XV Incontro della Rete Insieme per l'Allatamento
« Allatamento fra care e scienza »
30 settembre 2021, Trieste

Epigenetica, Perinatologia… e Allatamento

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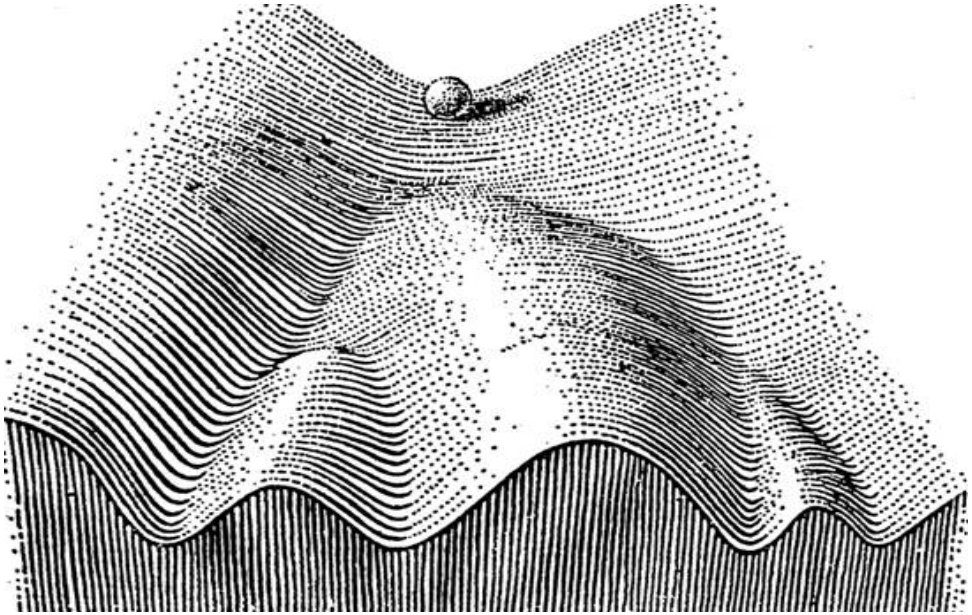
Breastfeeding

- Optimal nutrition for infants, with unique advantages:
  - Nutrients
  - Functional, bioactive components
  - Dynamic, adaptive composition
  - Mother-infant relationship

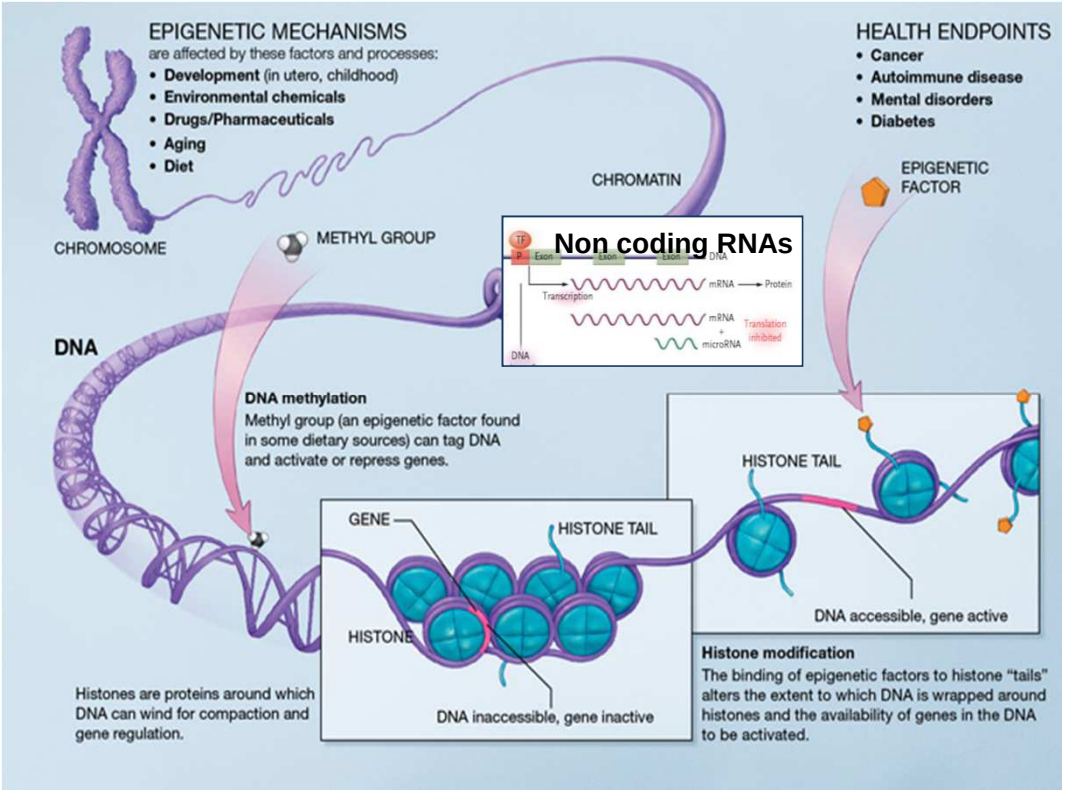
- Long term benefits to the infant:
  - Cognitive development (Victora C.G. et al, 2016)
  - Infectious diseases (Verduci E. et al, 2014)
  - Inflammatory responses (McDade T.W. et al 2014)
  - Blood pressure (Martin R.M. et al 2017)
  - Adiposity and obesity (Horta B.L. et al, 2014; Martin R.M. et al 2017)

Epigenetic landscape and biological bevelopment: How the environment affects genes regulation and development



C Waddington (1957)

