IL
PESO DELLA GLICEMIA

DIABETE E OBESITÀ TRA RISCHIO
CARDIO-RENALE, EPATICO E NEUROLOGICO

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CARDIO-RENALE, EPATICO E NEUROLOGICO

Sesto San Giovanni (MI)
IRCCS MultiMedica

SID
Società Italiana
di Diabetologia

Obesità e infiammazione

Paola S. A. Morpurgo

ASST FATEBENEFRATELLI SACCO

Milano

la dr.sa Paola Silvia Anna Morpurgo dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- Abbott
- Sanofi
- Novo Nordisk
- Eli Lilly

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

Editorial

Inflammation: The Cause of All Diseases

Inflammation is an essential biological process that serves as the body's first line of defence against harmful stimuli, including pathogens, damaged cells, and irritants.

While acute inflammation is crucial for healing and recovery, **chronic inflammation** can lead to a variety of diseases, including cancer, cardiovascular disorders, and autoimmune conditions

Cells **2024**, 13, 1906.

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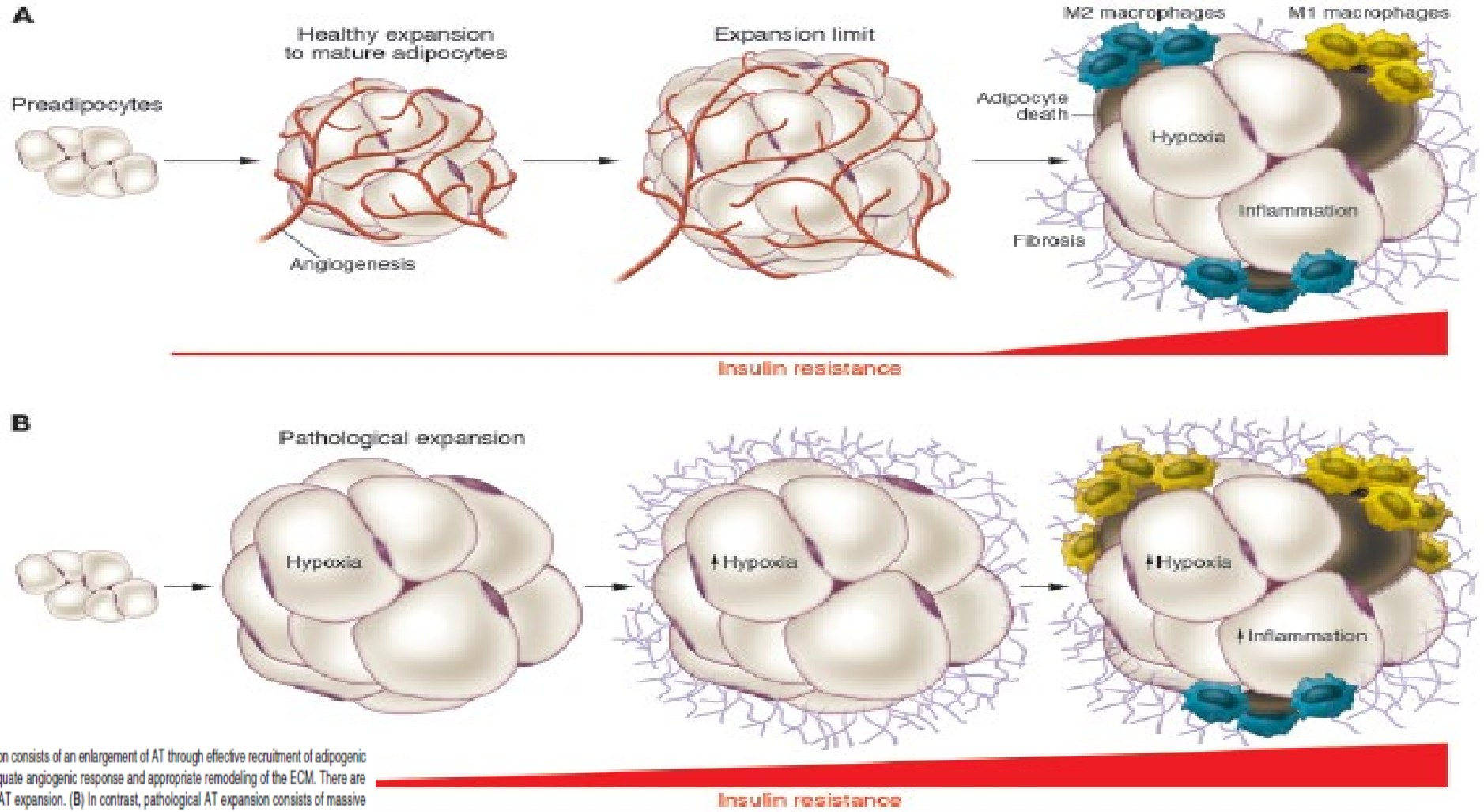
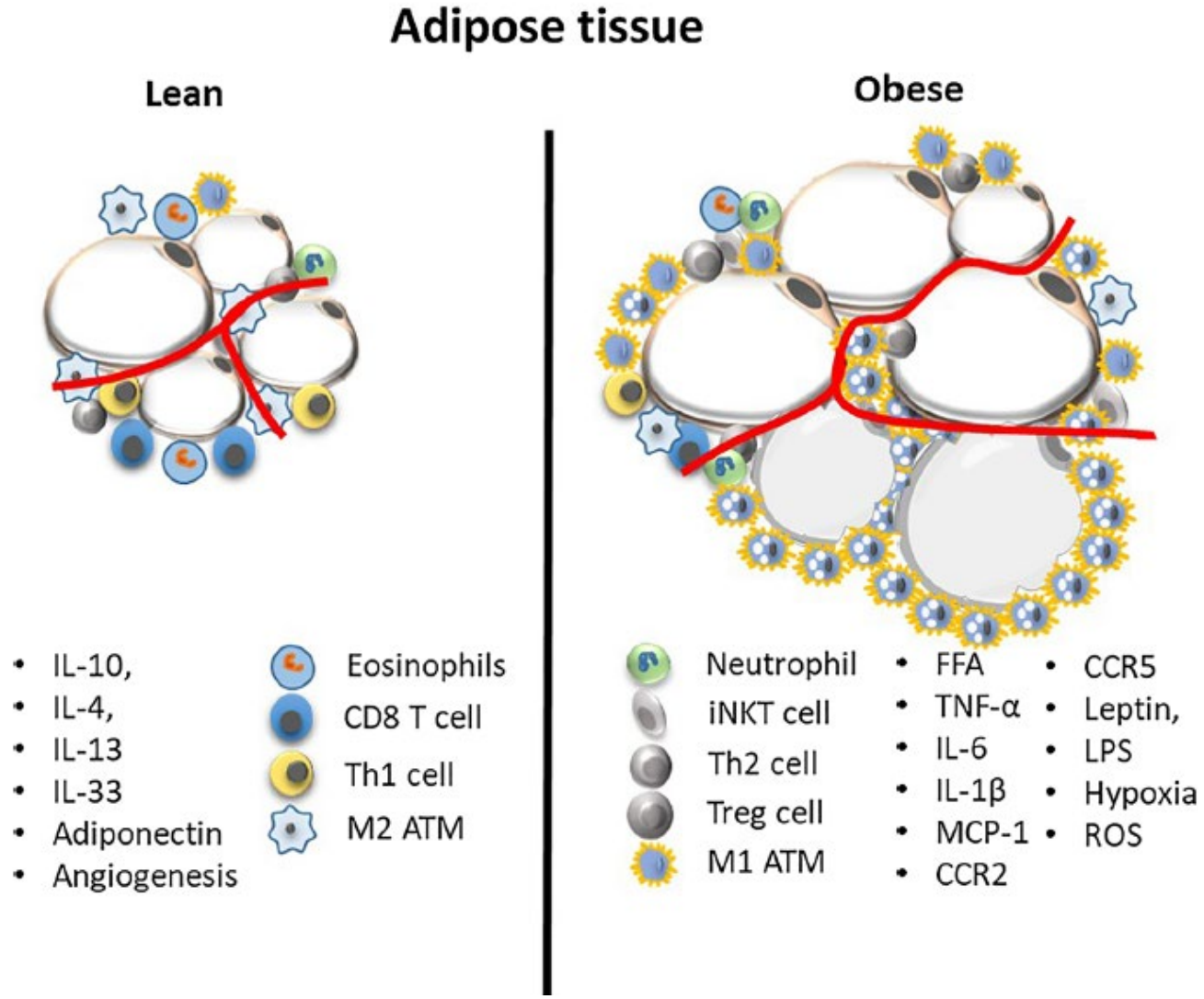


Healthy and unhealthy AT expansion. (**A**) Healthy AT expansion consists of an enlargement of AT through effective recruitment of adipogenic precursor cells to the adipogenic program, along with an adequate angiogenic response and appropriate remodeling of the ECM. There are strong individual differences with respect to the potential for AT expansion. (**B**) In contrast, pathological AT expansion consists of massive enlargement of existing adipocytes, limited angiogenesis, and ensuing hypoxia. As a result, HIF-1α is induced, which in turn can cause the induction of a fibrotic program. Ultimately, M1-stage macrophages prevail, leading to an inflammatory phenotype that is strongly associated with systemic insulin resistance.

