

Early high nutrition affects epigenetics related to lipogenesis in grass-fed Wagyu



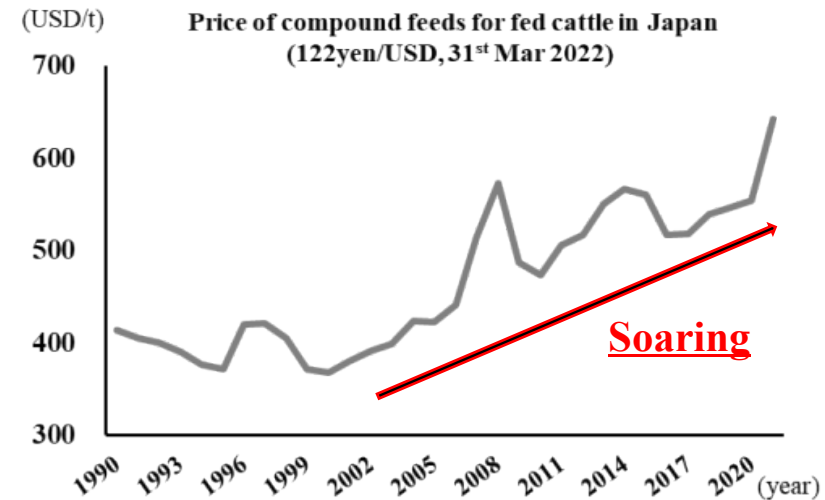
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Marbled beef production system



Soaring grains prices
Feed-food competition
Animal welfare etc.



No other effective feeding system
to produce marbled beef

Grazing

Sustainable system

Poor quality
and quantity

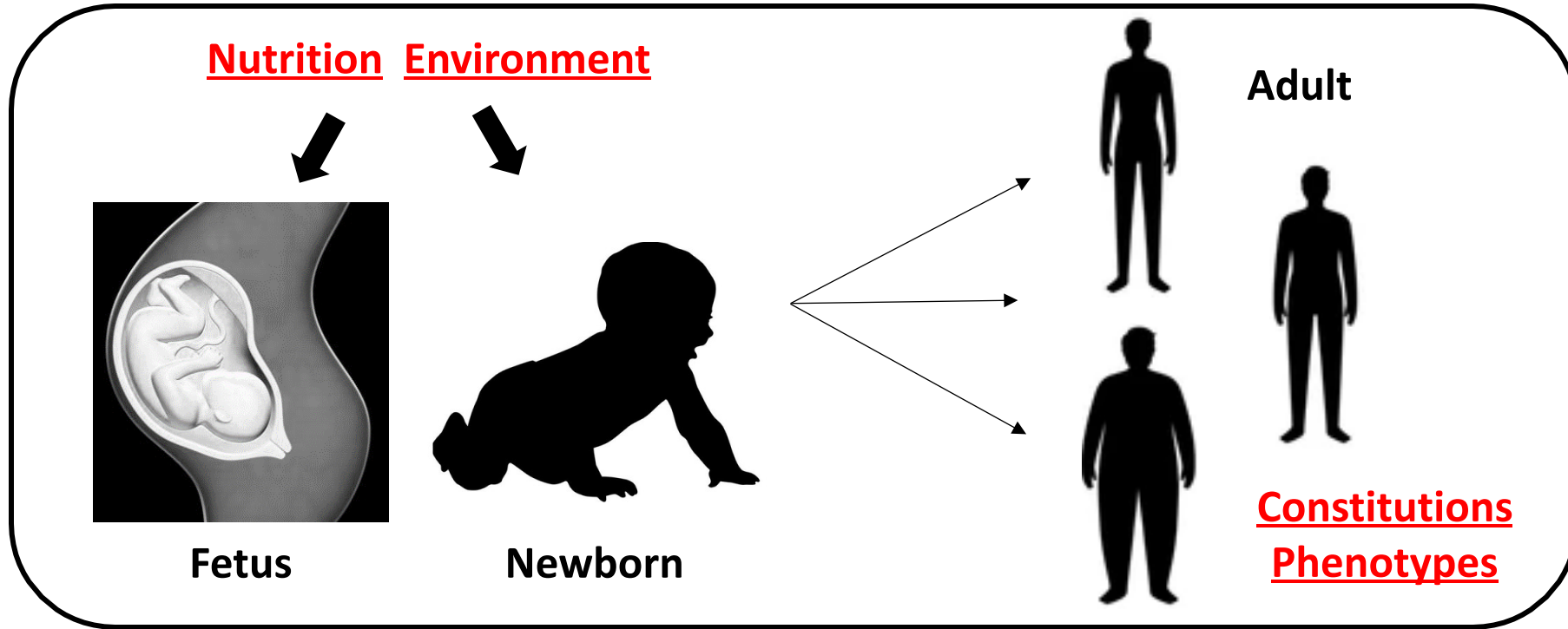


An innovative feeding system is required

DOHaD (Developmental Origins of Health and Disease)

