XLIV

GIORNATA MONDIALE ALIMENTAZIONE

IPSEOA "Angelo Celletti" FORMIA

Nutrizione tra alimentazione ed innovazione

Formia, 16 ottobre 2025

Renato Guttuso - Natura morta con la scure (Still life with the ax), 1947

La Nutrizione di precisione: maneggiare con cura

Prof.ssa Annamaria Colao

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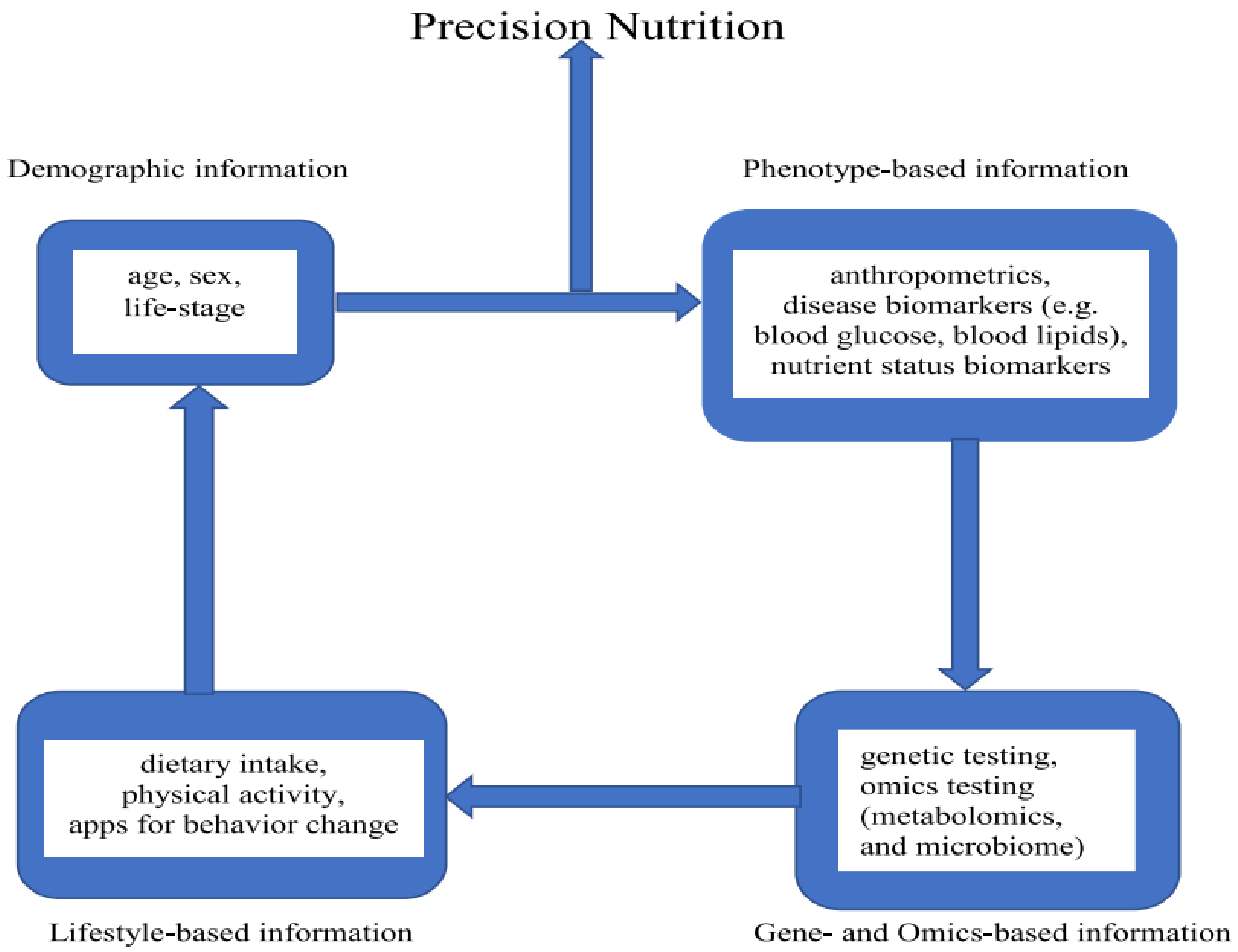
UOC di Endocrinologia, Diabetologia, Andrologia e Nutrizione

Vice Presidente del Consiglio Superiore di Sanità

UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II



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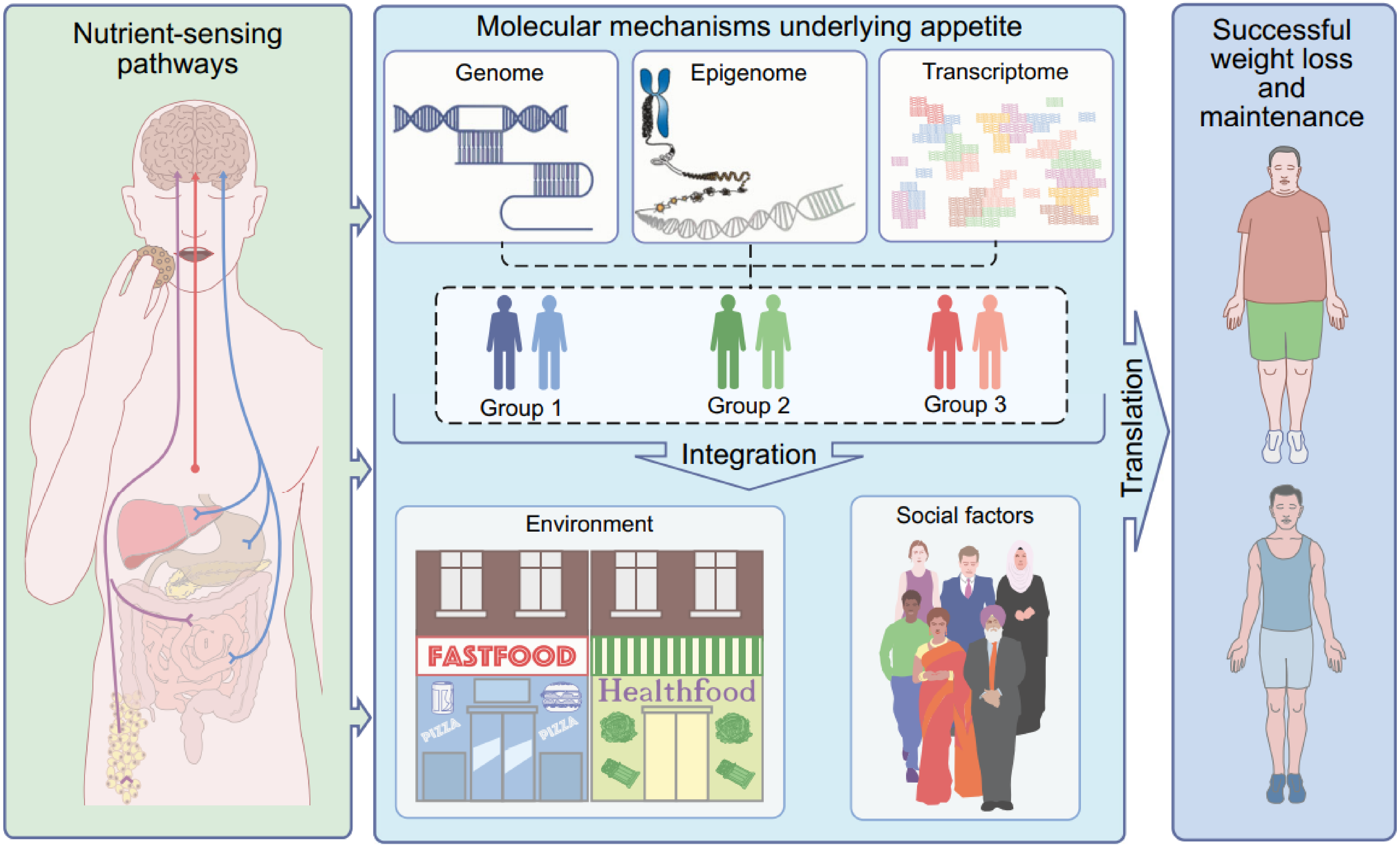