Adipose tissue remodeling and obesity

Kai Sun,[1] Christine M. Kusminski,[1] and Philipp E. Scherer[1,2]



Disfunctional adipocytes and M1 macrophages induces several factors (FFAs; TNF-alfa; iL-6; iL-1beta; MCP-1; CCR2; CCR5, Leptin and LPS) wich creates complex systemic environments.

Adipose tissue remodeling and obesity

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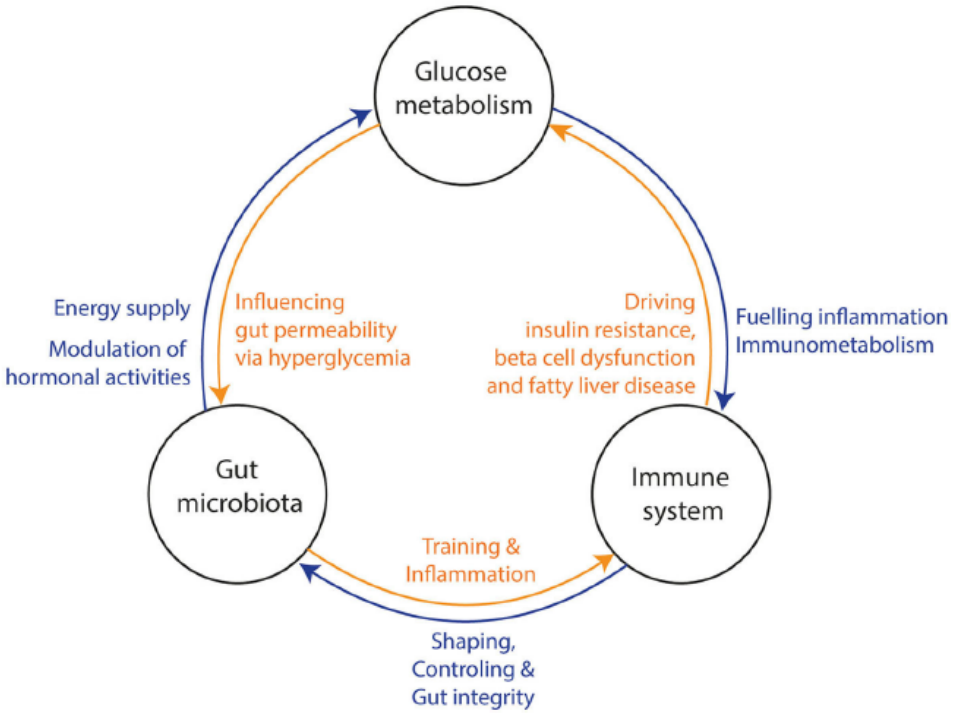
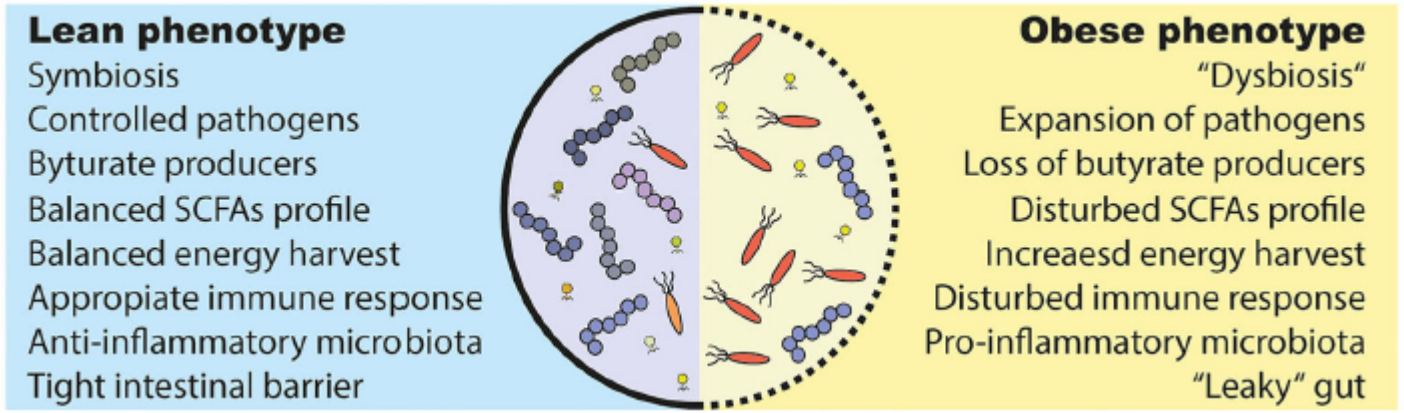
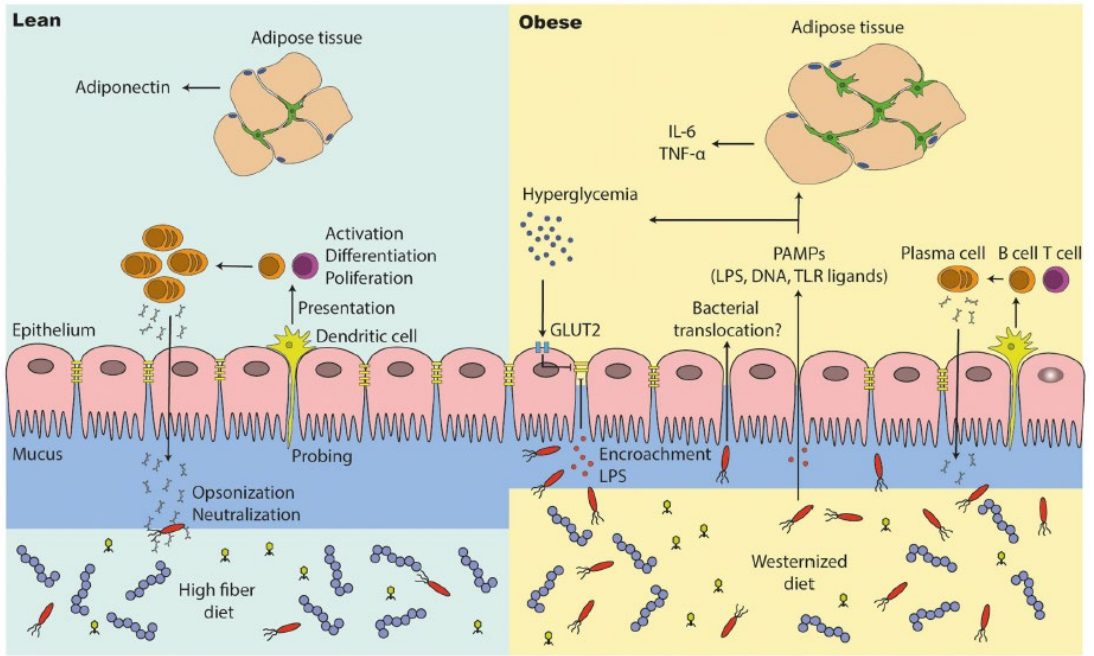
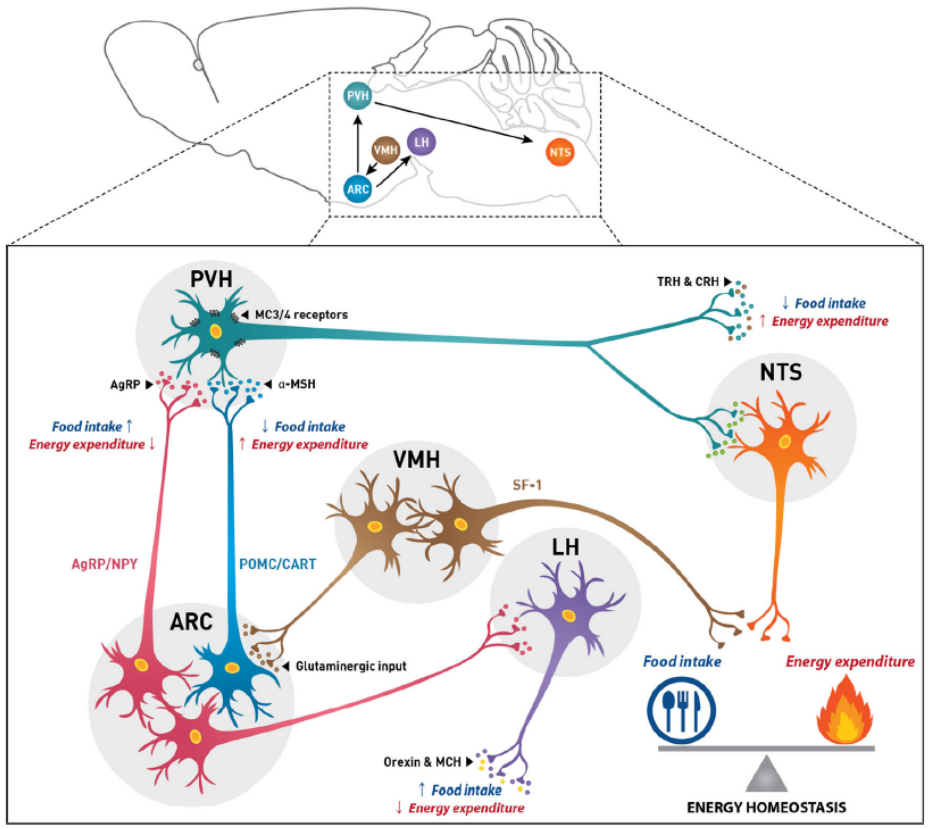