The Dutch Famine

Undernutrition during the fetus stage \Rightarrow Obesity, Dyslipidemia, Chronic disease



[Neonatal period]

[Adult]

High-fat,
calorie diet

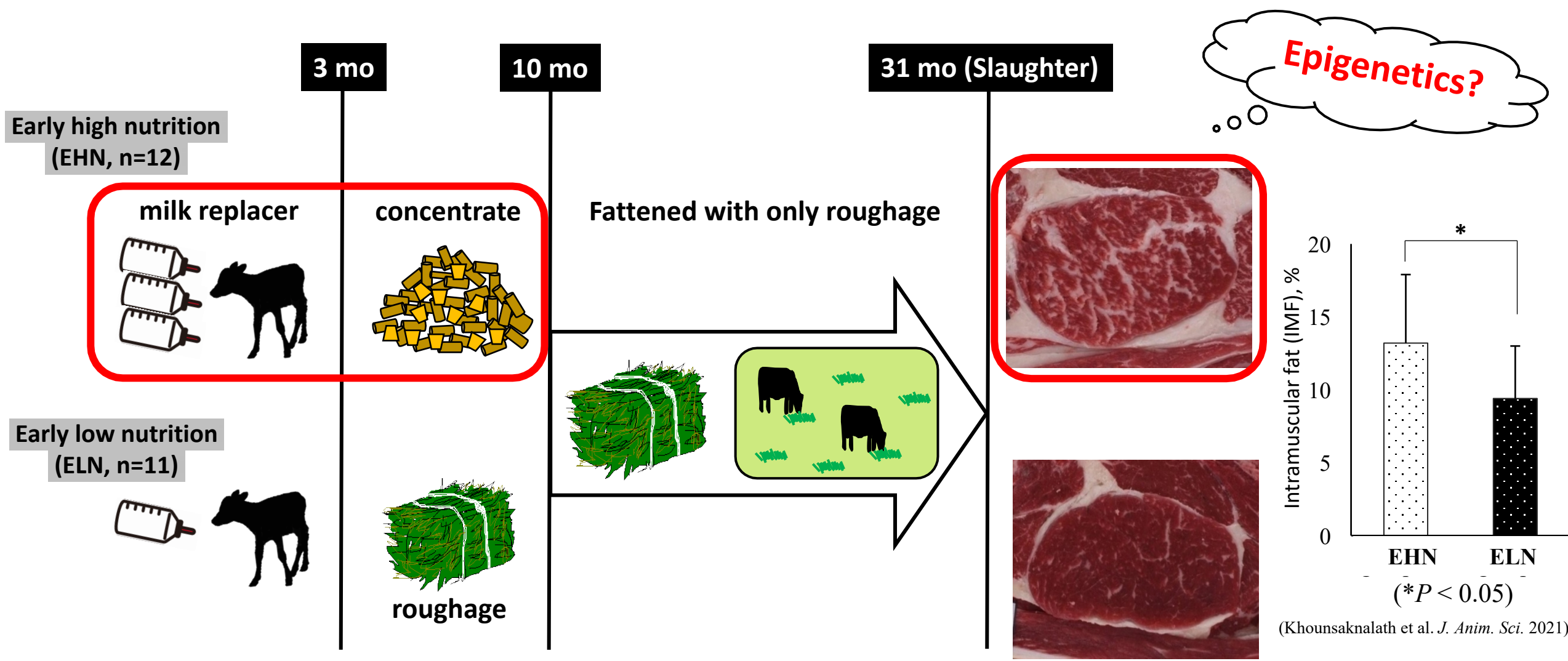


Obesity

?

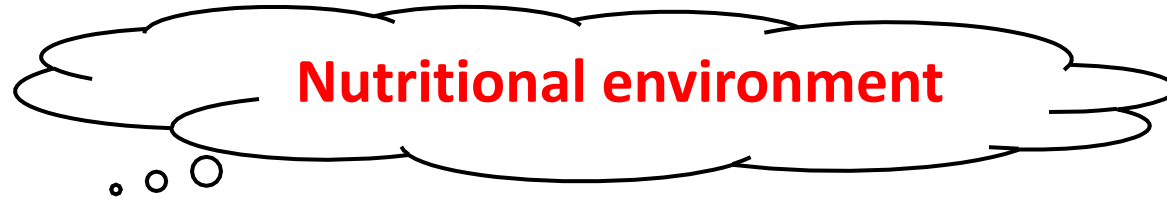
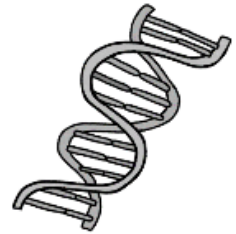
Efficient beef production?