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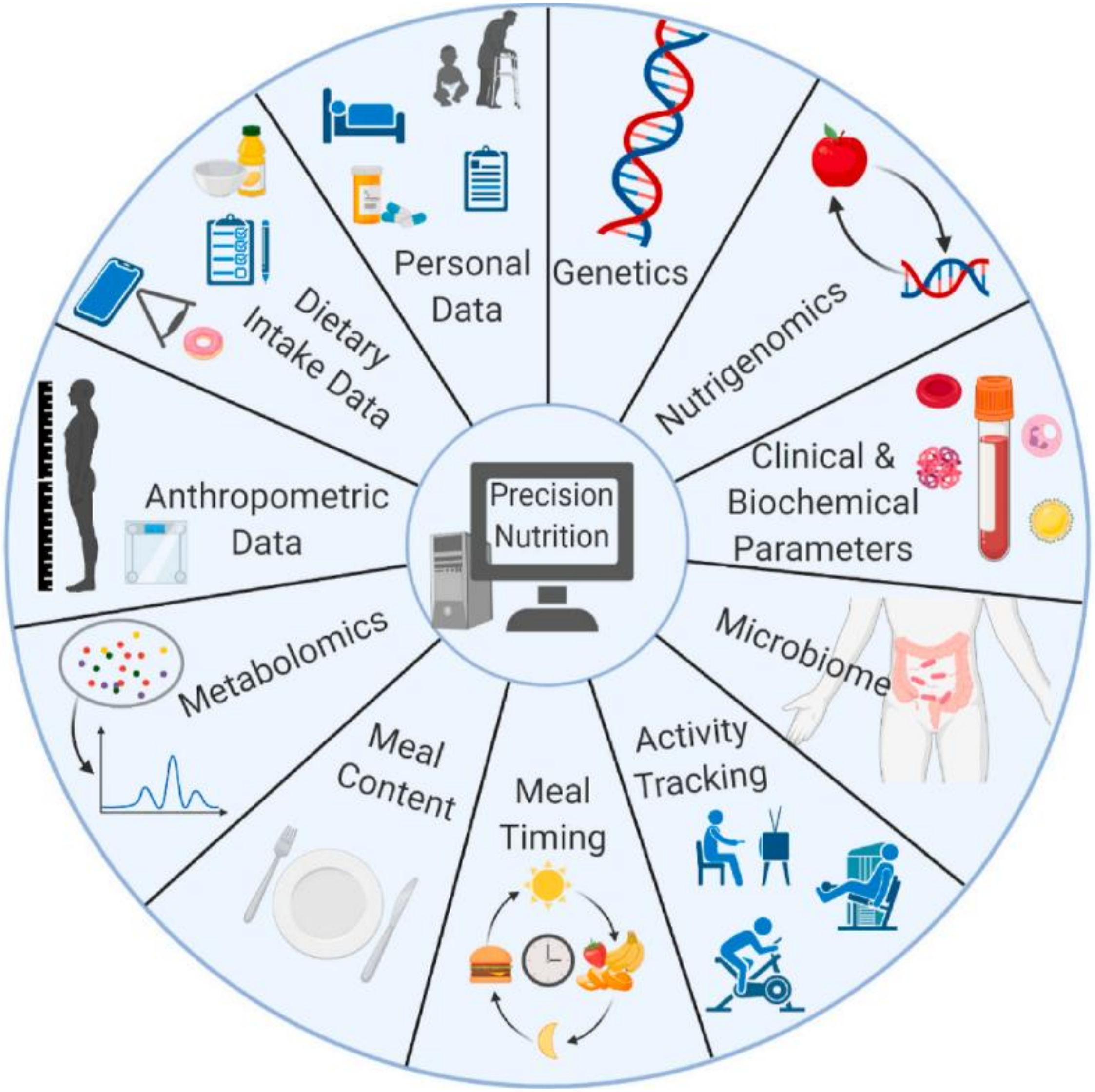
Precision Nutrition is founded upon the concept of biological variability between individuals in response to nutrition



If the variables responsible for causing this variation and their effect on a desired outcome variable can be known, the outcome variable can be predicted, and this can be translated into nutrition advice.

There is no set of fixed variables that will provide any given output. Instead, features thought to be of importance to predicting the outcome are selected on a per situation basis. In some cases, this can reach to large numbers of individual features. However, they can be separated into groups, here referred to as PN elements.

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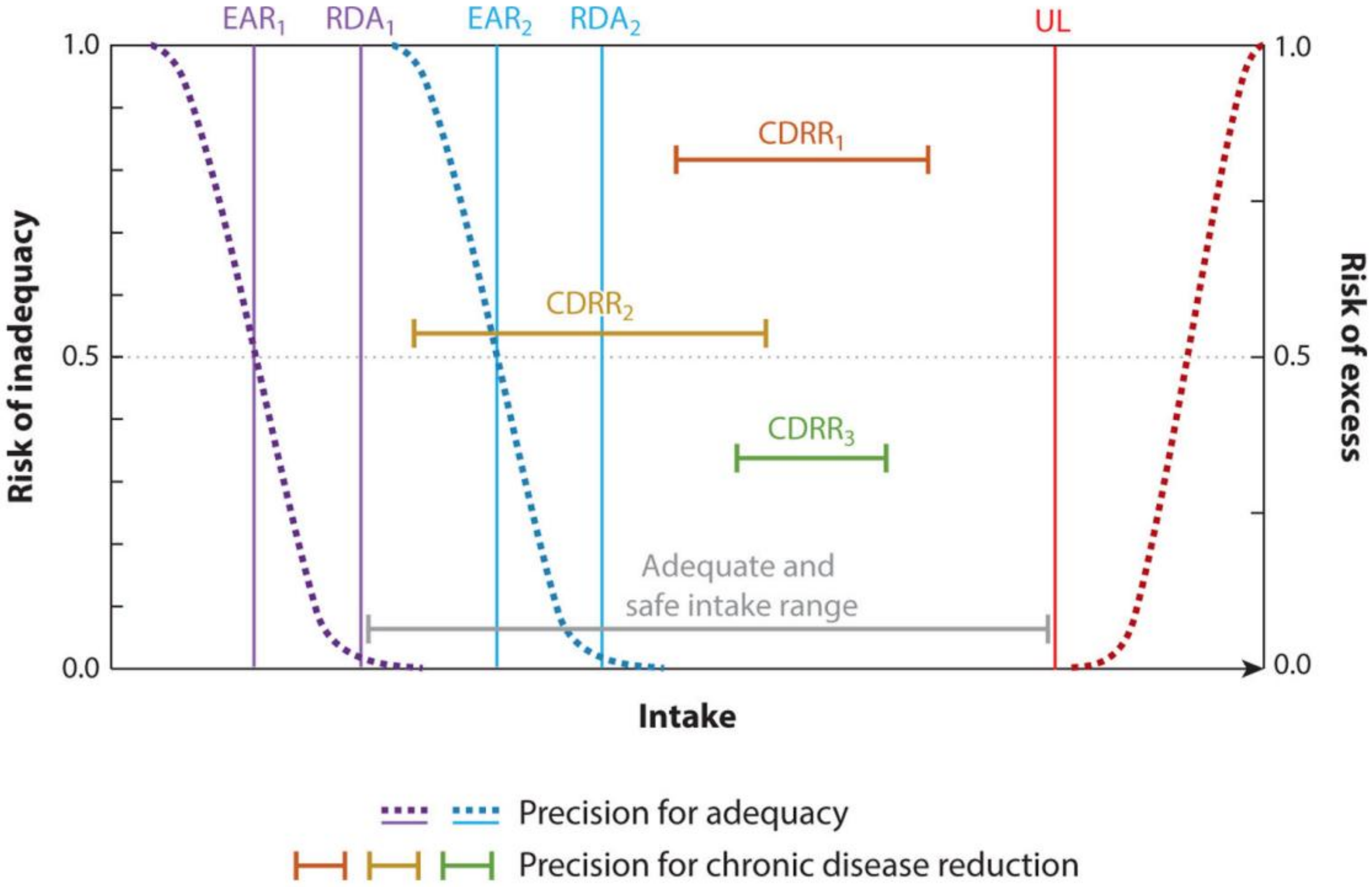