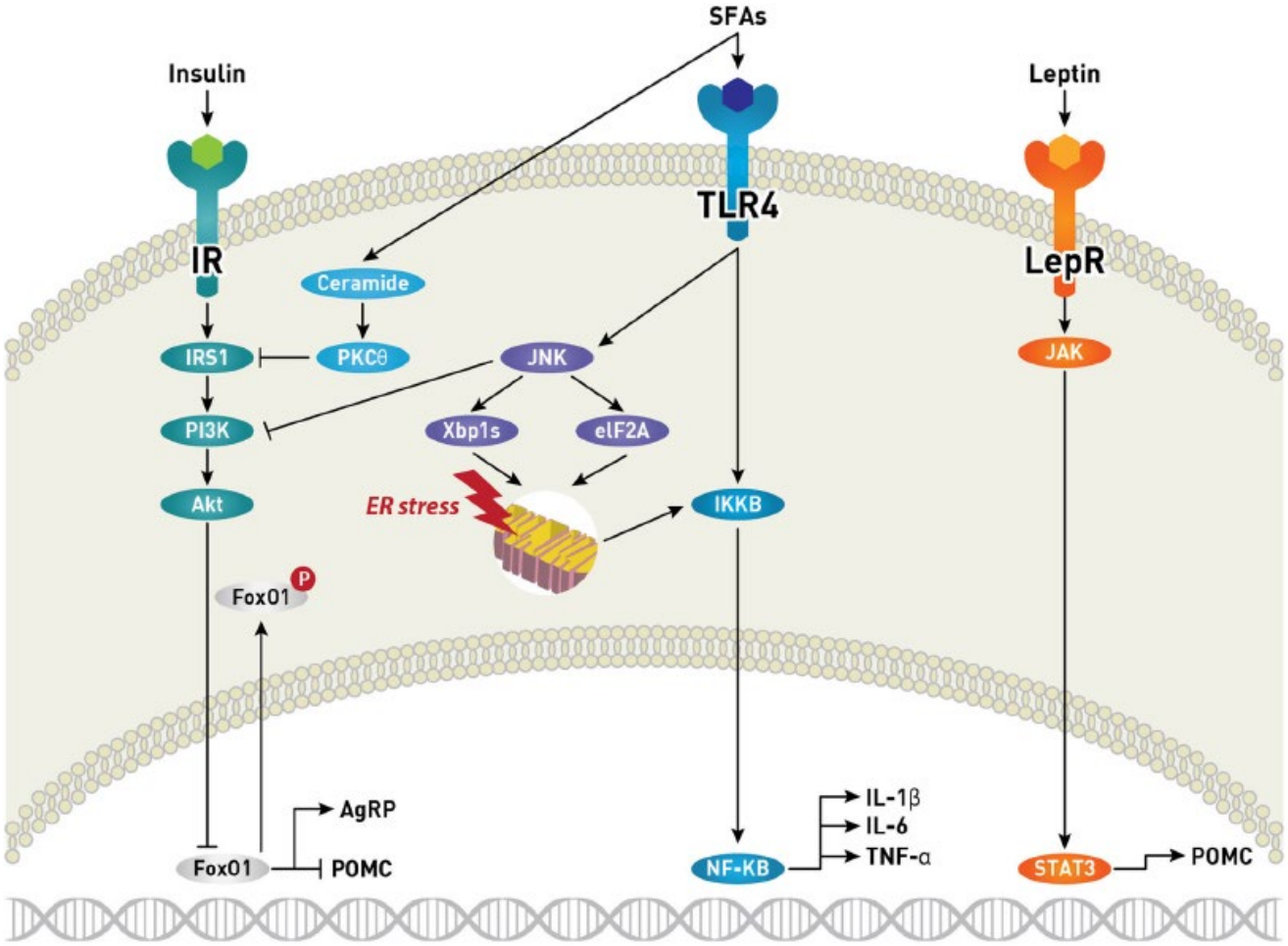




Front. Immunol. 11:571731.