Previous research



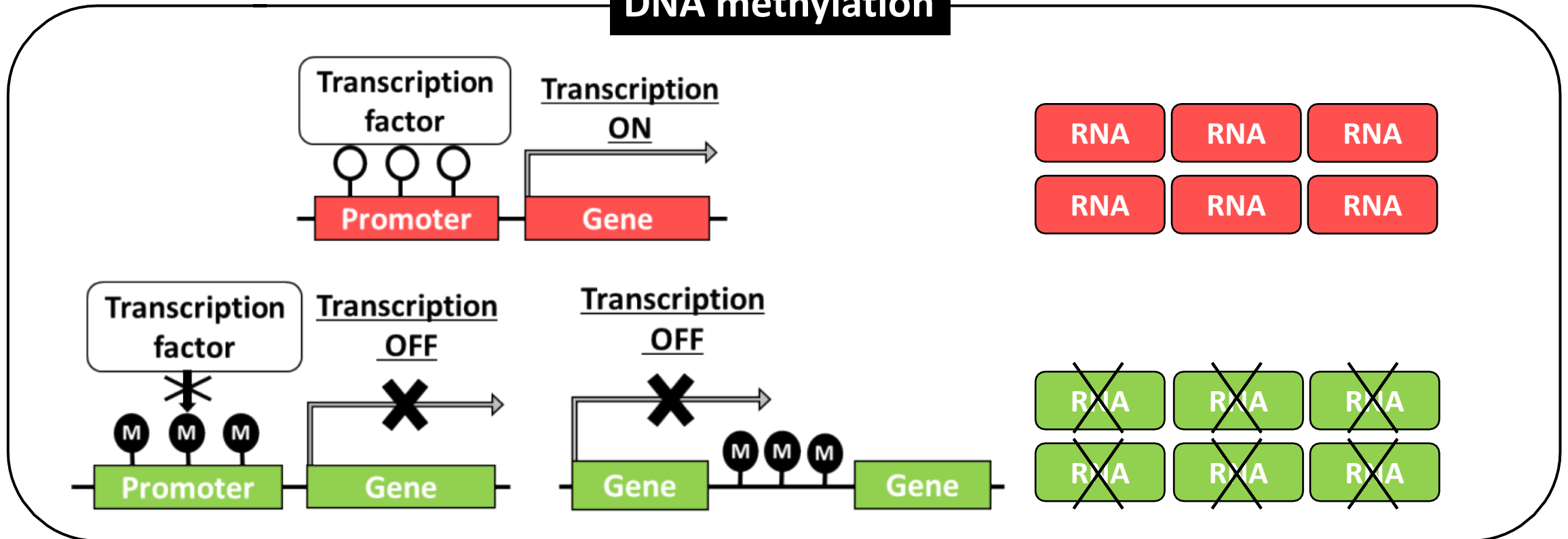
EHN contributed to the accumulation of IMF