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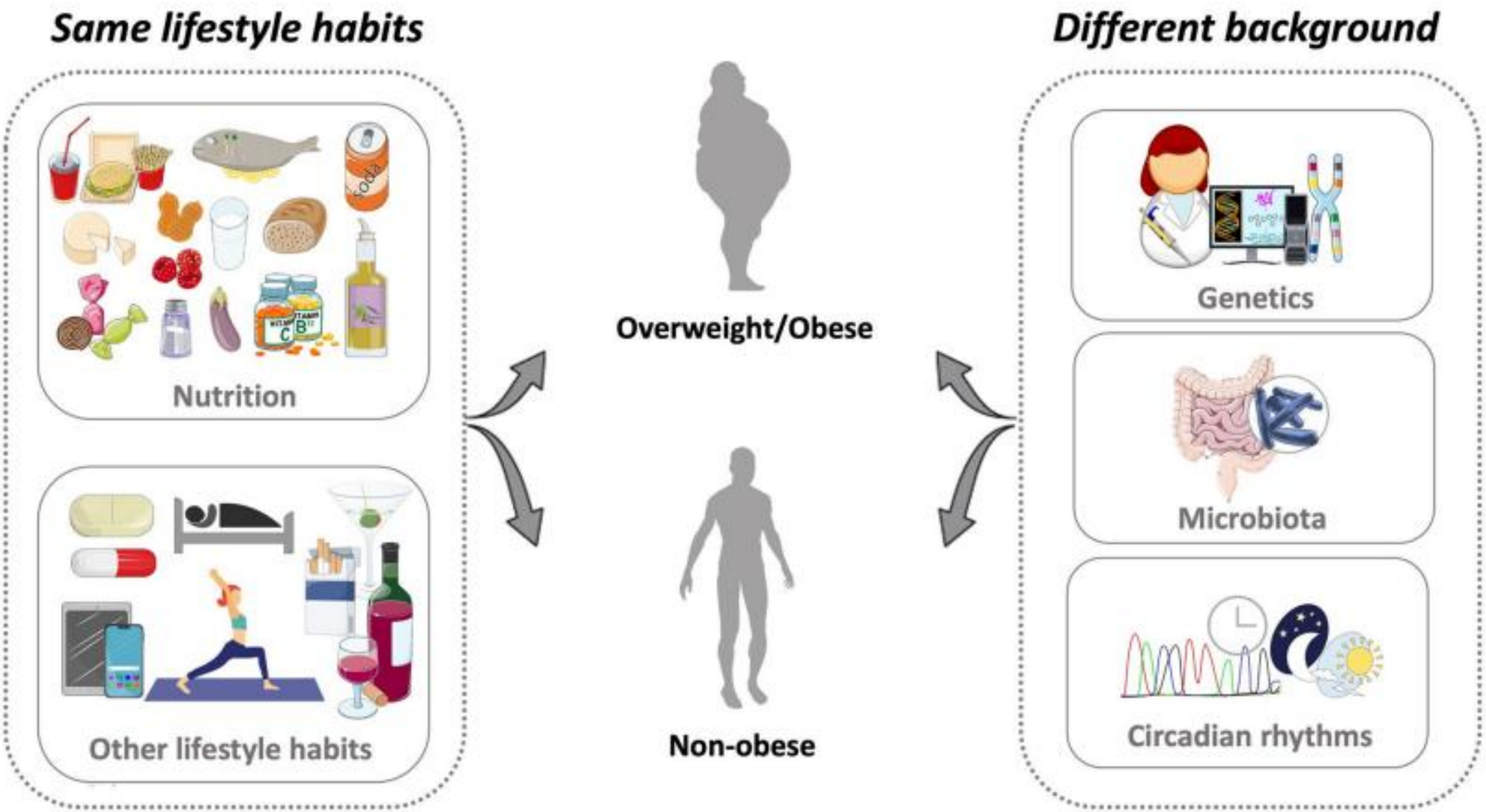
La Nutrizione di Precisione in prevenzione e gestione dell'obesità



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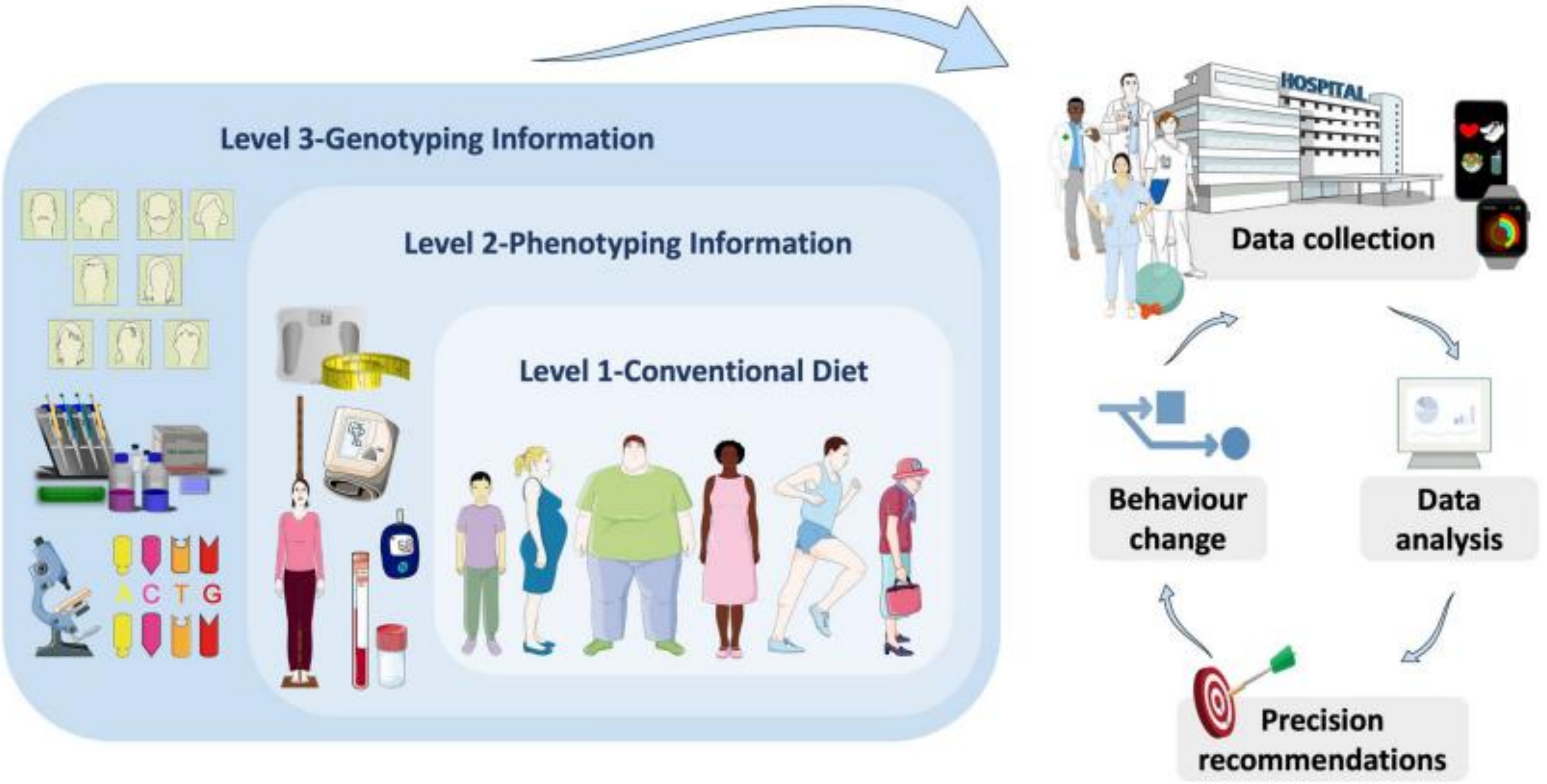

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TABLE 1. ***Summary of nutrigenetics of obesity phenotypes***

Variant of Interest	Gene	Type of Study	Sample Size	Nutrient/Dietary Intake	Outcome	Population	Conclusion	Reference(s)
rs9939609 rs1121980	*FTO*	Cohort	339,000	Total fat	BMI	European and Hispanic adults	TT allele of both SNPs associated with higher BMI with higher SFA intake	Corella et al. (53)
rs9939609	*FTO*	Intervention	86	Mediterranean diet	Weight loss	Italian	A allele was associated with less weight loss than TT carriers	Franzago et al. (58)
rs662799	*APOA5*	Cohort	3266	Red meat	Metabolic syndrome	Korean	G carriers and in highest tertile of red meat consumption had 1.7 HR as compared to those with A allele	Choi and Shin, (103)
GRS of 4 SNPs		Cohort	302	Total fat, SFA, MUFA, and PUFA	Waist circumference	Ghana	GRS >3 and high intake of fat, SFA, PUFA, and MUFA linked to increased waist circumference	Alsulami et al. (52)
				Fiber	Body fat		GRS >3 and high intake of fiber had lower total body fat as compared to low fiber intake	
GRS of 94 SNPs		Cohort	362,496	Alcohol	BMI	UK adults (UK Biobank)	Increase in BMI per GRS is higher in infrequent drinkers as compared to frequent drinkers	Rask-Anderson et al. (104)
rs6722579	*CAB39*	Cohort	50,808	Fat intake	Abdominal obesity	Korea	A carriers were at higher risk for abdominal obesity in those who had fat intake >DRI	Kwon et al. (54)
rs59465035	*CPQT*						T carriers are at lower risk for abdominal obesity in those who had vitamin C >DRI	
rs17782313	*MC4R*	Cohort	282	Carbohydrate intake	BMI	Iranian	Higher carbohydrate intake was associated with higher BMI and waist circumference in C carriers	Alizadeh et al. (51)
rs1801282	*PPARG*	Intervention	327	Diet therapy vs. diet therapy + metformin	Weight loss		CC carriers had a greater weight loss than others	Valeeva et al. (48)
rs59465035	*CP*	Cohort	50,808	Vitamin C	Waist circumference	Korean	T-allele carriers had lower risk of abdominal obesity as compared to others in those who consumed vitamin C higher than DRI	Kwon et al. (54)
rs10401670	*RETN*	Intervention	284	High-fat hypocaloric diet	BMI	Spain	T-allele carriers had greater weight loss than others	De Luis et al. (57)
5 SNP PRS		Cohort	>53,000	Fried foods	BMI	Korean	High PRS and menarche linked with higher BMI	Park et al. (56)
rs1761667,	CD36	Cohort	142	Fat and sugar intake	BMI percentiles	African American females	AA and altered fat perception linked to BMI increase	Primeaux et al. (55)
rs35874116	TAS1R2						TT and sugar intake linked to BMI increase	
rs713598	TAS2R38						CC and energy intake linked to BMI increase	