Hypothalamic inflammation and obesity



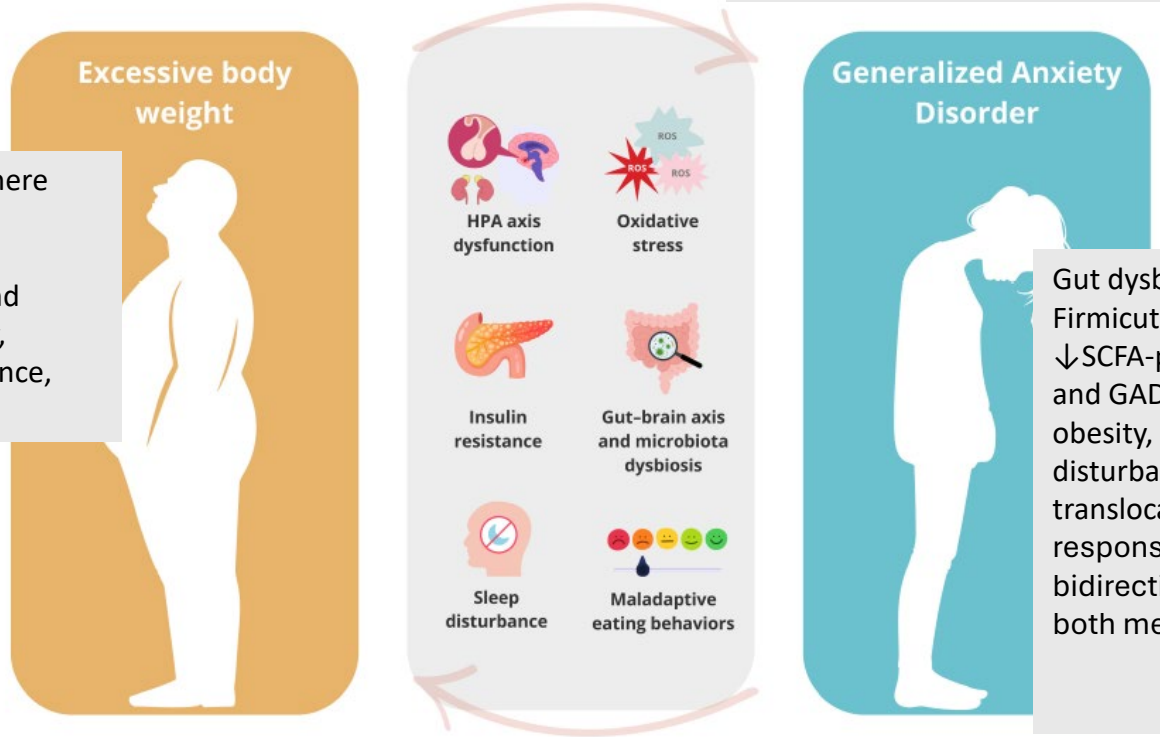


Arch. Pharm. Res. (2019) 42:383–392

Generalized Anxiety Disorder and Obesity: Overlapping Neuroendocrine, Metabolic, and Behavioral Pathways

Oxidative stress and obesity-related low-grade inflammation (↑IL-6, TNF-α) disrupt neurotransmitter balance (↓serotonin, altered GABA), impair neural function, and promote anxiety. Shared mechanisms include chronic inflammation, mitochondrial dysfunction, NADPH oxidase activity, and reduced antioxidant defenses, leading to ROS overproduction, oxidative brain damage, appetite dysregulation, and a mutually reinforcing relationship of metabolic and neuropsychiatric disturbances