Possibility of epigenetics



DNA → RNA → Protein → Phenotype

DNA methylation

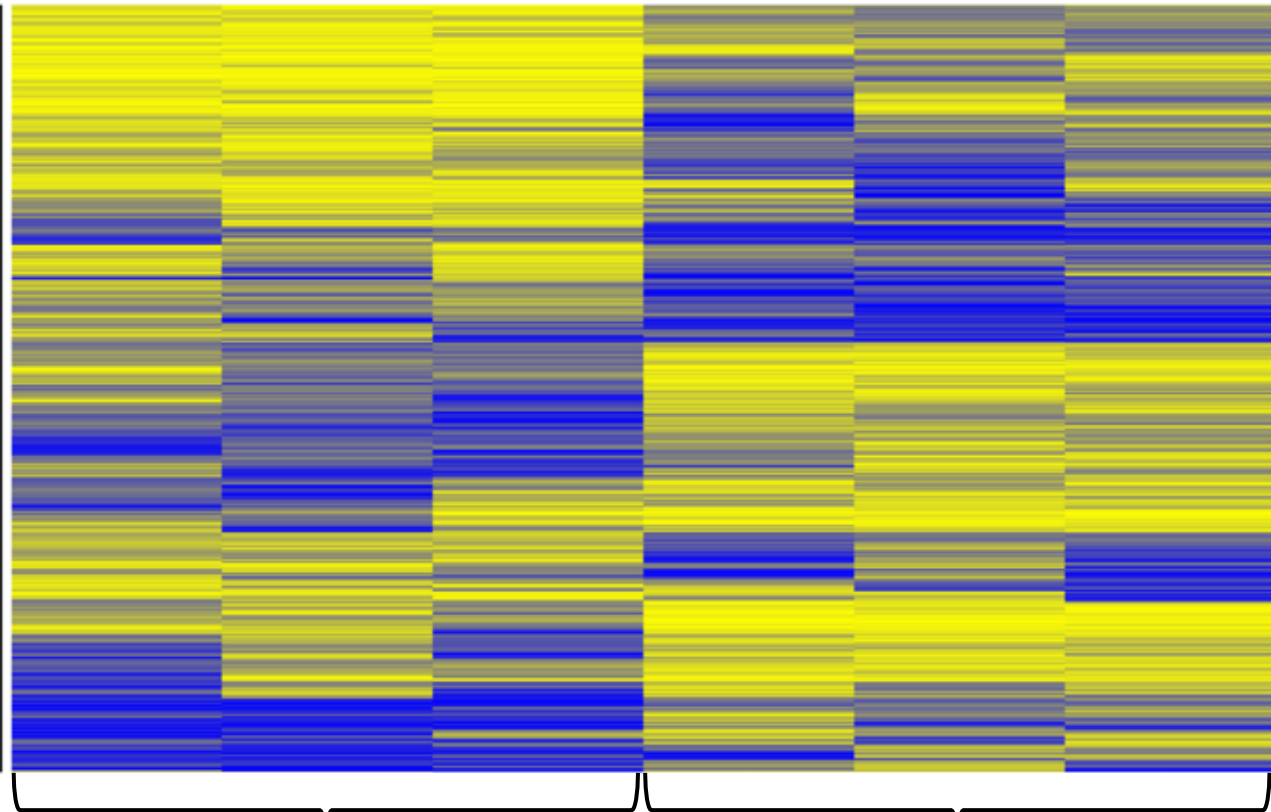


(Anastasiadi et al. Epigenetics & Chromatin 2018, Nam et al. Clinical Epigenetics 2020)

Hypothesis

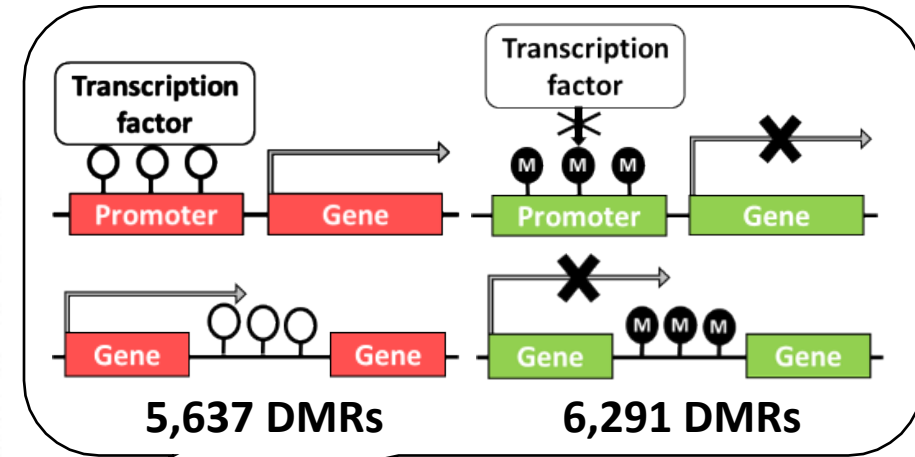
Comparison of DNA methylation levels in longissimus muscle at 31 mo by WGBS (EHN/ELN)

Differentially methylated region (DMR)



EHN

ELN (Nishino et al. ICoMST. 2022)