GRS, genetic risk score; PRS, polygenic risk score; BMI, body mass index; SNP, single nucleotide polymorphism; SFA, saturated fatty acid; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; DRI, dietary reference intake.

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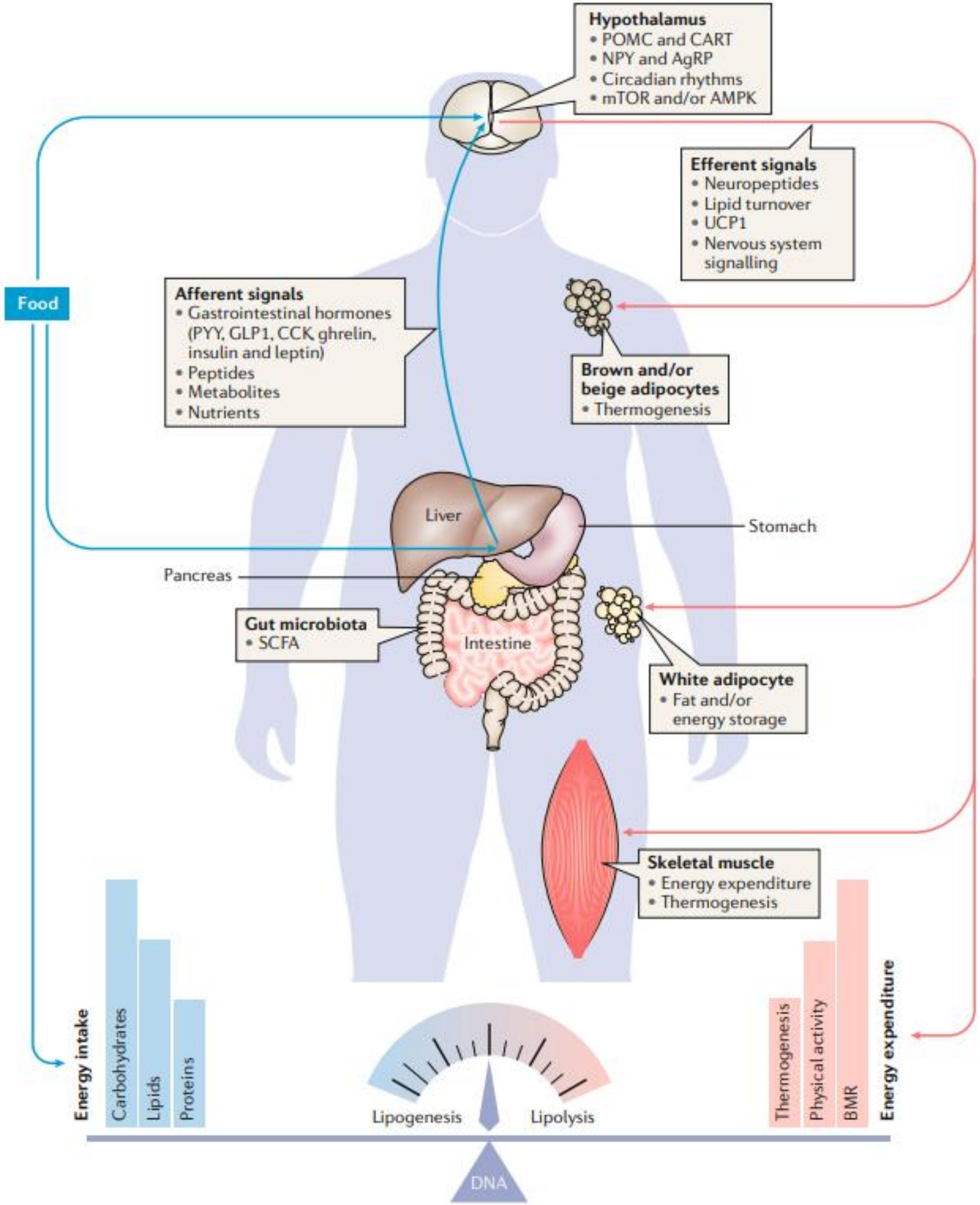

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Table 1 | **Associations between genetic background, macronutrient intake and obesity traits**

Dietary components	Genes	Population characteristics	n	Reported relationship	Outcome and/or traits	Ref.
Energy						
Energy	*FTO*, *LEP* and *LEPR*	Men in the overweight BMI category	40	+	Appetite or feeling of fullness	105
Energy	*MC4R*	US women	5,724	+	Body weight	108
Energy	*FTO* and *MC4R*	Heterogeneous	Review (39 articles)	None reported	Weight maintenance	109
Energy	*FTO*	US adult twins	114	+	Feeling of fullness	106
Total fat	*FTO*	From 56 studies	213,173	–	Obesity risk	107
Carbohydrates						
Carbohydrates	*ADBR2*	Spanish	313	+	BMI	110
Carbohydrates	*PPARG*	Spanish	313	+	Obesity risk	111
Fibre	*LIPC*	European women with obesity	549	–	Obesity risk	112
Fibre	*GRS* (16 SNPs)	Spanish adults	711	–	Adiposity markers	103
Starch	*AMY1* (CNV)	Swedish population	4,800	–	BMI	114
SSB	*GRS* (32 SNPs)	US population	>32,000	+	BMI	113
Fat						
Total fat	*FTO*	Saudi Arabian individuals	240	+	Early onset of obesity	116
Total fat	*FTO*	Spanish adolescents	652	+	Adiposity	117
Total fat	*APOA5*	US adults	2,280	–	BMI	118
Total fat	*APOA5*	Mediterranean adults	1,465	+	BMI	119
Total fat	*PPARG*	Three case–control studies	2,141	+	Obesity risk	120
Total fat and SFA	*GRS* (63 SNPs)	Two US studies	2,818	+	BMI	127
Total fat and SFA	*GRS* (95 SNPs)	White European adults	48,170	–	BMI and waist circumference	126
SFA	*FTO*	French adults	1,754	+	BMI and waist circumference	123
SFA	*APOA2*	European and Asian individuals	4,602	+	BMI	125
MUFA	*PPARG*	Spanish men and women	60	–	BMI and fat oxidation	121
MUFA	*PPARG*	Mediterranean population	1,465	–	BMI and body fat	122
Protein						
Protein	*FTO 9939609*	Heterogeneous	177,330	+	BMI	128
Protein	*CTSS* (3 SNPs)	European adults	11,091	+	Obesity risk	131
Protein (animal and/or plant)	*FTO*	Adolescents of several ethnicities	1,491	Ethnic differences	BMI, waist circumference and food intake	132
Vegetable protein	*GRS* (16 SNPs)	Spanish adults	711	–	Adiposity markers	103

+, positive association between the SNP (or SNPs); –, negative association between the SNP (or SNPs); CNV, copy number variation; MUFA, monounsaturated fatty acid; SFA, saturated fatty acid; SNP, single-nucleotide polymorphism; SSB, sugar-sweetened beverage.