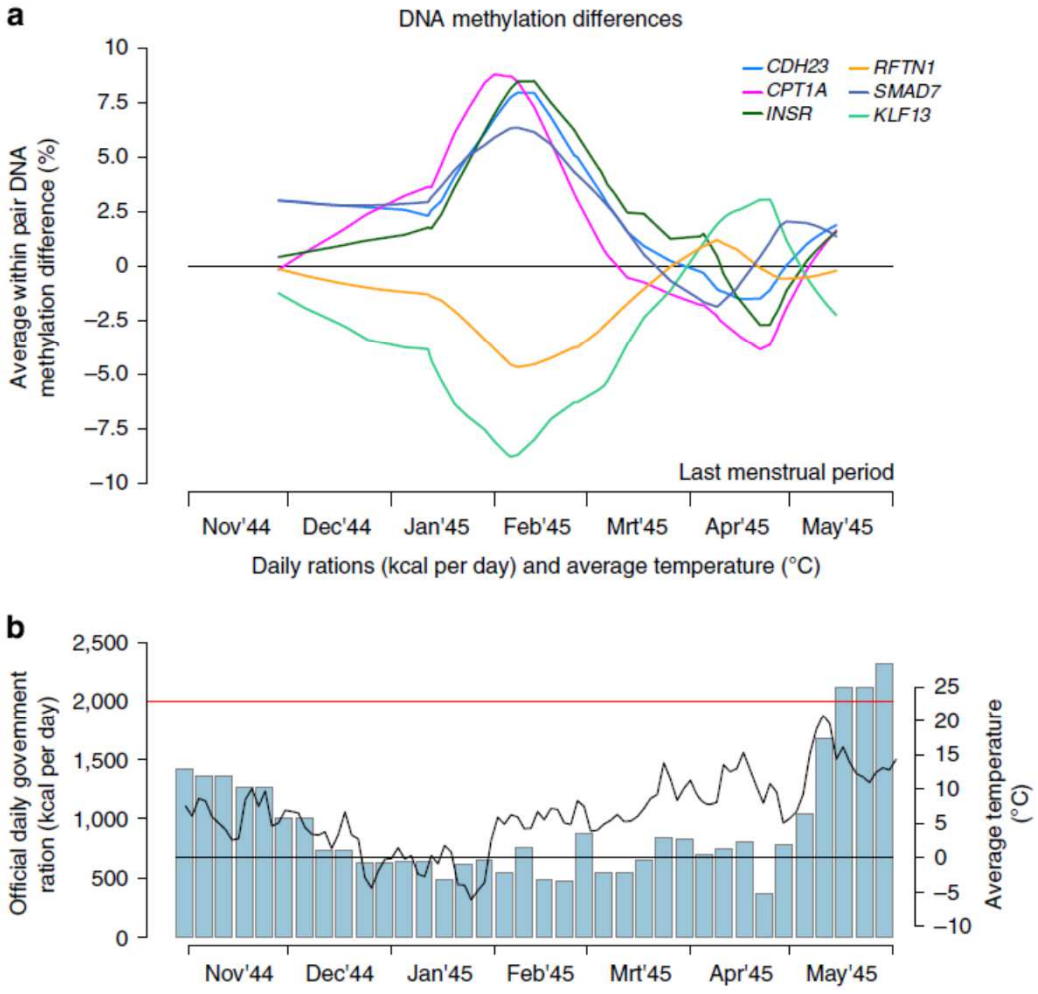
Epigenetics: a long lasting, heritable molecular translation of early genome-environment interactions, in the absence of gene sequence alteration



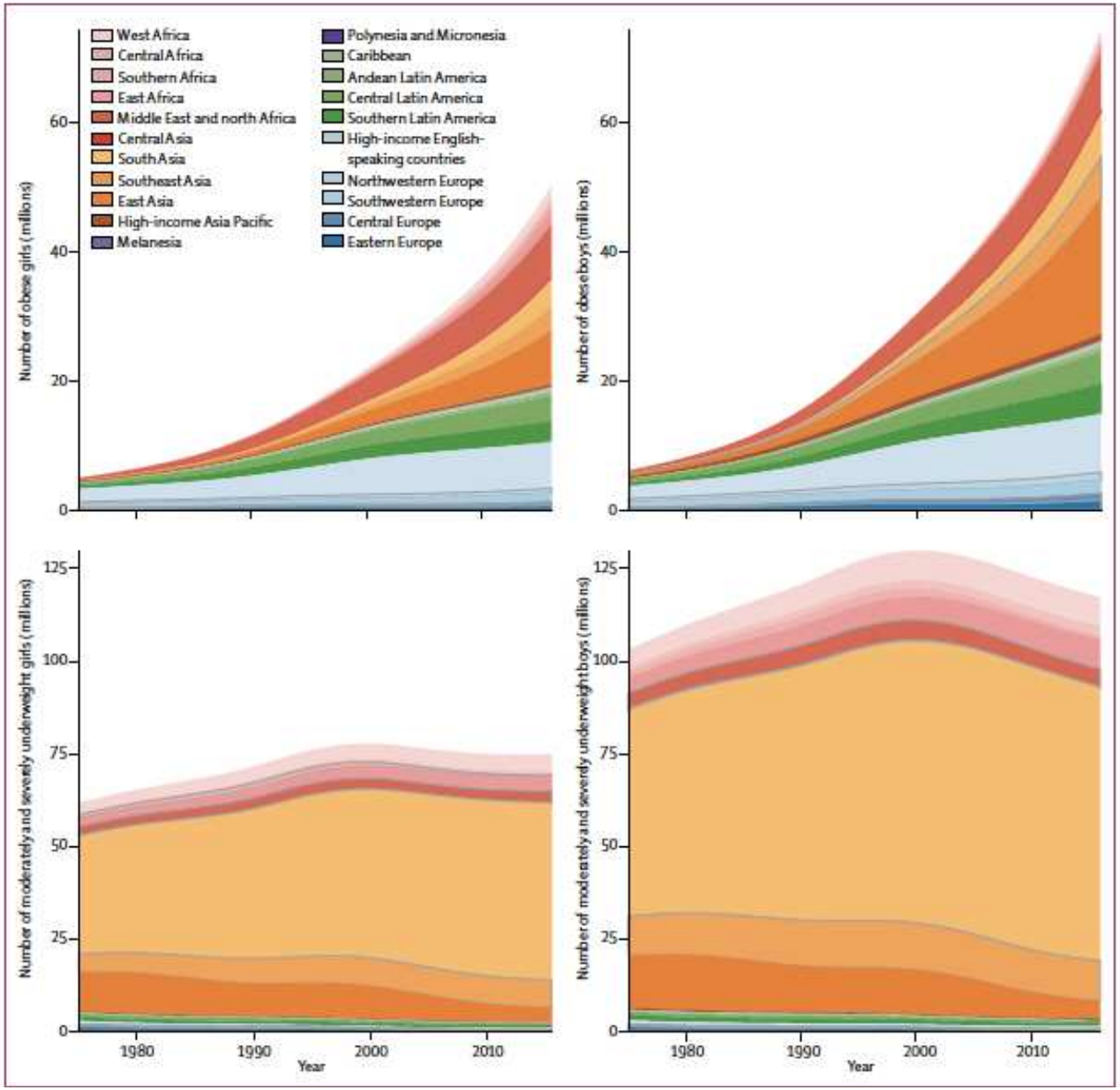
DNA methylation signatures link prenatal famine exposure to growth and metabolism

Increased risk in offspring:

- Obesity
- Dyslipemia
- Type 2 Diabetes
- Schizophrenia



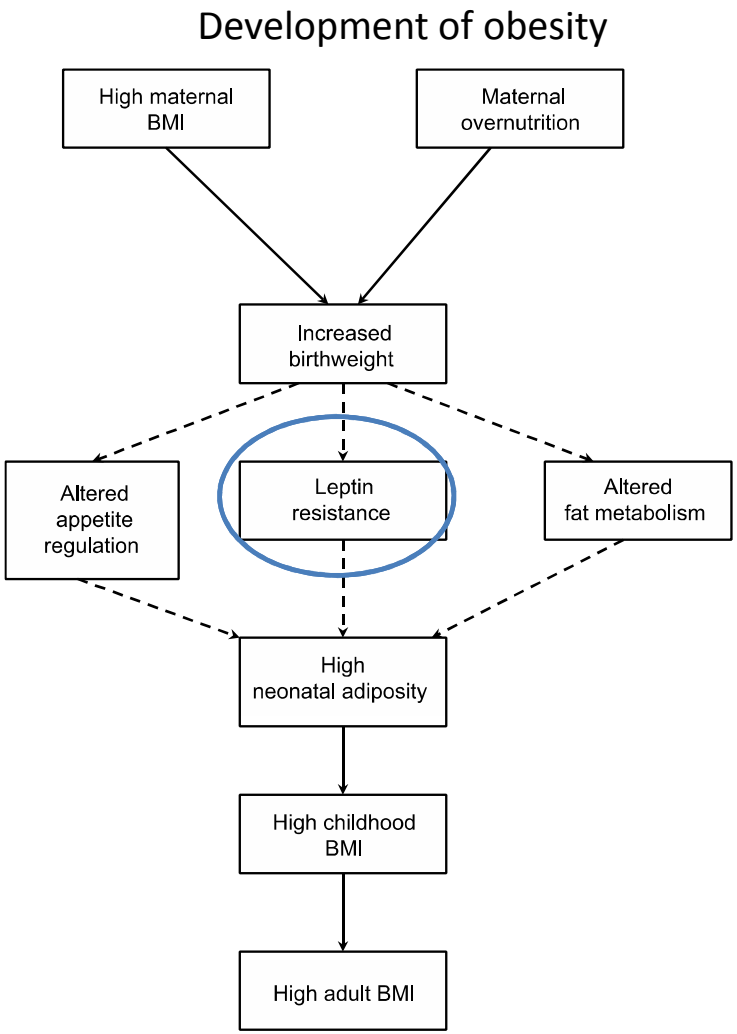
Tobi EW et al, Nature, 2014

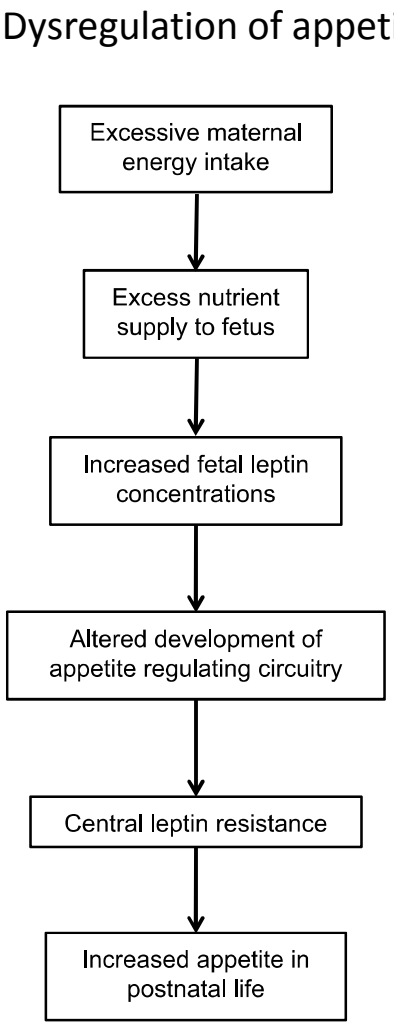


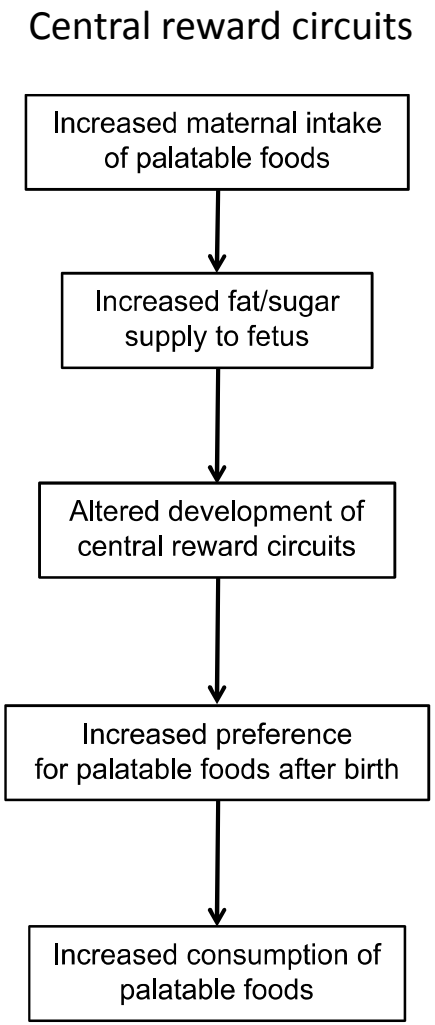
Trends in the number of children and adolescents with obesity and with moderate and severe underweight by region

NCD-RisC Lancet 2017

Maternal overnutrition and metabolism programming in the offspring







Muhlhausler B et al, 2013

Figure 3 Summary of the mechanisms throu

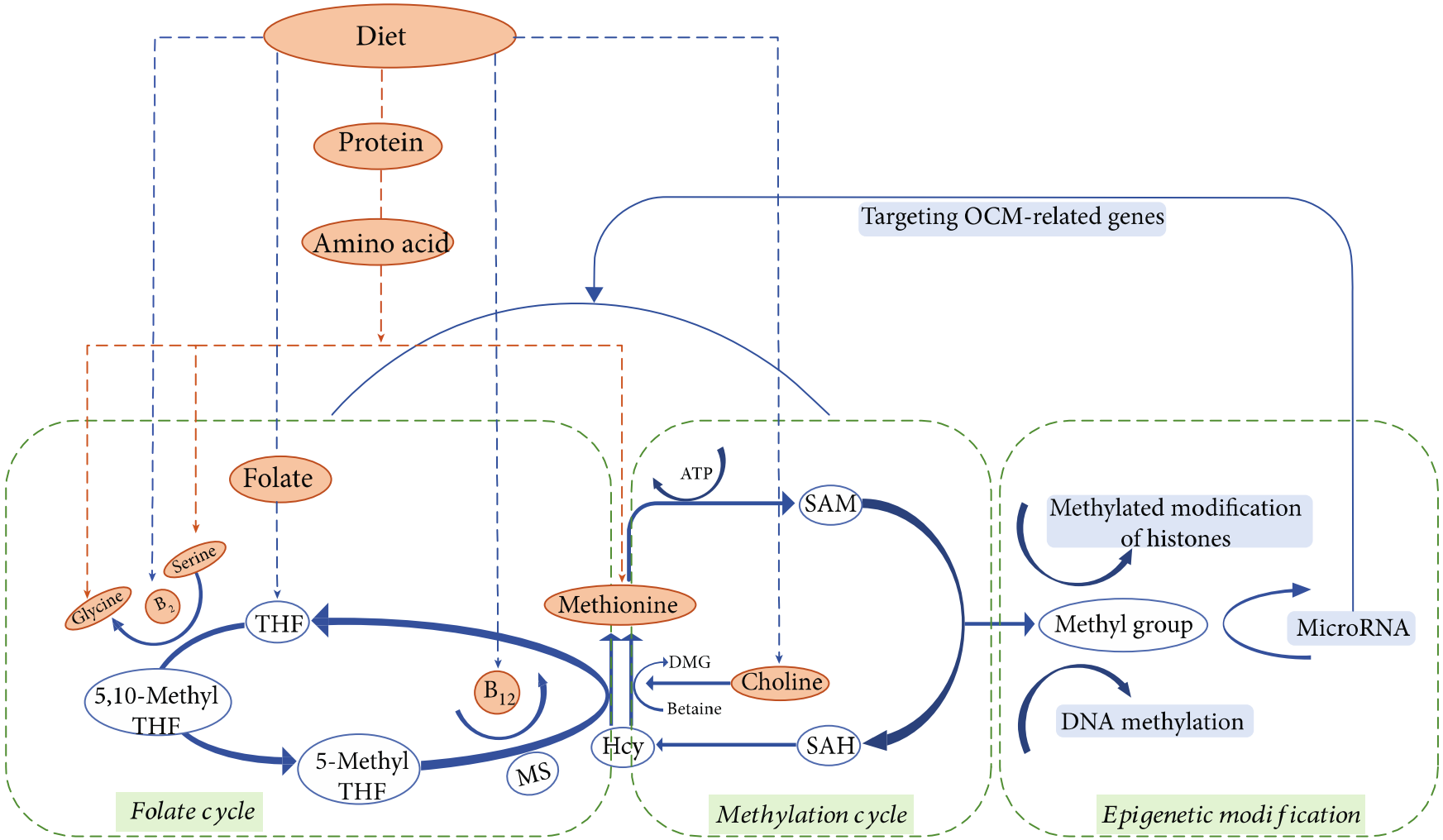
Breastfeeding, early life environment and LEP methylation in 17 month old children