Early nutrition

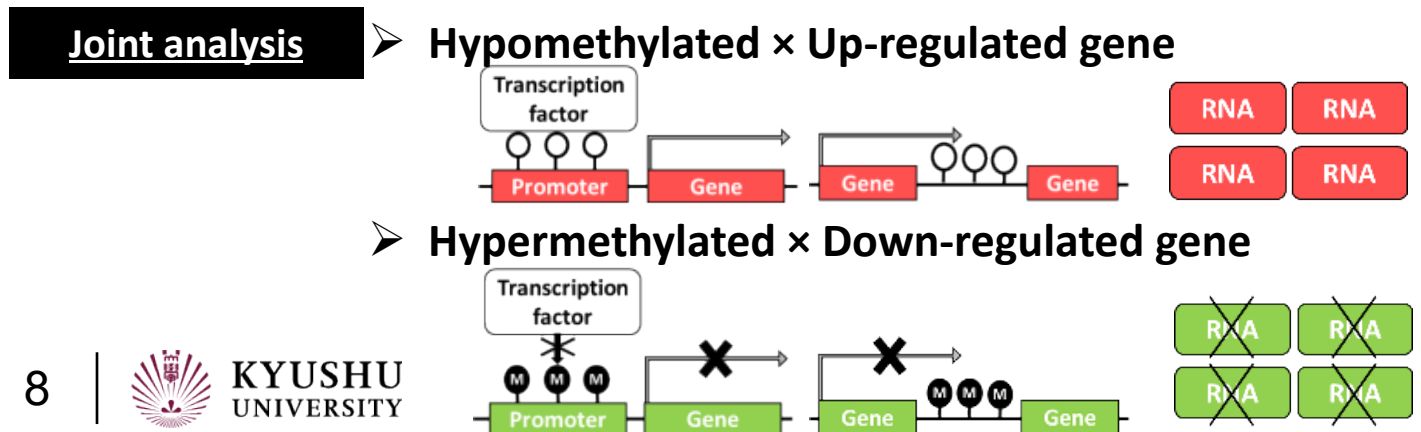
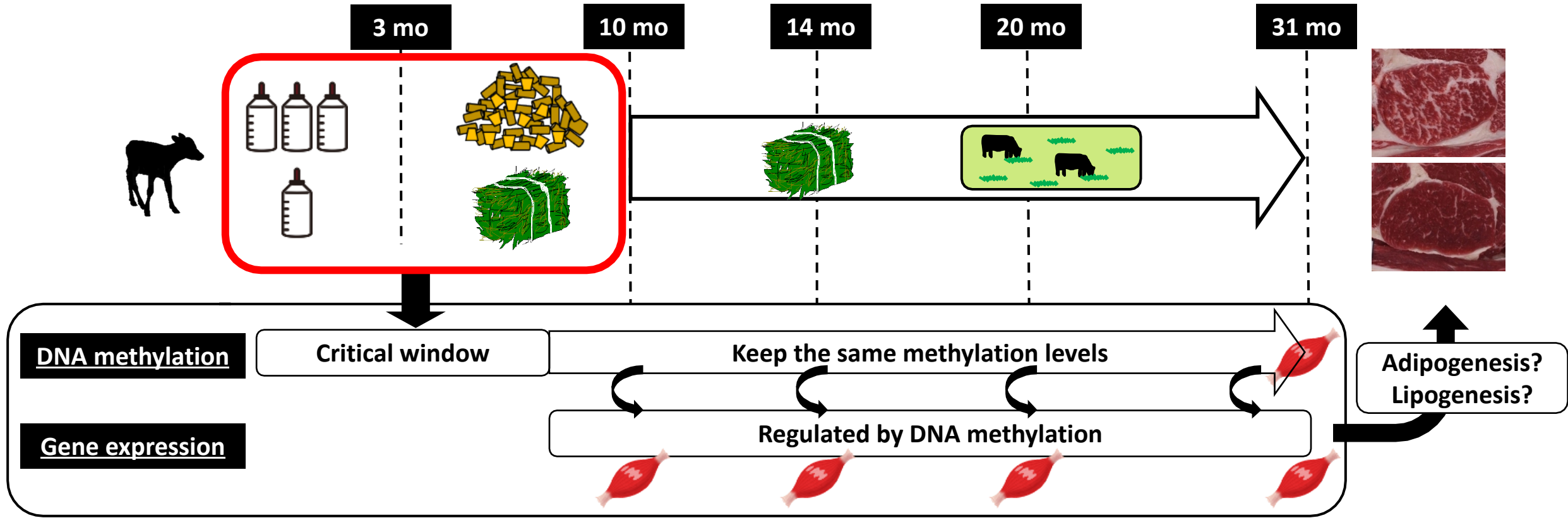
DNA methylation

Gene expression

Phenotype

Exploration of candidate genes that contribute to IMF increase through DNA methylation regulation

Materials and Methods



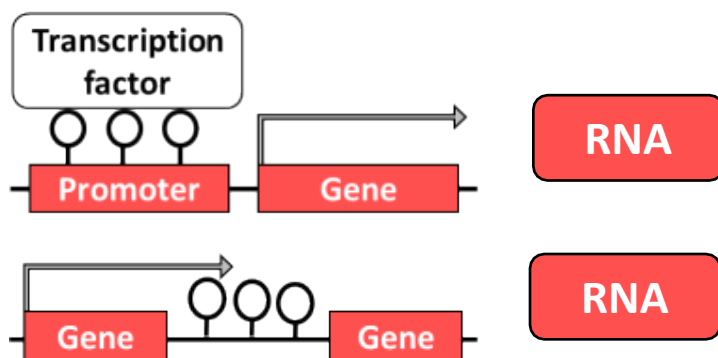
Hypo or Hyper methylated gene (EHN/ELN)
 |methylation difference| > 25%, P-value < 0.01

Up- or Down-regulated gene (EHN/ELN)
 |Log₂(EHN/ELN)| > 0.5 at all time points
 (10, 14, 20, and 31 mo)

