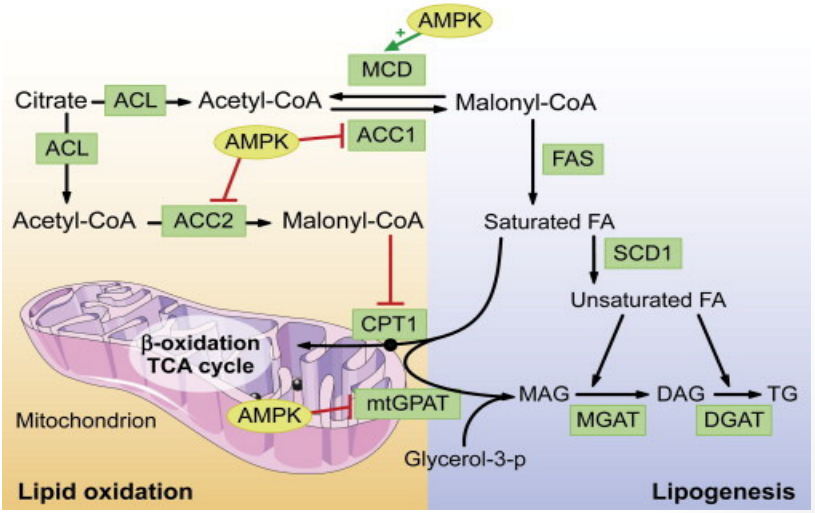


D



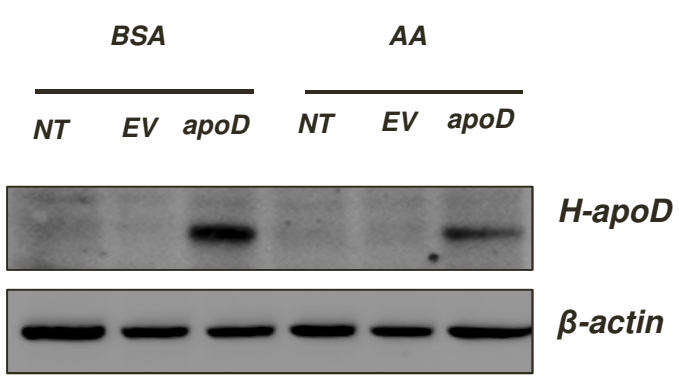
E

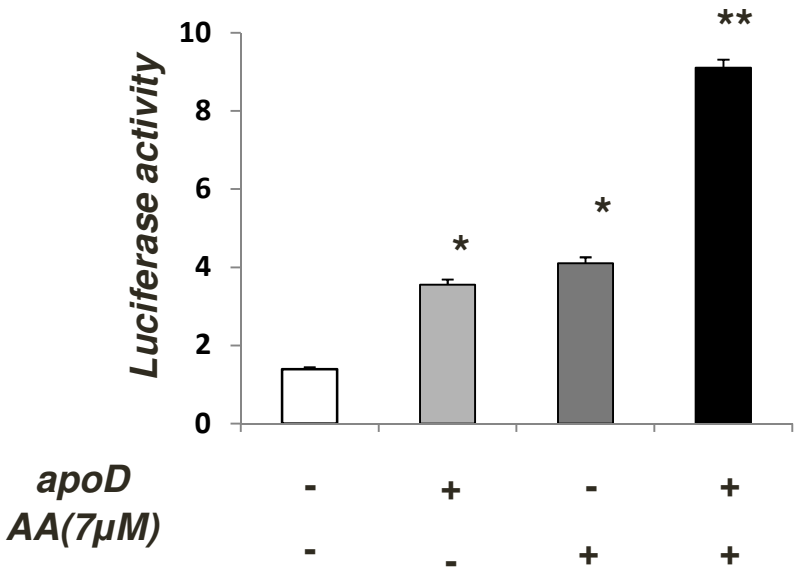




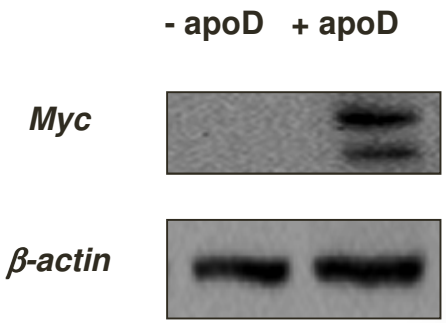
Labrie et al. 2014 BBA-lipids submitted

ApoD in hepG2 cells



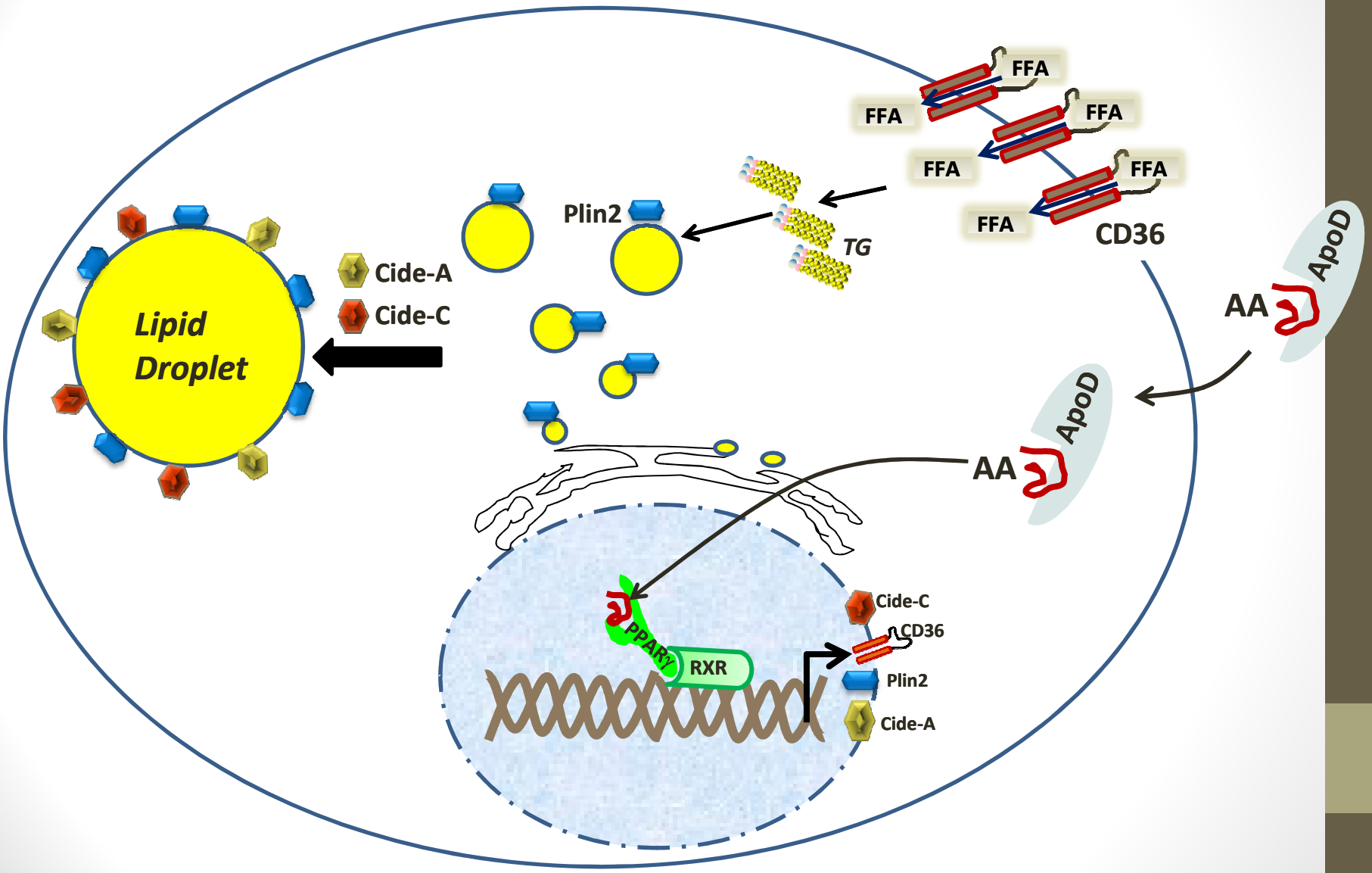






Labrie et al. 2014 BBA-lipids submitted

ApoD mechanism of action



Labrie et al. 2014 BBA-lipids submitted

Acknowledgments



UQÀM
Université du Québec à Montréal

Maryline Labrie
Simon Lalonde
Ouafa Nagyb
Dr. E. Rassart



CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

CRSNG
NSERC

FONDATION DES MALADIES DU CŒUR DU QUÉBEC
À la conquête de solutions.