Obernann-Borst S et al, 2012

Associations between methylation of *LEP* and several variables

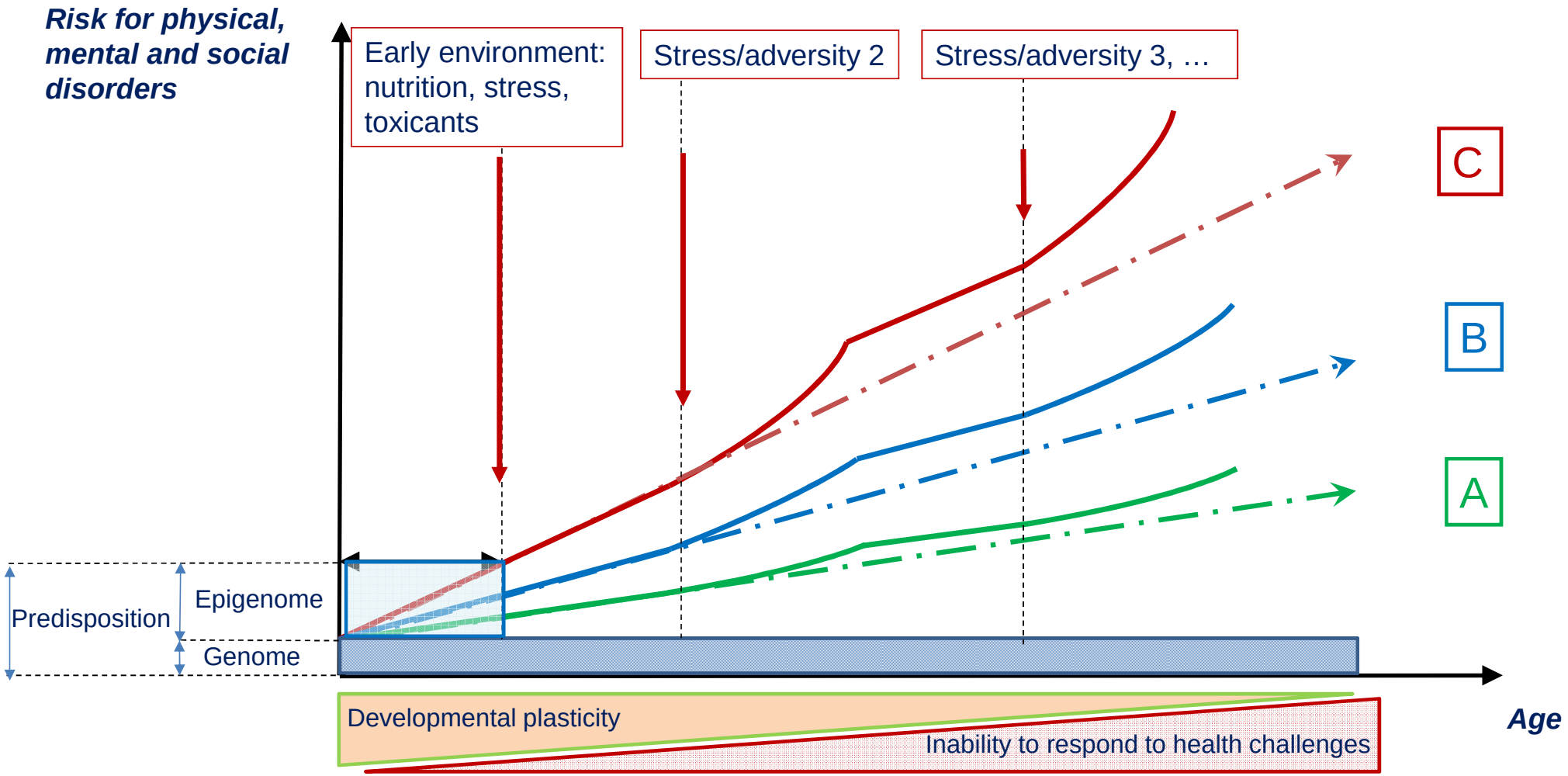
	Model 1			Model 2		
	% Absolute methylation change (SE)[a]	% Relative methylation change (SE)	*P*[b]	% Absolute methylation change (SE)[a]	% Relative methylation change (SE)	*P*[c]
Early environmental factors						
Low education	+2.1 (0.8)	+9.1 (3.5)	0.008	+1.0 (0.8)	+4.2 (3.4)	0.233
No folic acid, periconception	+0.1 (0.8)	+0.0 (0.8)	0.910			—
Smoking, periconception	+1.3 (0.8)	+5.6 (3.4)	0.094	+0.6 (0.8)	+2.5 (3.3)	0.454
Duration of breastfeeding[d]	−0.7 (0.3)	−2.9 (1.2)	0.011	−0.6 (0.3)	−2.5 (1.3)	0.040
Constitutional factors						
Gender, male	−1.8 (0.7)	−7.3 (4.1)	0.010	−2.3 (0.8)	−9.0 (3.9)	0.005
Birth weight[e]	−1.2 (0.4)	−5.0 (1.7)	0.005[f]	−0.6 (0.5)	−2.5 (2.1)	0.159[f]
Growth rate[e,g]	0.0 (0.4)	0.0 (0.3)	0.985			—
BMI[e]	−0.8 (0.4)	−3.3 (1.7)	0.043	−0.3 (0.4)	−1.2 (1.6)	0.514
Biomarker concentration						
Leptin, serum[e]	−0.4 (0.4)	−1.7 (1.7)	0.035	−1.2 (0.5)	−4.9 (2.0)	0.028

The interplay between one-carbon metabolism and epigenetic modifications: the role of nutrition