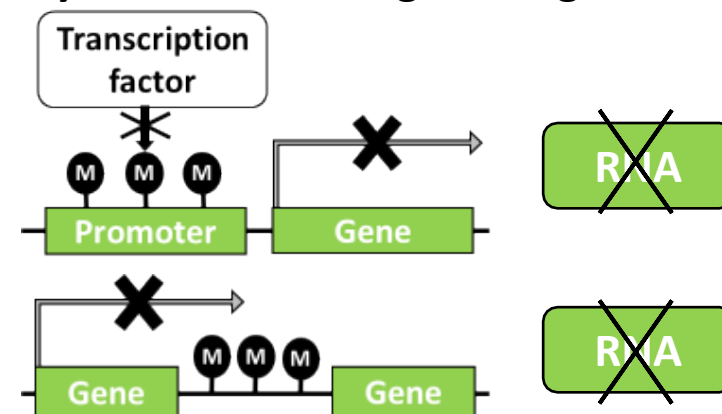
Candidate Genes

Gene symbol	DNA Methylation	Microarray ($\log_2[\text{EHN}/\text{ELN}]$)				Gene name
		10 mo	14 mo	20 mo	31 mo	
CACNA2D3	Hypo	0.95	0.68	1.51	0.64	calcium voltage-gated channel auxiliary subunit alpha2delta 3
MTUS2	Hyper	-1.14	-1.29	-1.10	-0.98	microtubule associated scaffold protein 2
RGS1	Hyper	-2.08	-1.32	-0.76	-0.67	regulator of G protein signaling 1
DPYSL5	Hyper	-0.77	-0.91	-0.55	-1.68	dihydropyrimidinase like 5
FAM163A	Hyper	-1.08	-1.52	-0.76	-0.66	family with sequence similarity 163 member A
FOXO1	Hyper	-0.86	-1.24	-1.10	-0.73	forkhead box O1
TMEM163	Hyper	-1.18	-1.26	-0.61	-0.67	transmembrane protein 163