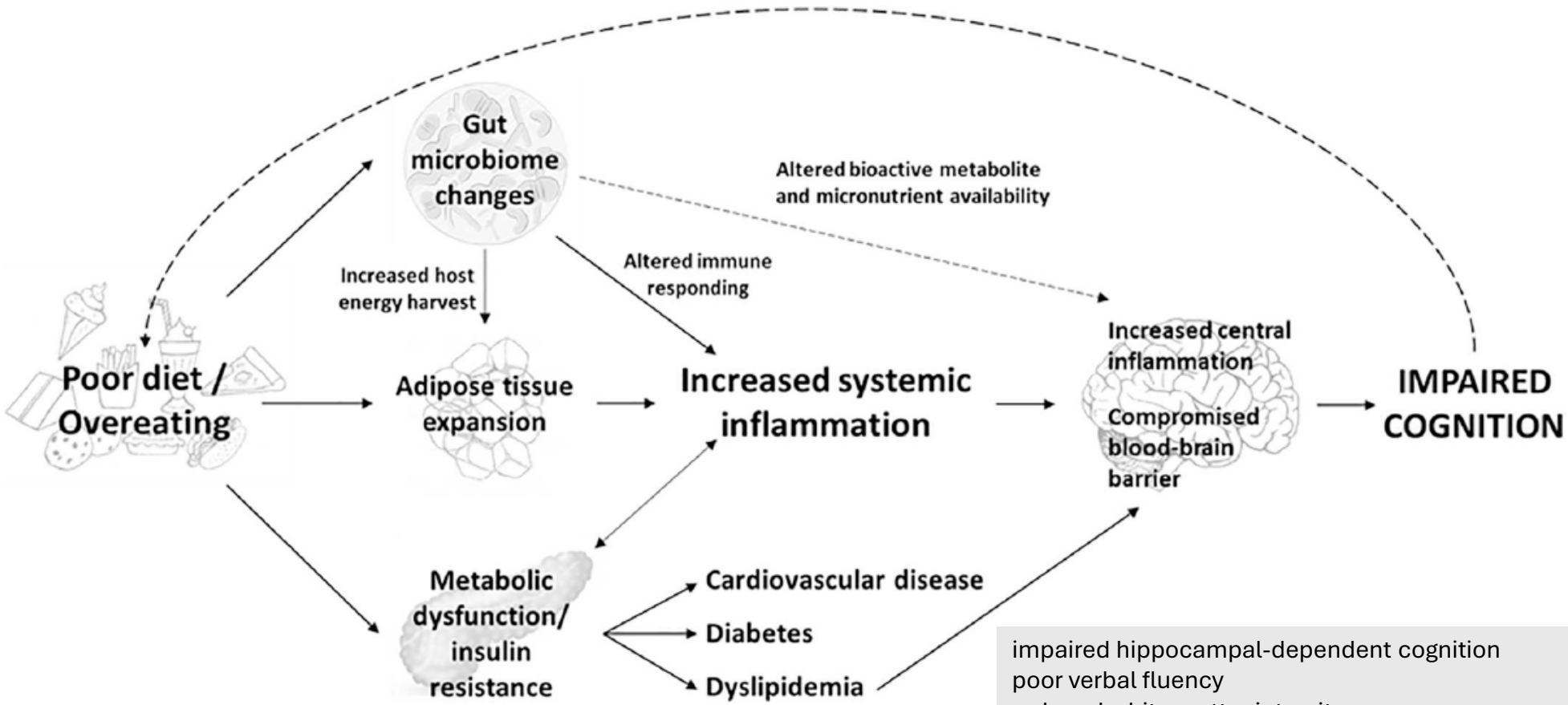
IR is closely associated with visceral obesity, where chronic low-grade inflammation (↑IL-6, TNF-α) disrupts insulin signaling. Reduced insulin action in the CNS may affect the frontal lobe and hippocampus, leading to HPA axis hyperactivity, cortisol dysregulation, and serotonergic imbalance, which could increase susceptibility to GAD.



Gut dysbiosis (↓diversity, altered Firmicutes/Bacteroidetes ratio, ↓SCFA-producing bacteria) is observed in both obesity and GAD. In obesity, it enhances energy harvest, fat storage, bile acid disturbances, and systemic inflammation via LPS translocation. These changes activate immune responses and HPA axis dysregulation, creating a bidirectional gut–brain feedback loop that exacerbates both metabolic and anxiety symptoms.