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Table 2 | **Associations between macronutrient intake, gut microbiota and obesity in humans**

Dietary substrate	Effect on gut microbiota	Association[a]	Outcome and/or functionalities	Rationale	Putative metabolic mechanisms concerning obesity (host metabolism)	Ref.
Energy						
Total energy intake	↑ Firmicutes to Bacteroidetes ratio	+	Increased energy harvest of ≈150 kcal, overfeeding in lean individuals	Greater fractional decrease in stool energy loss	Efficiency of nutrient absorption	185
Caloric restriction	↑ *Akkermansia muciniphila*, ↑ gene richness	+	Healthier fasting plasma levels of glucose, plasma levels of triglycerides and body fat distribution	*A. muciniphila* produces SCFAs (such as acetate)	SCFAs presented an anorectic effect and displayed greater improvement in insulin sensitivity and other clinical parameters	186
Carbohydrates						
Total carbohydrates	↓ *Roseburia* spp., *Eubacterium rectale* and *Bifidobacteria* with carbohydrate reduction	+	Reduction in faecal butyrate supply to the colonic mucosa, which affected gut health	Association of butyrate-producing bacteria with the faecal butyrate	Butyrate-induced suppression of orexigenic neuron activity that expresses neuropeptide Y in the hypothalamus	160
Fibre	↑ Diversity, ↓ Bacteroidetes, ↑ Firmicutes (Ruminococcaceae and Lachnospiraceae)	+	Long weight maintenance with reduced weight gain independently of energy intake	The fermentation of fermentable carbohydrates yields the increase of SCFAs	Appetite reduction by PYY and GLP1; energy expenditure increase by thermogenesis through the expression of the genes encoding PPARγ and UCP1	187
Fibre (arabinogalactan and inulin)	↑ *Gemmiger*, *Dorea*, *Roseburia*, *Alistipes*, *Lactobacillus* and *Bifidobacterium* (lean participants), ↑ *Bifidobacterium adolescentis*, *Bifidobacterium* and *Faecalibacterium prausnitzii* (lean participants and those with obesity)	+	Differences in gut microbiota and metabolites between lean individuals and those with obesity	Microbiota from lean individuals presents more n-butyrate from the fermentation of both substrates than the microbiota from those with obesity	Butyrate products can reduce levels of neuropeptide Y in the hypothalamus	188
Prebiotics (inulin)	↑ *Bifidobacterium* spp., ↓ *Bacteroides vulgatus*	+	Body weight z-score, body fat and truncal fat	NA	NA	189
Fat						
Total fat and SFA	↑ Bacteroidetes and Actinobacteria, ↓ Firmicutes and Proteobacteria	+/–	BMI and enterotypes remained stable during 10 days of intervention	Firmicutes and Actinobacteria are associated with obesity-enriched genes and reduced functional diversity	Promotion of pro-inflammatory pathways associated with obesity	172
Unsaturated fatty acids	↑ *Bifidobacterium longum*	+	Higher *B. longum* abundance in lean participants, possible interaction with fibre	Unsaturated fats affect the cell membrane fluidity, regulate neurotransmitter function and reduce cytokine production	Promotion of membrane integrity and pro-inflammatory pathways associated with obesity	190
Protein						
Total protein	↓ Total bacteria, ↓ *Roseburia* and/or *E. rectale* and Bacteroidetes	–	Increase of branched-chain fatty acids, pH, phenylacetic acid and *N*-nitroso compounds in faeces	Increase in isovalerate and isobutyrate concentrations reflect the increase in amino acid (valine and leucine) fermentation	The pH increase might induce the reduction of butyrate-producing bacteria	169

↑, increase; ↓, decrease; NA, not available; SCFA, short-chain fatty acid; SFA, saturated fatty acid. [a]Association between nutrient and/or dietary substrate and gut microbiota.

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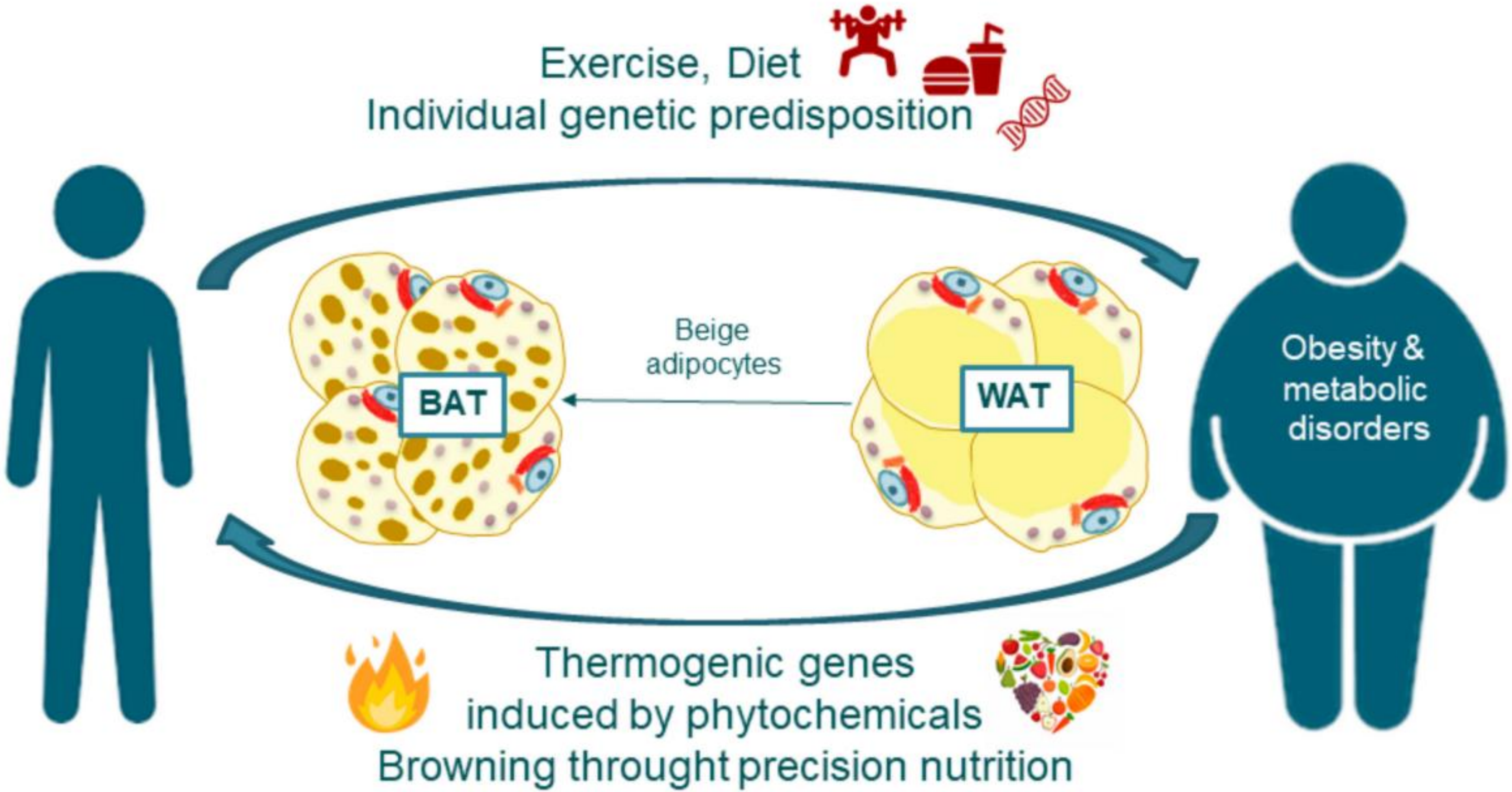