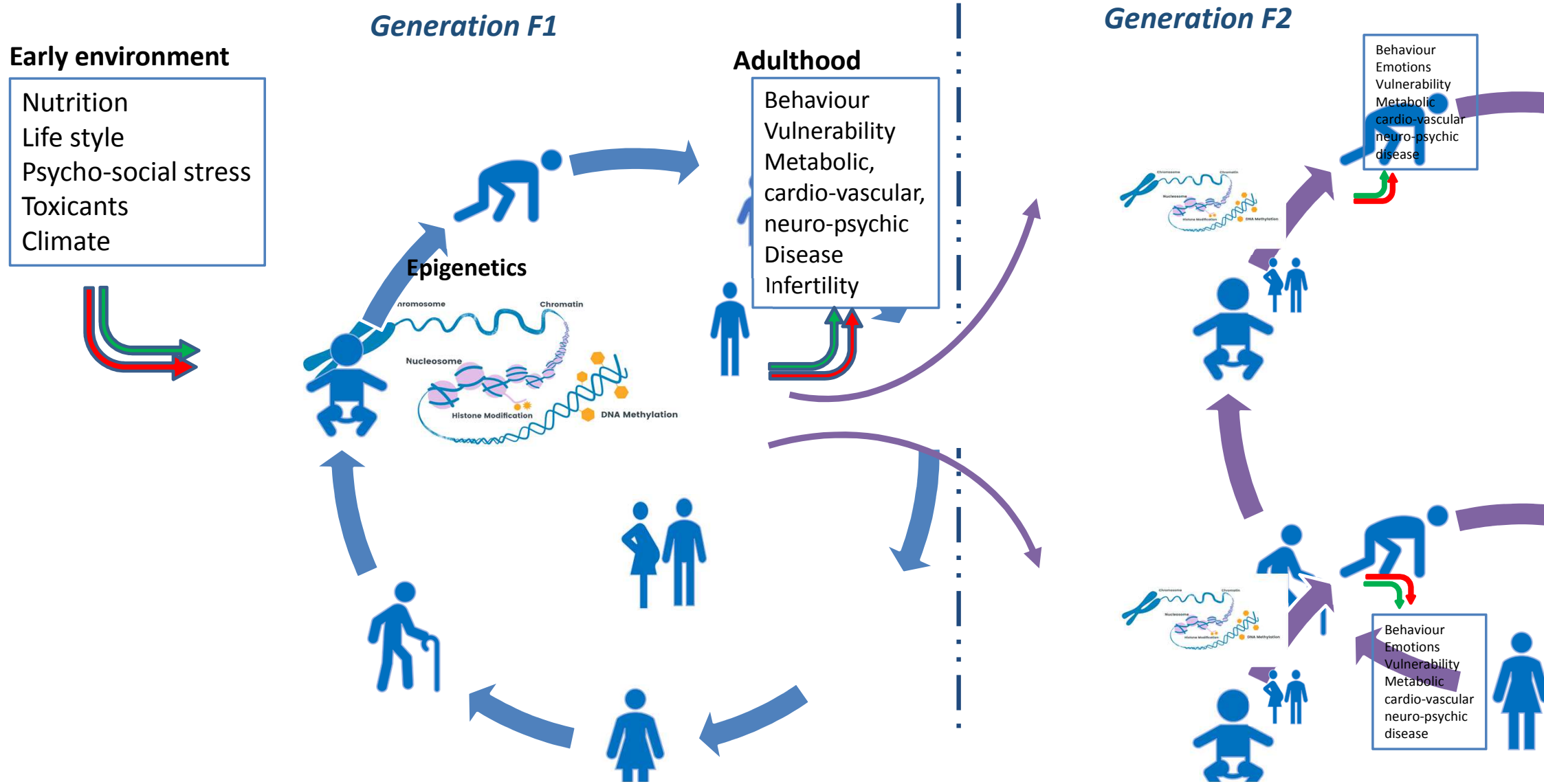


Wu et al, 2019

Developmental Origins of Health and Disease: Predisposition & life trajectories

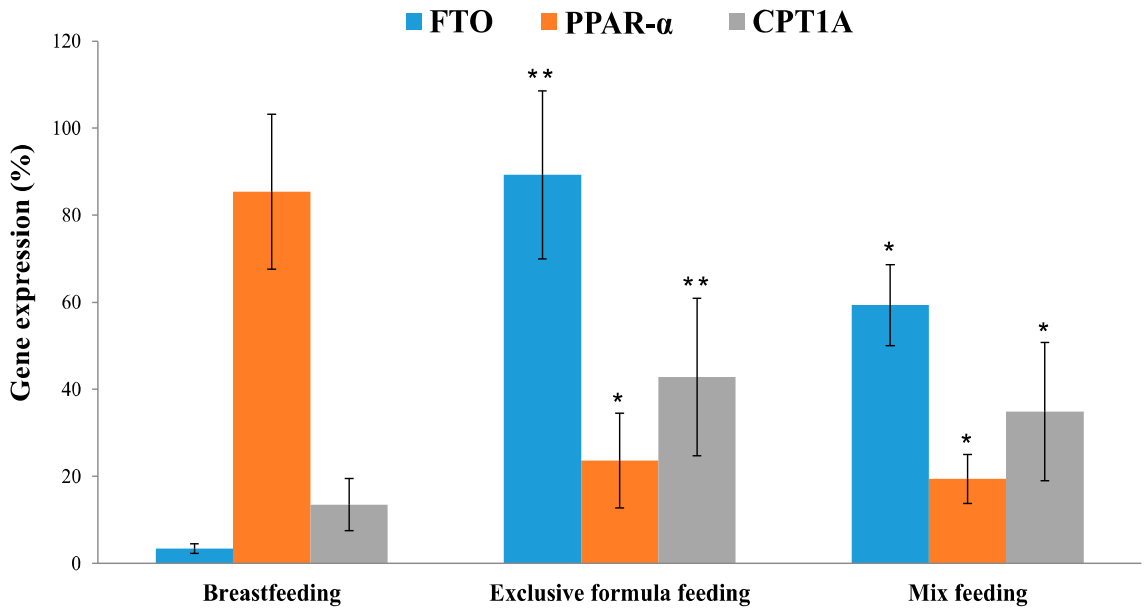


Developmental programming: trans-generational inheritability of acquired epigenetic imprinting



DNA methylation *vs* breast feeding

Effects of Breastfeeding and Formula Feeding on the Expression Level of *FTO*, *CPT1A* and *PPAR-α* Genes in Healthy Infants



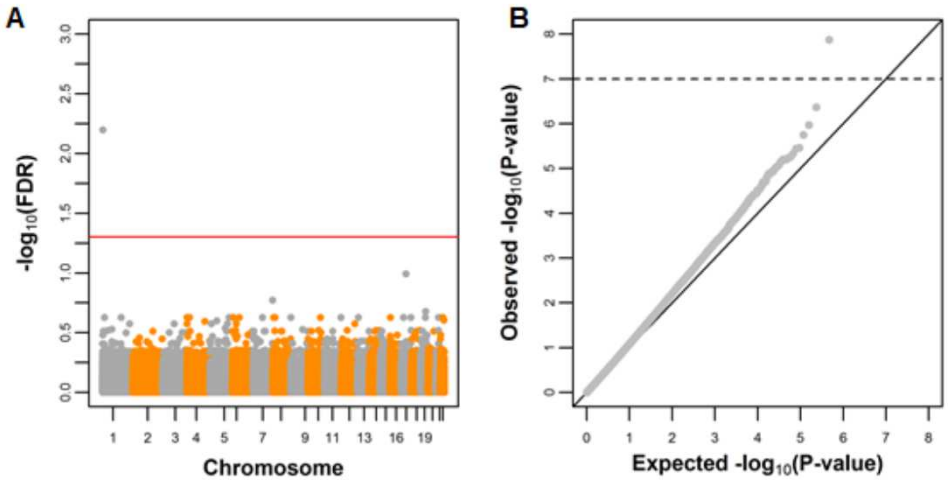
Chesmeh et al, 2020

Association between Breastfeeding and DNA Methylation over the Life Course: Findings from the Avon Longitudinal Study of Parents and Children (ALSPAC)