Hypomethylated × Up-regulated gene

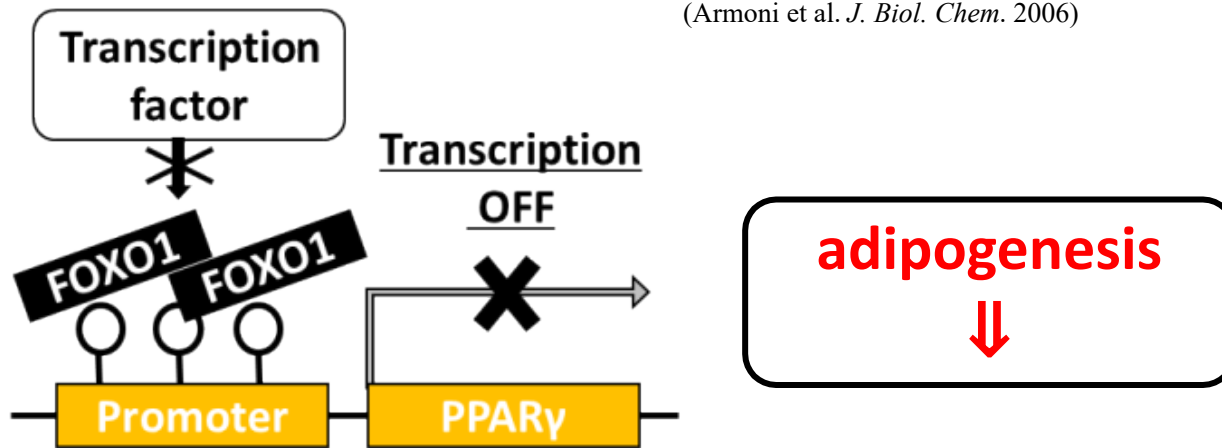


Hypermethylated × Down-regulated gene



PPAR γ

FOXO1 inhibits PPAR γ transcription

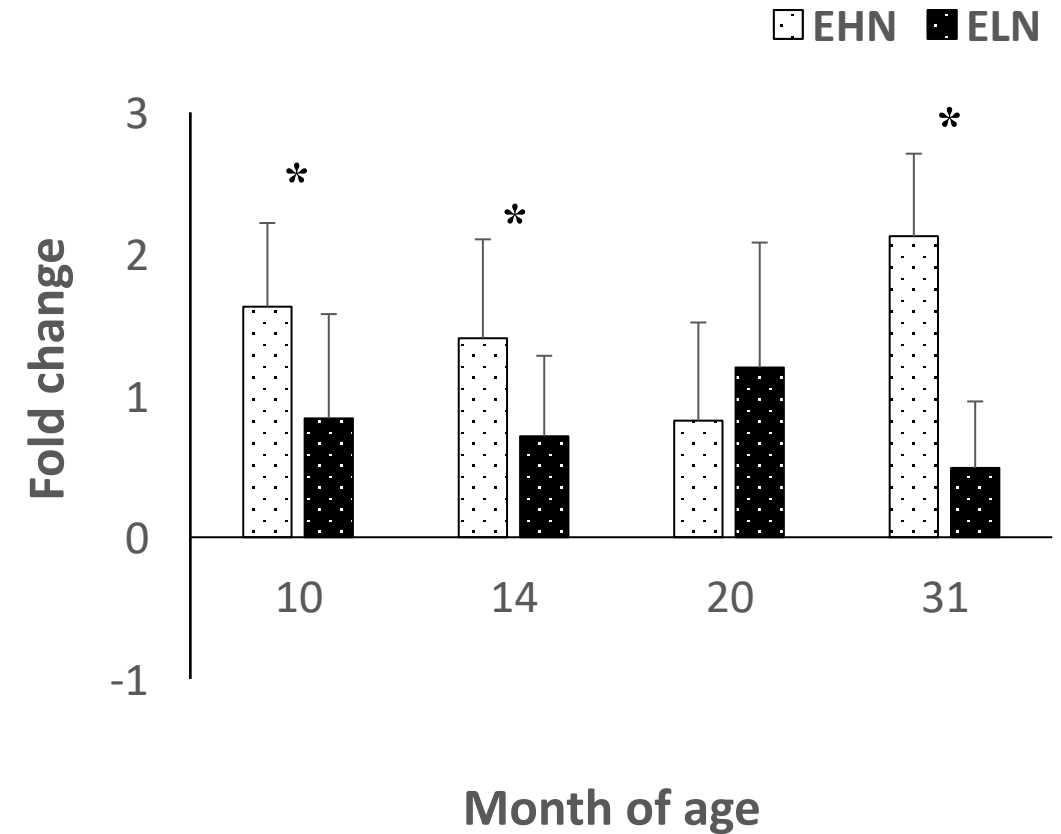


PPAR γ (Peroxisome Proliferator-Activated Receptor γ)

- Primary regulator of adipogenesis
- Necessary for adipocyte differentiation

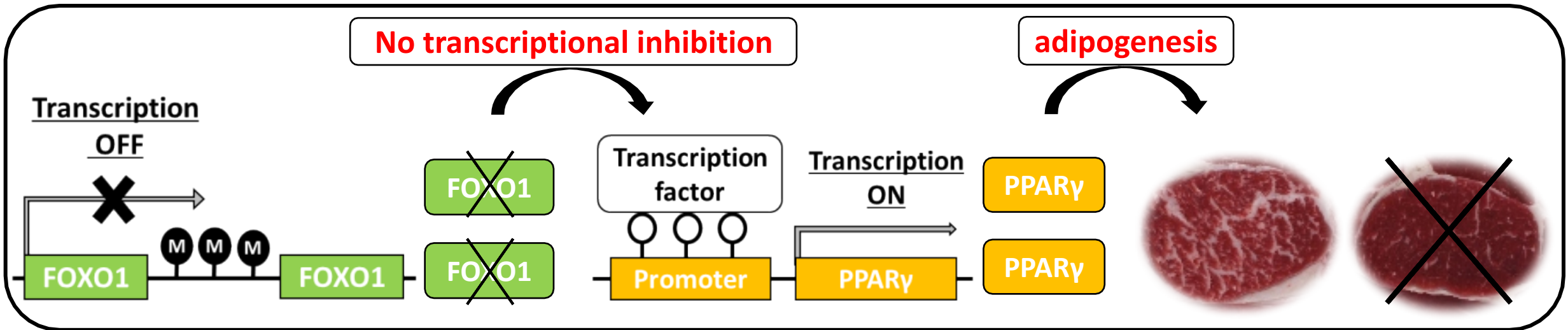
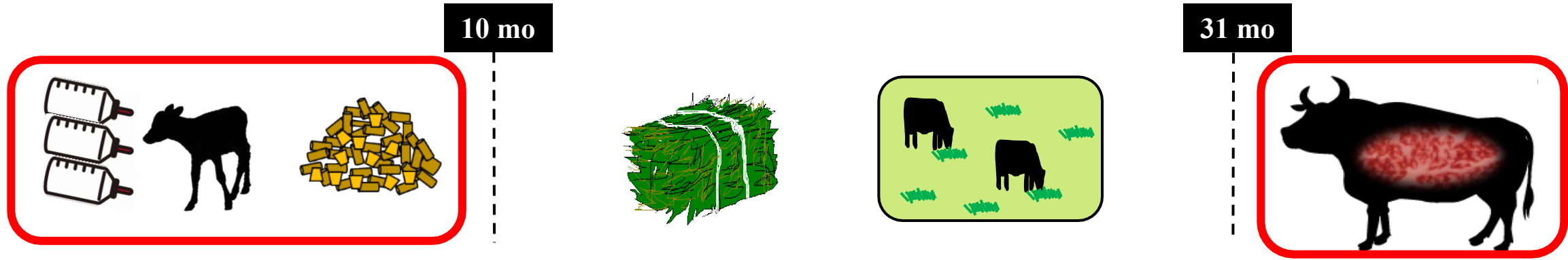
(Ali et al. *Eur. J. Cell. Biol.* 2013)

PPAR γ expression (qPCR)



EHN steers had greater PPAR γ expression

Summary



EHN might enhance adipogenesis by inducing FOXO1 hypermethylation and less expression, and promoting PPAR γ transcription