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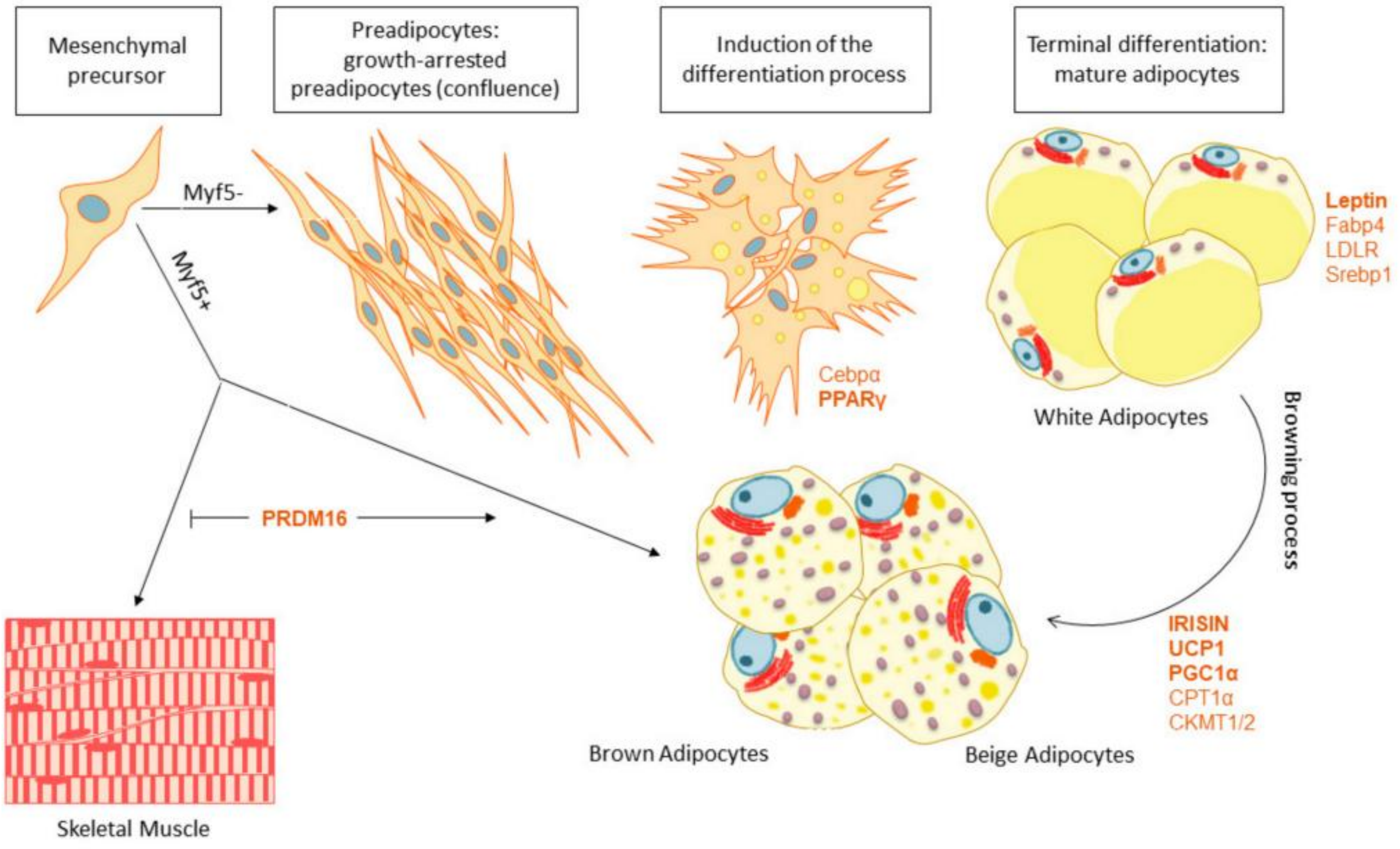

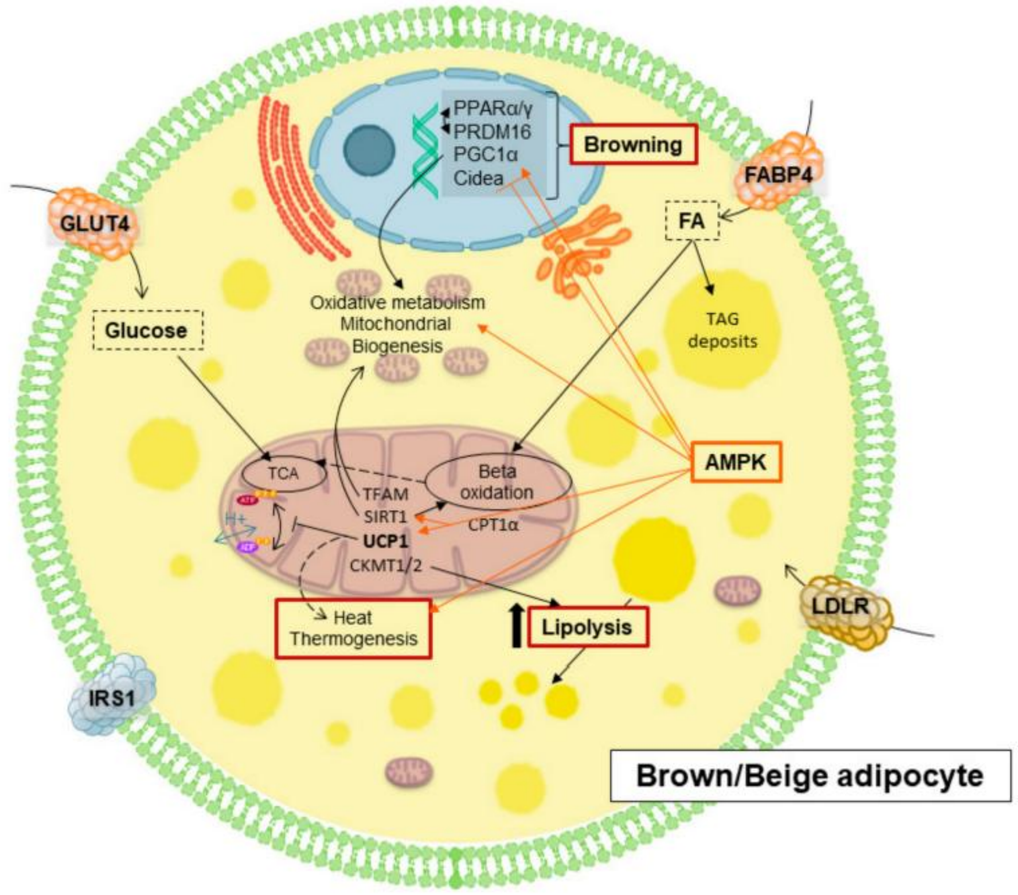

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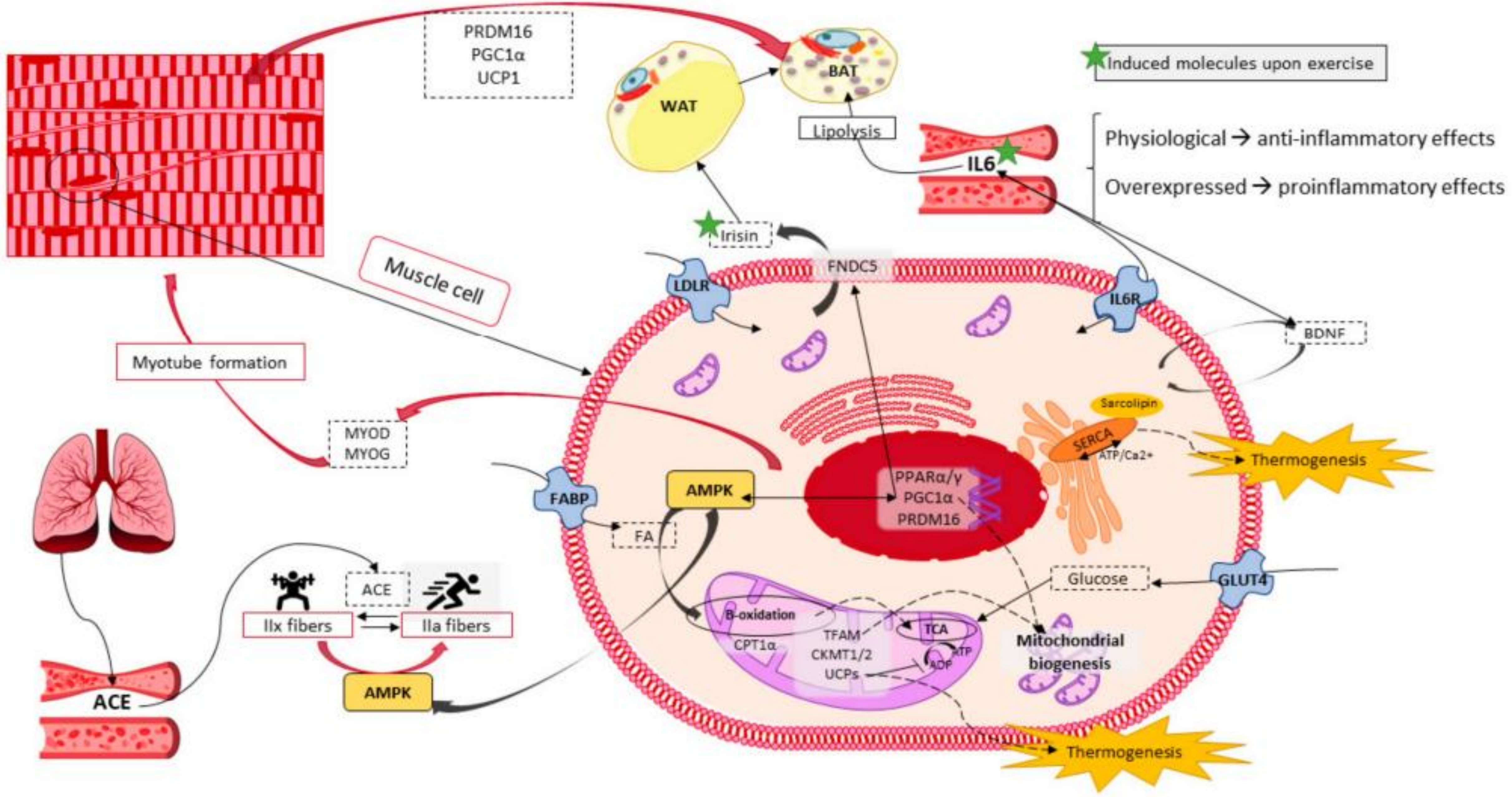