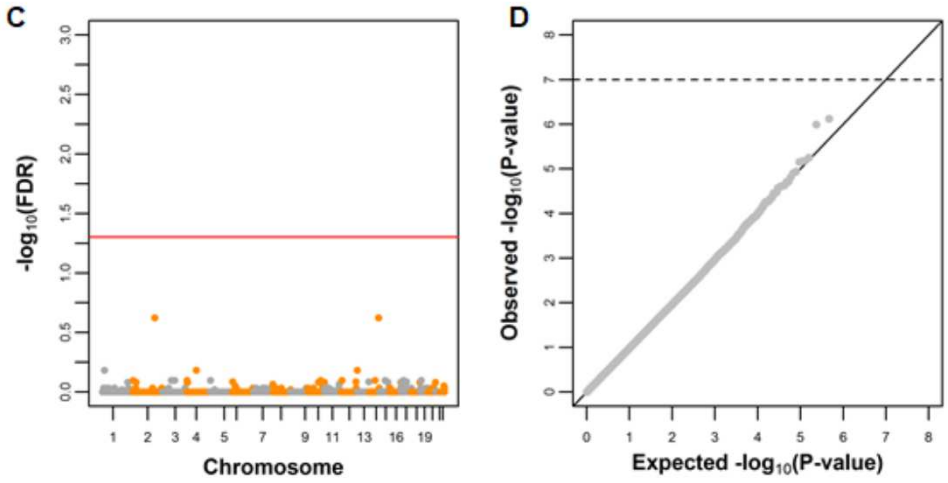
Manhattan plots

Q-Q (quantiles) plots

Comparison between never/ever breastfed individuals
(FDR: false discovery rate)



Comparions according to categories of breastfeeding duration

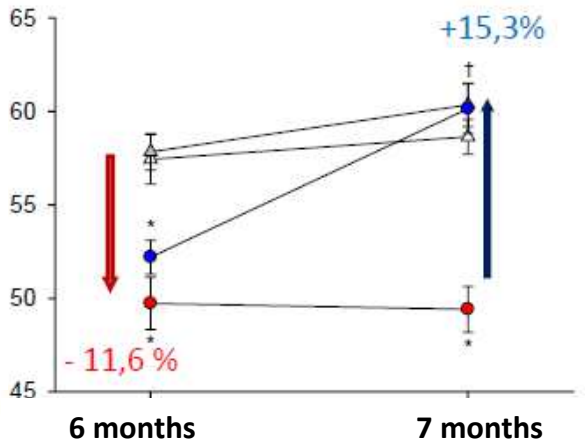


Hartwig F.P. et al, 2020

MicroRNAs associated with offspring overnutrition during lactation

Early, transient overnutrition during lactation alters myocardial function at adulthood and is reversible by late caloric restriction