*Thank you
for your attention.*

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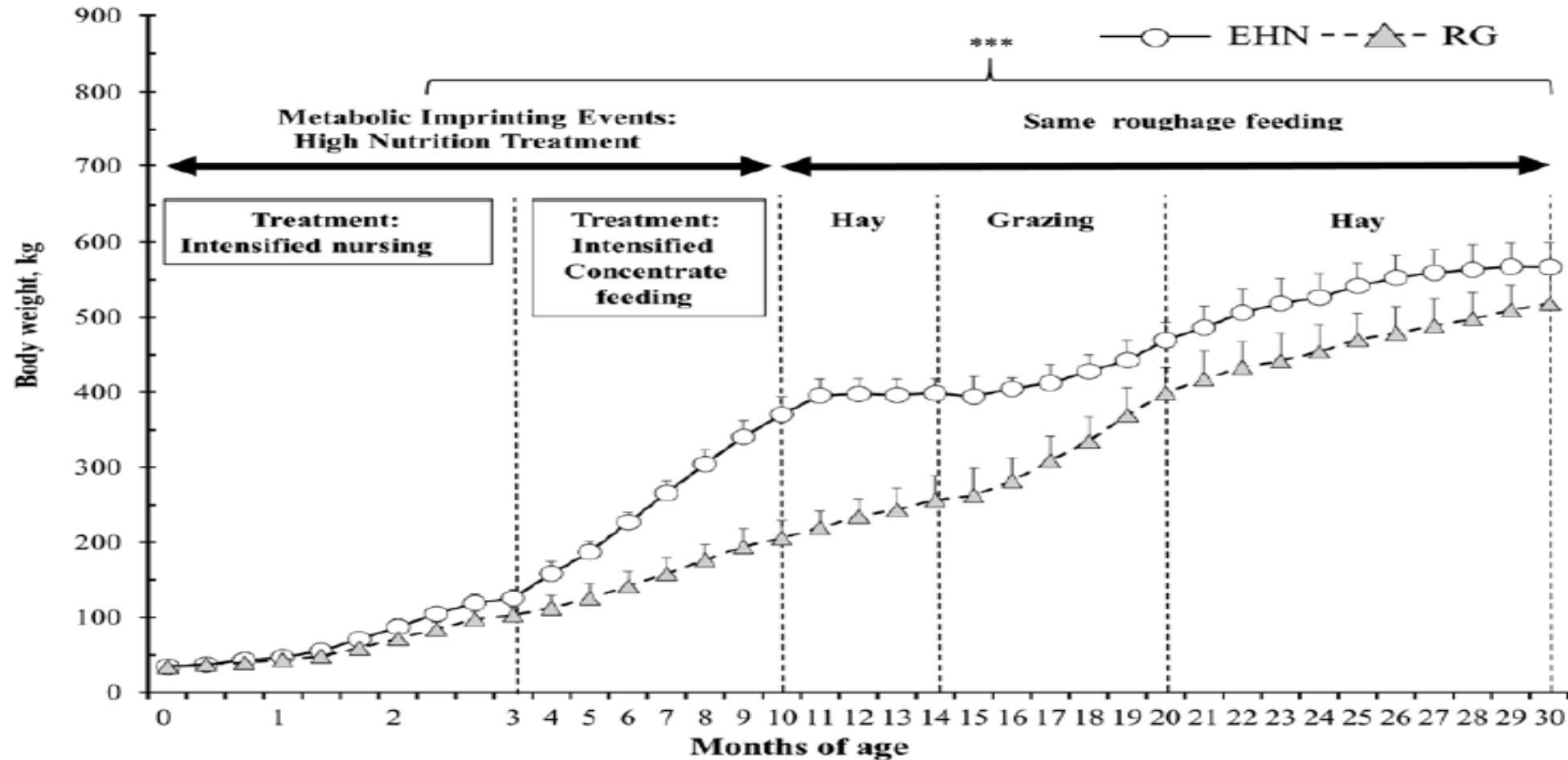
Doctoral Course

Faculty of Agriculture, Kyushu University

Special Research Student, Hokkaido University



Changes in mean body weight over the experiment



- ① 実験モデル（栄養量のサブスライドも）
- ② これまでのデータ：表現型に加え、IMF（要強調）→エピジェネティクスの可能性
- ③ エピジェネティクス、特に直接的な制御を施すDNAメチル化に着目。制御機構の説明
- ④ DNAメチル化のヒートマップ（メチル化は変わらないのか？要リファレンス、サブスライド）
- ⑤ 本研究の仮説「初期栄養→10moまでにDNAメチル化確定（そもそもcritical windowはいつまで？要Ref）
→遺伝子発現→IMF」
- ⑥（10moまでに確定したであろう）メチル化と遺伝子発現の解析対象時点の説明
- ⑦（10moまでに確定したであろう）30moにおけるDNAメチル化と10mo後に一貫した発現変動を示した遺伝子の統合解析
- ⑧ In EHN, 1 gene was hypo-methylated and highly expressed, and 6 genes were hyper-methylated and consistently under-expressed.
- ⑨ FOXO1に着目、脂質形成に関するFOXO1の報告（FOXO1とPPAR γ の関連）
- ⑩ PPAR γ の遺伝子発現（10, 14, and 31 moで高発現）
- ⑪ FOXO1の高メチル化・低発現によりPPAR γ が抑制されず、脂質形成を促進？