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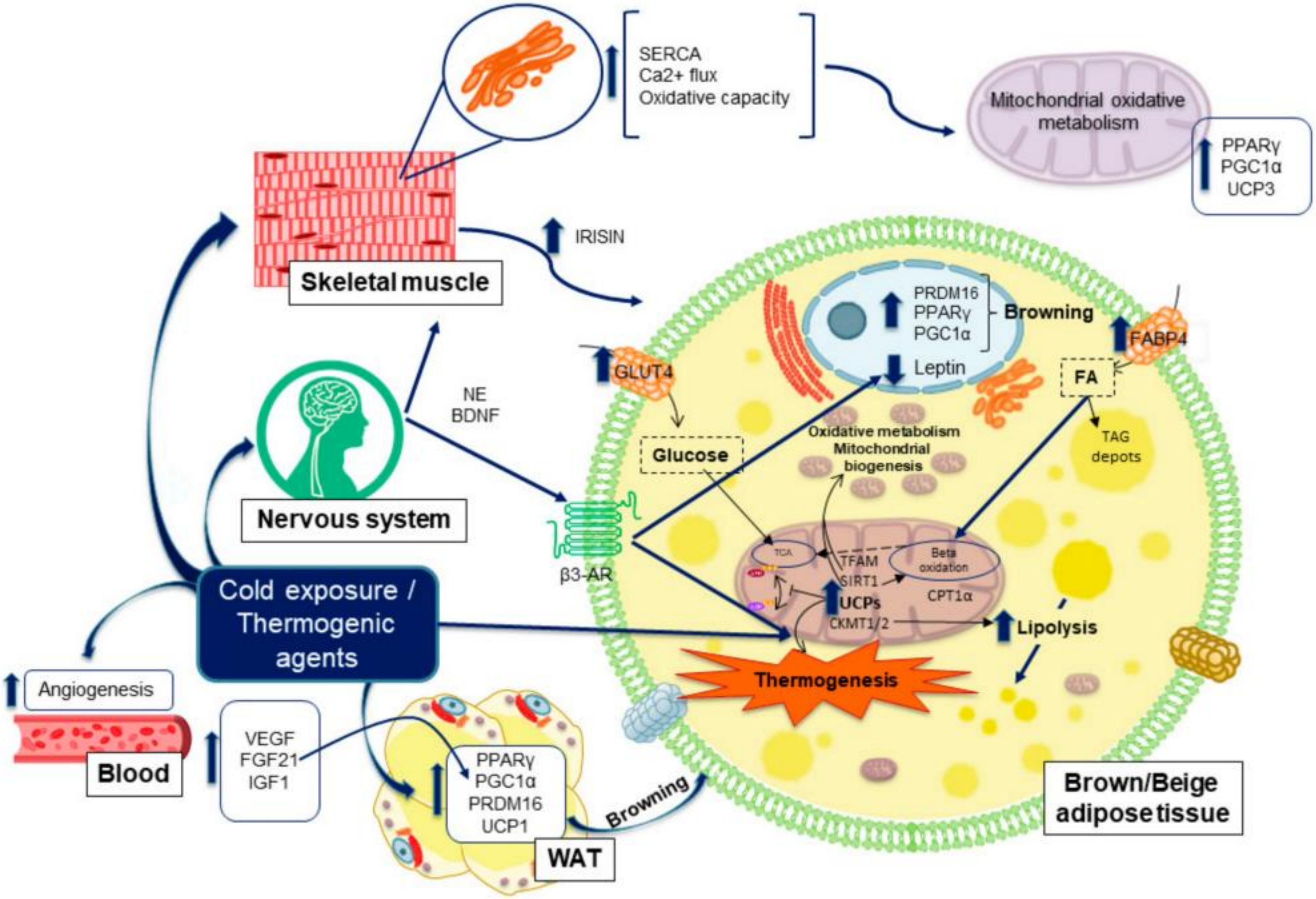

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Pomegrate

↑ adipogenesis, TG, lipase, PPARG, GLUT4, FABP4, adiponectin

↓ Ch, TG, glc, BW, appetite

↑ AMPK, PGC1a pathway

↓ oxidative stress, inflammation markers (IL1, 4, 6, TNFa), hyperlipidemia, hepatic lipid deposition
↑ FAO, PGC1a

↑ Insulin sensitivity
↓ BW, WAT mass

↑ immune function (CD4+)
↓ apoptosis in PBMC, inflammation, oxidative stress

↑ Browning and thermogenesis (T3), improves glucose and insulin homeostasis.
↓ BW

↓ muscle damage markers, fatigue, recuperation time

Ginko biloba

↑ AMPK, adiponectin pathways, no effects in PPARG nor adipogenesis

Antiadipogenic effects
↓ differentiation, TG accumulation,
↑ AMPK, CPT1a, HSL, lipolysis

↓ Lipid accumulation, adipogenesis and differentiation (Cebpd, PPARG)

↓ NFkb
↑ Adiponectin

Antiadipogenic effects
↓ PPARG, Ch.
↑ Apoptosis via ROS in WAT

Antiadipogenic. ↓ differentiation, STAT5, PPARG, Cebpa
↑ hypertrophy AT in mice

↓ Intake, BW, NFkb, TNFa
IR ↑ IL10, Akt-P

↓ Intake, IR
↑ Akt-P, IRS1

↓ BP, Nitrite level
↑ eNOS mRNA, iNOS prot, TNFa, IL6, IL1, GSH

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Milk Thistle

↓ PPARG, FABP4, FASN, SREBP1c, Cebpa en WAT, terminal differentiation, lipogenesis in mature adipocytes

↓ PPARG, FABP4, FASN, SREBP1c, Cebpa en WAT
↑ SIRT1, PGC1a, UCP1

↓ Lipid accumulation (TG, FA), adipogenesis and differentiation (Cebpd, PPARG, FABP4), adipocyte size,
↑ AMPK

↓ BMI, IR, TG, LDL
↑ Leptin sensitivity

↓ Lipid accumulation, IR, BP, BW, inflammation
Improve glucose metabolism

↑ HDL, ABC transporter, CytP450
↓ TG, Ch in serum

↓ AT inflammation, hypertrophia, BW, IR, restore lipid and glucose homeostasis

↑ Serum lipid profile, SOD, GSH, Adiponectin, FAO
↓ IR, Resistin, Oxidative stress, FA synthesis

↓ IR, visceral fat, gluconeogenesis, TG
↑ Lipolysis

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↑ fat tissue apoptosis
↓ food intake, BW, parametrial and inguinal fat

↓ BW, lipogenesis, adipogenesis
↑ FAO, lipolysis, Akt-P, mTOR inhibition

↓ BW, WAT mass, serum leptin, insulin, TG in muscle and liver
↑ AMPK, ACC, FAO, mitochondrial biogenesis (PGC1a, TFAM) in muscle and fat

↑ UCP1, WAT lipolysis, Leptin sensitivity in hypotalamous, adipocyte perilipin
↓ SREBP1 and adipocyte size in WAT

↑ thermogenesis (UCP1, T3 in BAT)
↓ leptin and insulin in serum

↑ body temperature, T3 in serum
↓ hypercorticosteronism

↓ BW, fat in the liver, SCD
↑ FAO and UCP1 in BAT

↑ thermogenesis and browning (UCP1,2, 3, PPARa)
↓ WAT adipogenesis (PPARG)

↓ abdominal and subcutaneous fat, IL6
No effect in leptin/adiponectin

Soy

Antiadipogenesis, ↓ SREBP1c

↓ Cebpa, PPARG, LPL, Lipid droplet size
↑ TGFb1

↓ Adipogenesis and differentiation (PPARG, Cebpa, FABP4, FASN, SREBP1c)