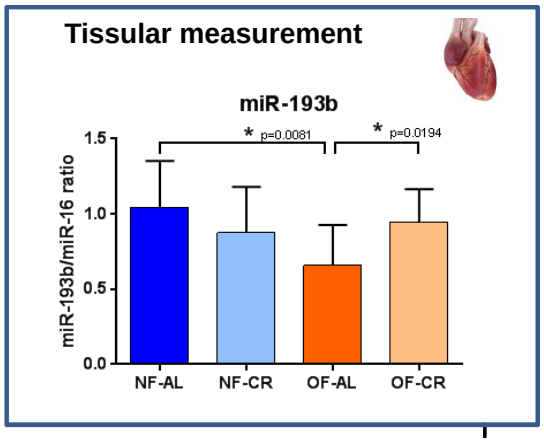
Left Ventricle Ejection Fraction

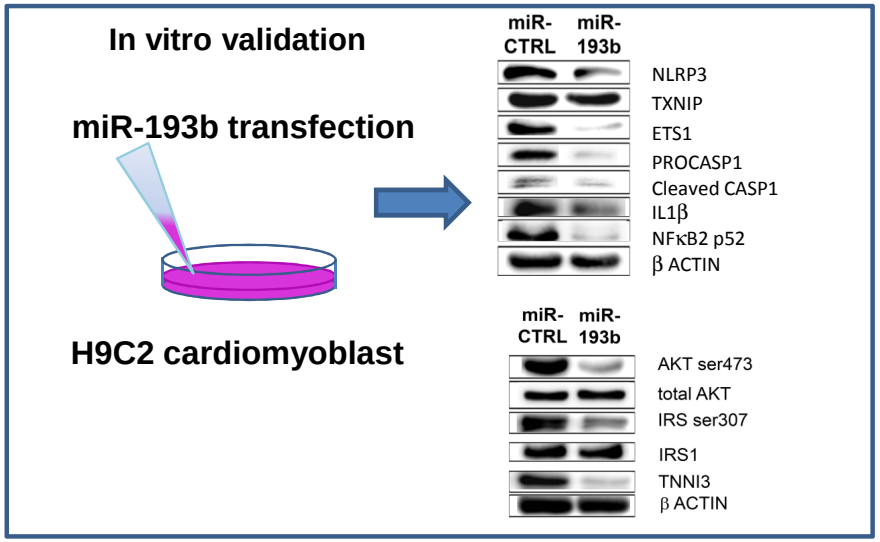


Postnatal Overfeeding

Calorie Restriction in Adulthood

Regulation of inflammasome by miR 193b



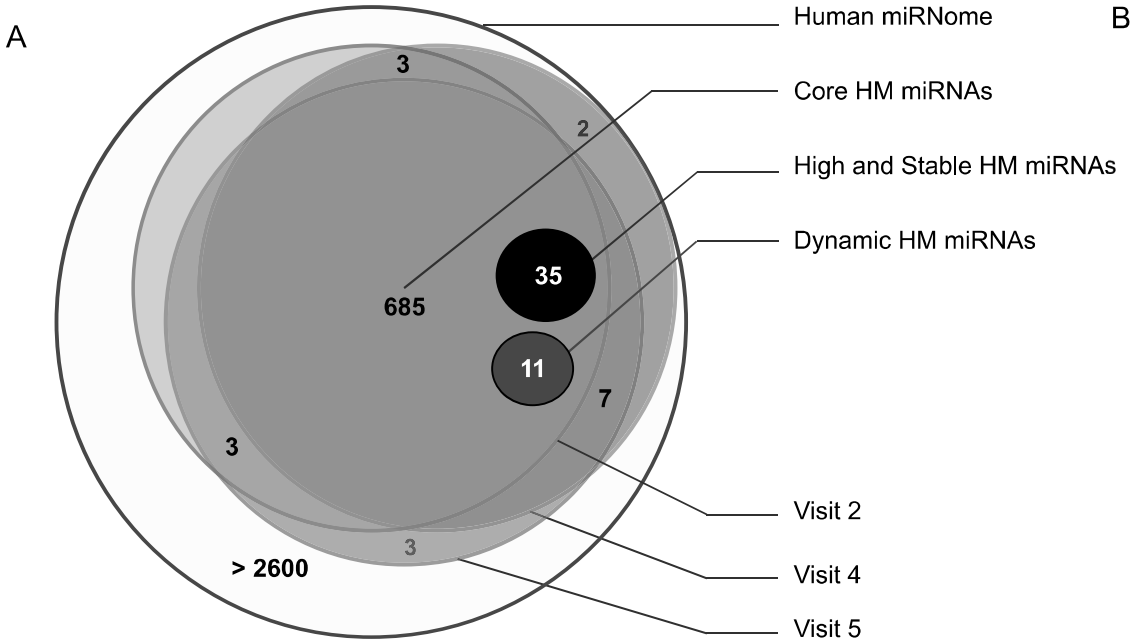


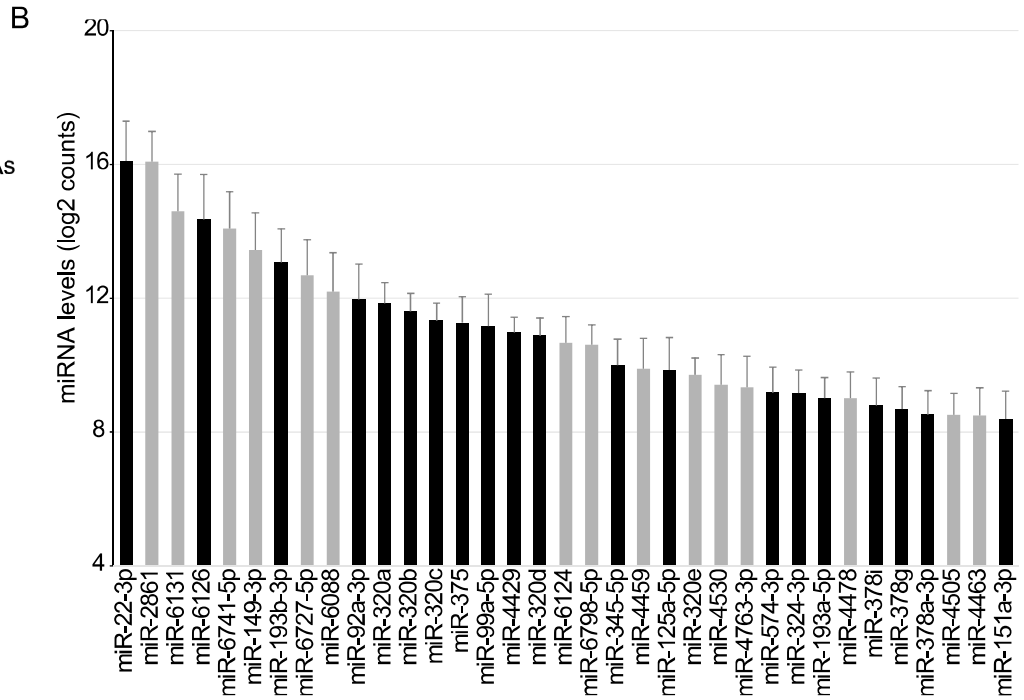
Li N et al, Sci Reports 2016

Siddek B et al, Nutr Metab Cardiovasc Dis 2018

Maternal modulation of infant’s genes expression and physiology through breat milk miRNAome

Longitudinal Human Milk miRNA Composition over the First 3 mo of Lactation in a Cohort of Healthy Mothers Delivering Term Infants

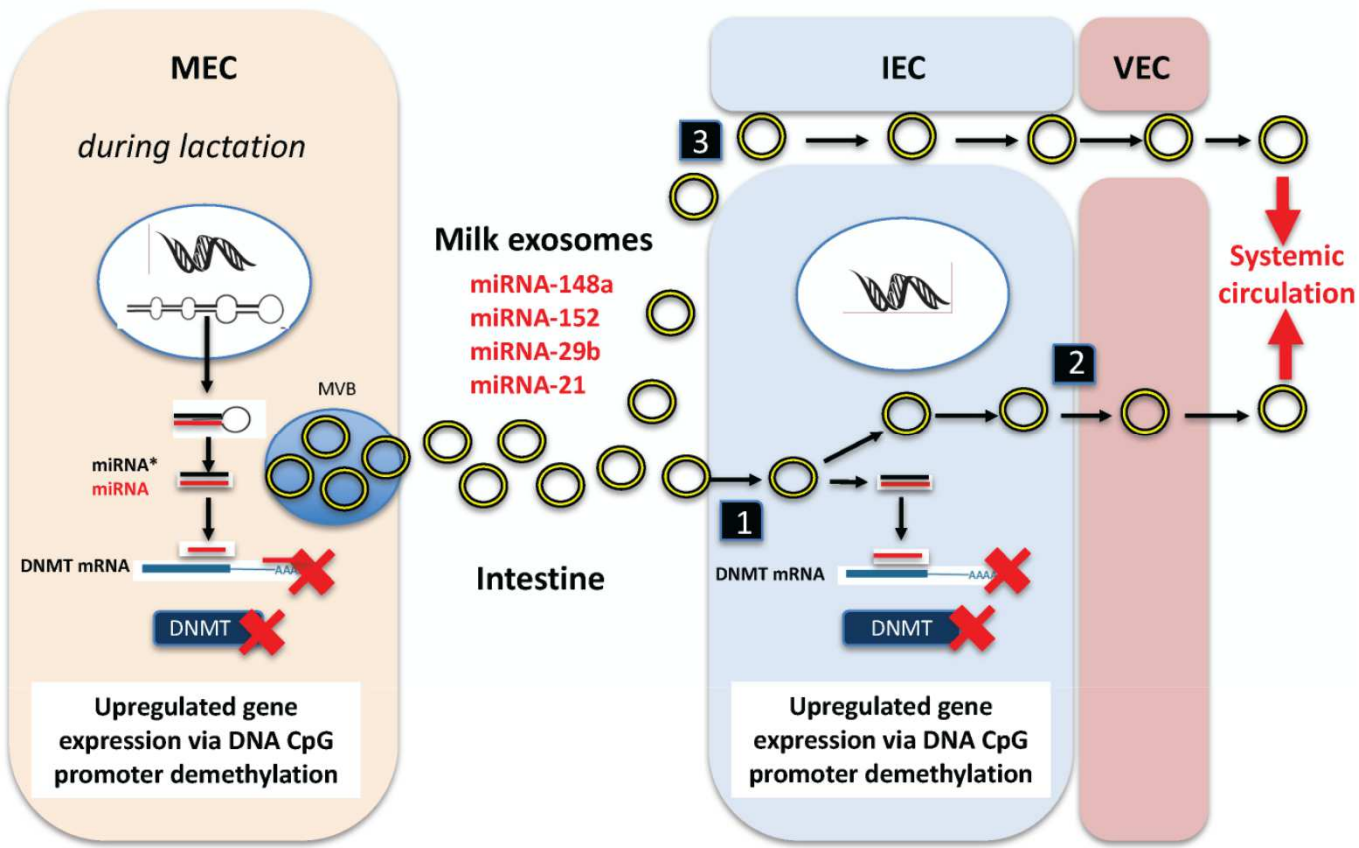




Raymond F et al, 2021

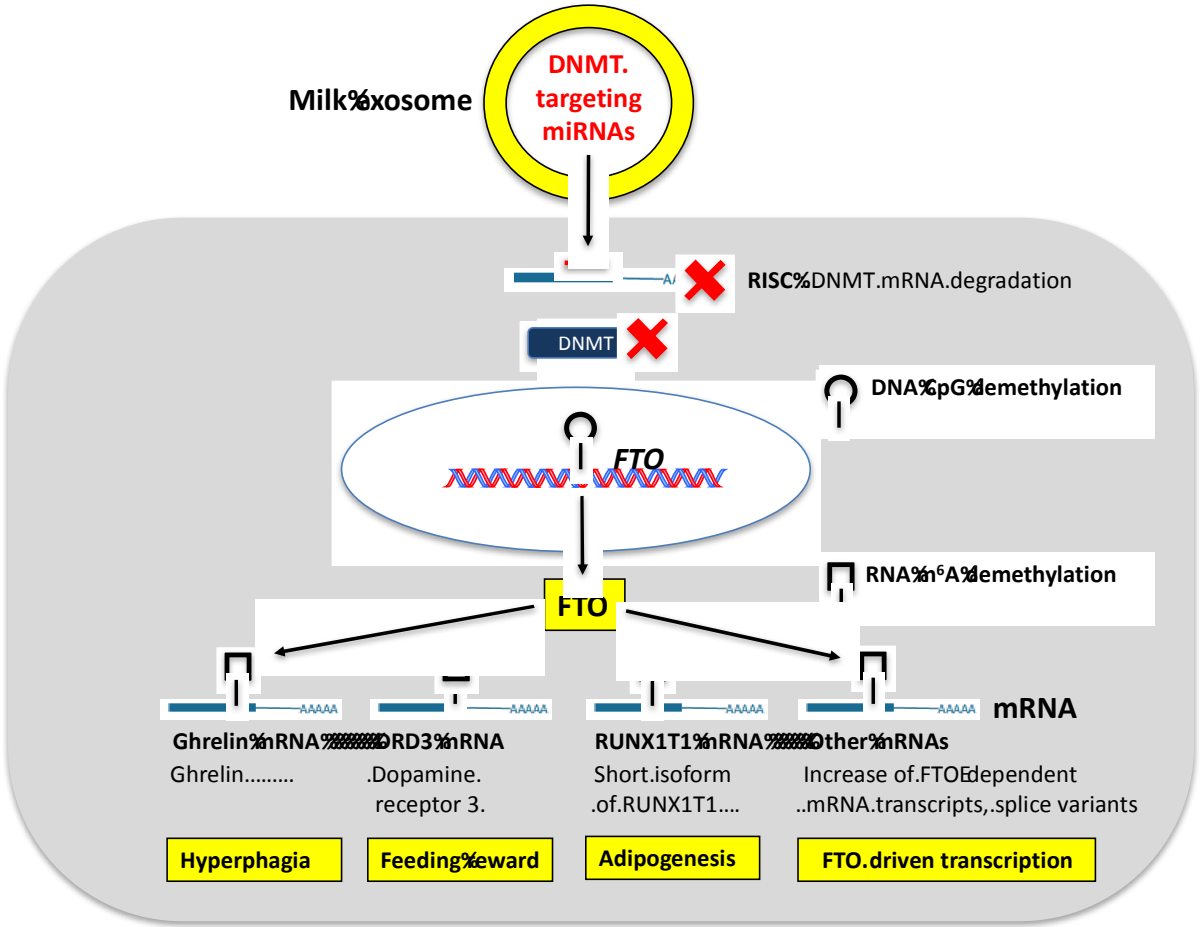
Milk's Role as an Epigenetic Regulator in Health and Disease:

Milk Exosomes: Long-Distance Transmitters of Lactation-Specific miRNAs



Melnik B.C. & Schmitz G., 2017

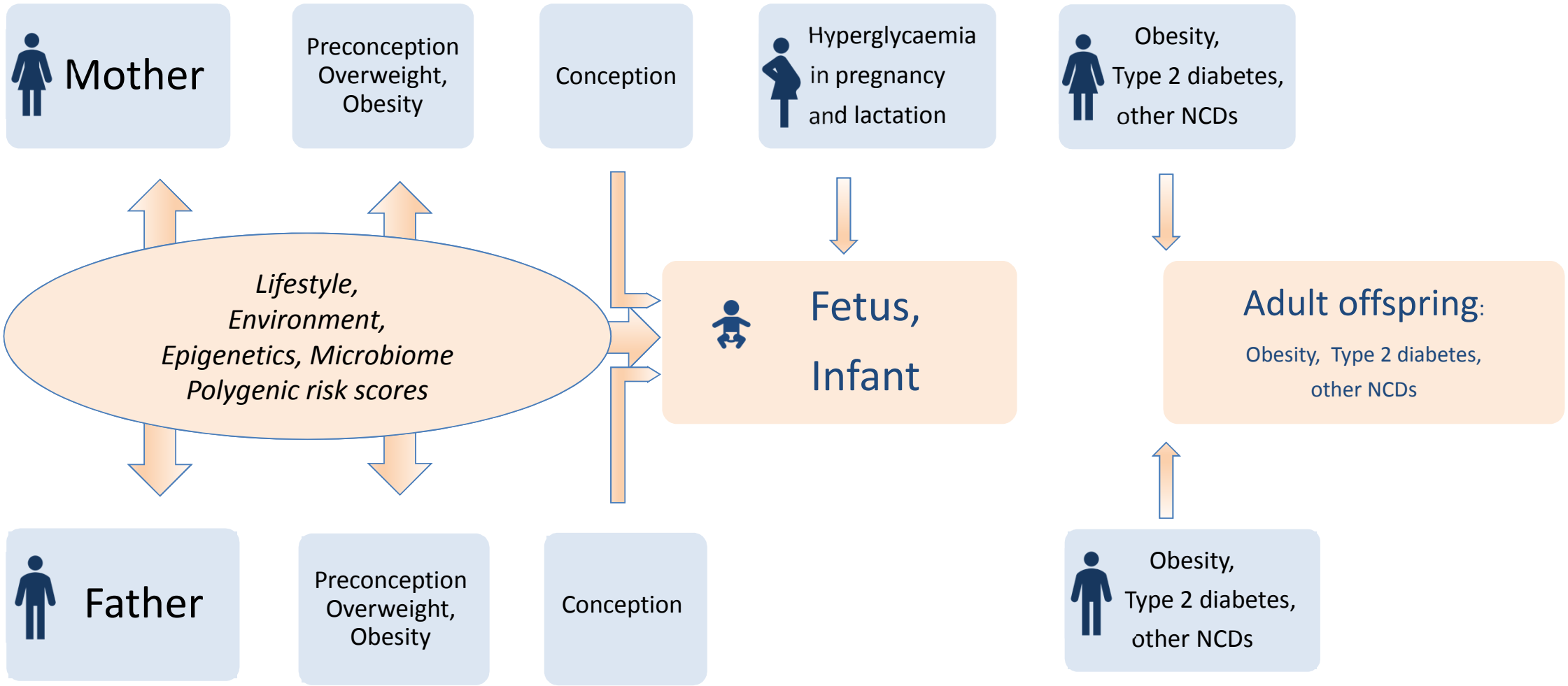
Appetite Control and Feeding Reward



FTO: Fat mass- and obesity-associated protein

Melnik B.C. & Schmitz G., 2017

Maternal, paternal and offspring risk induced by « diabesity »



Conclusion

- As an optimal source of nutrition, protection, and developmental programming for infants, mother milk consists of various bioactive components, including miRNAs.
- Fragmentary information shows associations of epigenetic changes in the expression of genes related to key physiologic and biologic functions with breast feeding. Further studies are necessary to understand the role of epigeneticchanges associated with breastfeeding.
- The concept that human milk miRNAome overall contribution to lactation regulation and/or to infant physiology through horizontal transfer of epigenetic material during breastfeeding is emerging but remains to be demonstrated.

The long term memory of early environmental cues