↓ adipocyte differentiation (PPARG, Cebpa, SREBP1c, GLUT4)

↑ FAO, browning induction (FNDC5) mitochondrial function in mice muscle (AMPK, PGC1a, PPARG)
↑ thermogenesis (UCP1, TMEM16), mitochondrial number and respiration rate in adipocytes 3T3L1

↑ Lipolysis, cAMP via AMPK activation
↓ TG

↑ AMPK, apoptosis in mature adipocytes
↓ adipogenesis

↑ mitochondrial biogenesis (SIRT1-PGC1a pathway), ATP synthase b

↓ adipogenesis and differentation (PPARG, Cebpa, FABP4 and perilipin)

↓ Adipogenesis (PPARG, Cebpa), lipid accumulation, PI3K-Akt pathway

↑ thermogenesis in BAT (UCP1, SIRT1, PGC1a, proton leak and oxygen consumption)
↓ Lipid accumulation in WAT (FASN, FABP4, HSL, resistin)

↑ mitochondrial biogenesis (PGC1a, TFAM, SIRT1 dependent), COX1

↑ SIRT1, AMPK activation
↓ myotube atrophy

↑ myotube diameter, MHC protein, IGF1 and IGF1R

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↑ FA release, ATGL via AMPK activation

↓ lipid deposition in WAT and liver, BW, differentiation capacity (PPARG and perilipin)

↑ mtDNA, oxydative capacity (CPT1a) and thermogenesis (UCP1)
↓ Lipogenesis and resistin

↑ EE, thermogenesis (UCP1), mtDNA, mitochondrial biogenesis (PGC1a, PPARA) and oxygen consumption in muscle fibers

↑ SIRT1, COX2, PGC1a and UCP1 protein

↑ mitochondrial biogenesis and function (PGC1a, NRF2, UCP1, ATP5a1, TFAM, SIRT1, AMPK activation, and maximal respiration rate)

↑ thermogenesis and mitochondrial function (UCP1, SIRT1, BMP7)

↑ iBAT mass, thermogenesis and browning (UCP1, AMPK, PRDM16)

↑ thermogenesis and mitochondrial function (UCP1, SIRT3, ↓ PGC1a acetylation)

↑ thermogenesis, browning and mitochondrial function in iWAT (UCP1, PRDM16, Cidea, PGC1a, AMPK, oxygen consumption and FAO)

↑ thermogenesis and mitochondrial function (UCP1, PRDM16, PPARA and adiponectin expression, SIRT1 and PGC1a activation)

↑ mitochondrial activity and mass in BAT, extrogen receptor a

↑ PPARG, UCP2 in WAT, MUFAs and PUFAs

↑ browning and thermogenesis (UCP1, PPARA, NRF) and oxidative capacity (CPT1a)

↓ Adipogenesis (↓ adipogenesis (PPARG, Cebpa, SREBP1c, FASN)
↑ SIRT1, AMPK activation, apoptosis, TNFa and lipolysis

↑ mitofusin 2 expression and respiration rates

↑ adiponectin. ↓ cell proliferation and differentiation (PPARG, Cebpa, FASN and resistin)

↑ oxygenase I
↓ Differentiation (PPARG, Cebpa, FABP4)

↓ Lipogenesis and lipogenic insulin effect

↓ adipogenesis and differentiation (PPARG, Cebpa, SREBP1c, FASN, FABP4) dose dependent

↑ mitochondrial biogenesis and mass (AMPK, ATAD3)
↓ lipogenesis

↑ SIRT1, AMPK, FOXO1 pathways, HSL
↓ Adipogenesis (FASN, PPARG)

Grape Resveratrol

↑ Browning and thermogenesis (UCP1, PRDM16, PGC1a SIRT1 dependent and FNDC5 in subcutaneous AT)

↓ Adipogenesis (FASN, leptin, PPARG, Cebpa, SREBP1c, FABP4), inflammation (TNFa, IL6, INFa and b), TG, BW, Ch, blood glucose

↓ adipogenesis and lipogenesis (PPARG, Cebpa, SREBP1c, FASN), BW, Ch, AT mass, ACC
↑ HDL

↑ muscle aerobic capacity
↓ muscle fatigue, CK, ammonia, lactate in serum

↑ Force isometric contraction, FAO, physical performance, mitochondrial number and function (oxydative metabolism), cardiac function (FAO)

↓ muscle fatigue index
↑ muscle glycogen content, insulin sensitivity, muscle hypertrophy

↑ Lipolysis
↓ adipocyte size

↑ SIRT1, PGC1a pathways in skeletal muscle ex vivo
No changes in BAT

No changes in BMI, AT mass
↑ resting EE, SIRT1, AMPK expression in muscle

↑ mitochondrial density, knee extensor muscle peak torque
↓ muscle fatigue index

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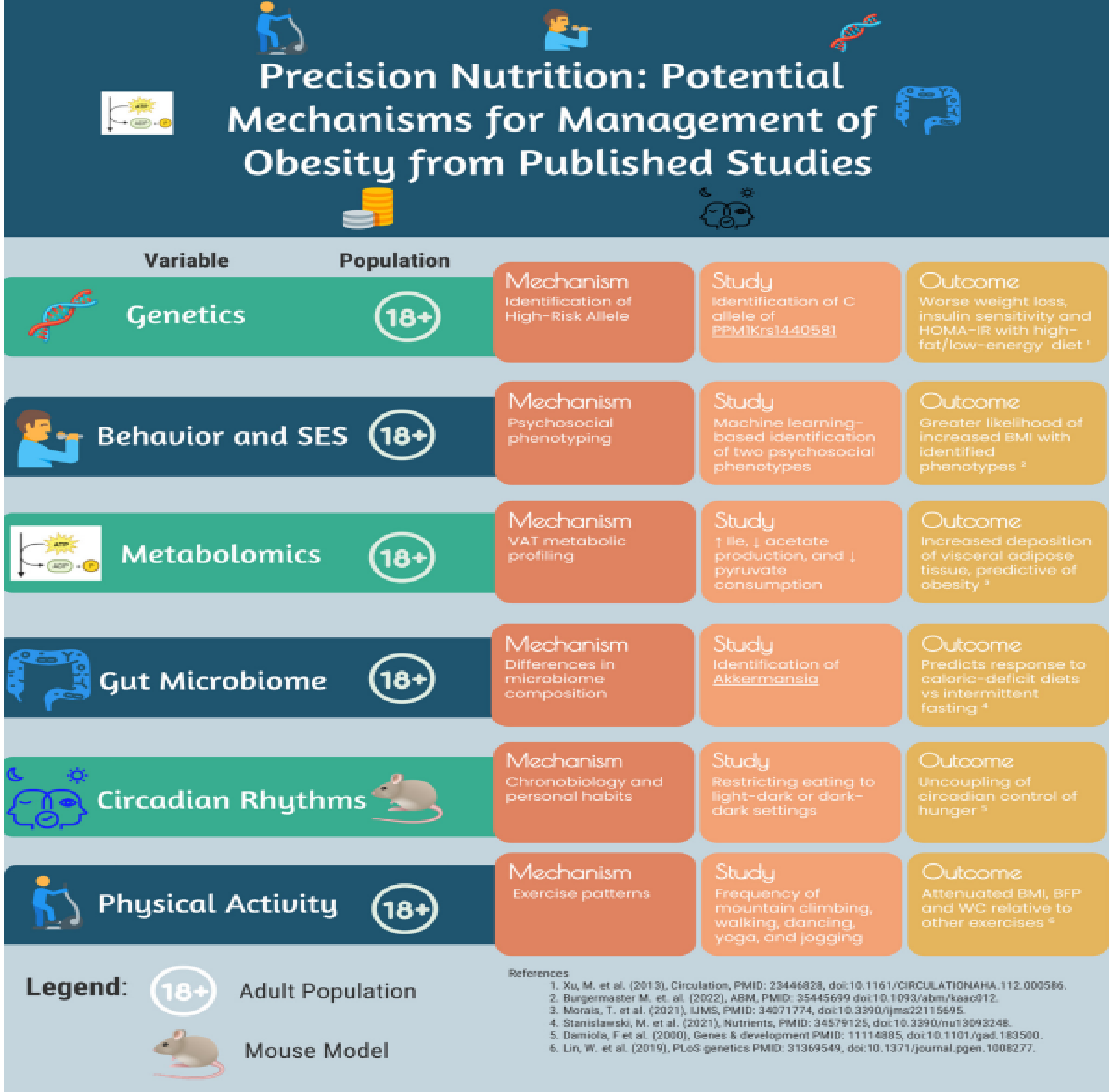

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