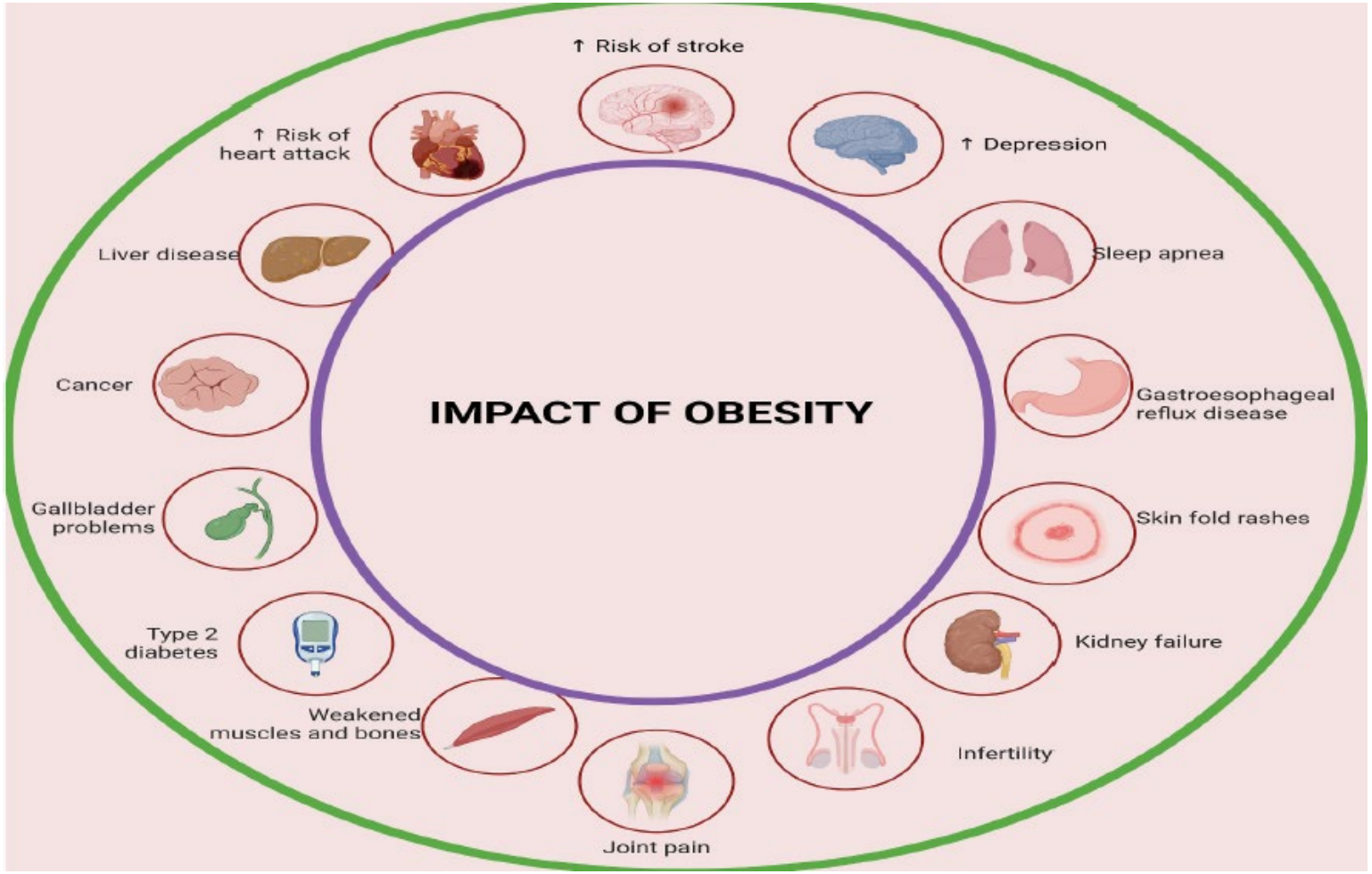
Nutrients **2025**, 17, 2835

Diet, inflammation and the gut microbiome: Mechanisms for obesity-associated



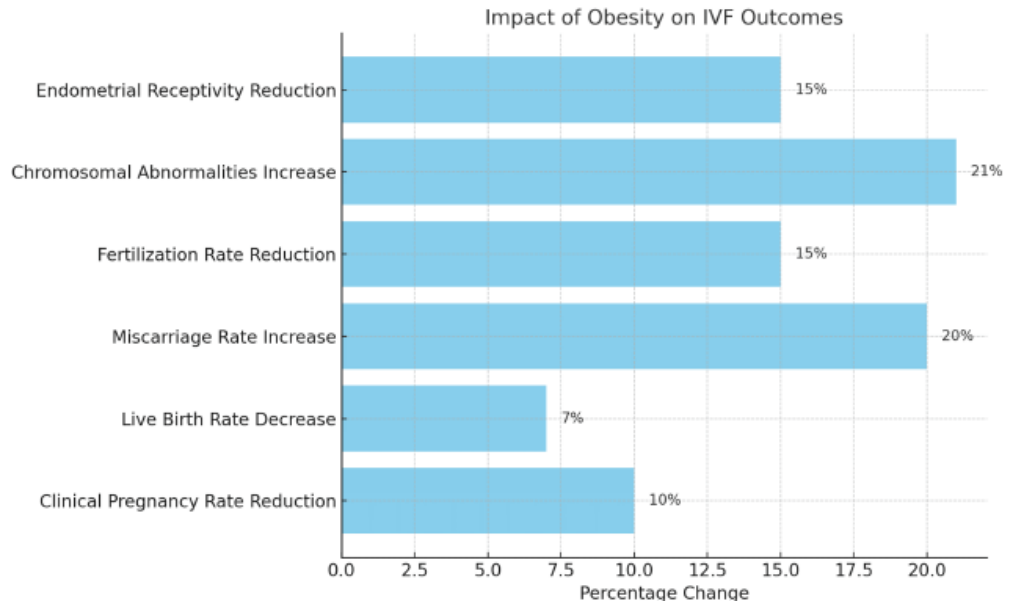
impaired hippocampal-dependent cognition
poor verbal fluency
reduced white matter integrity

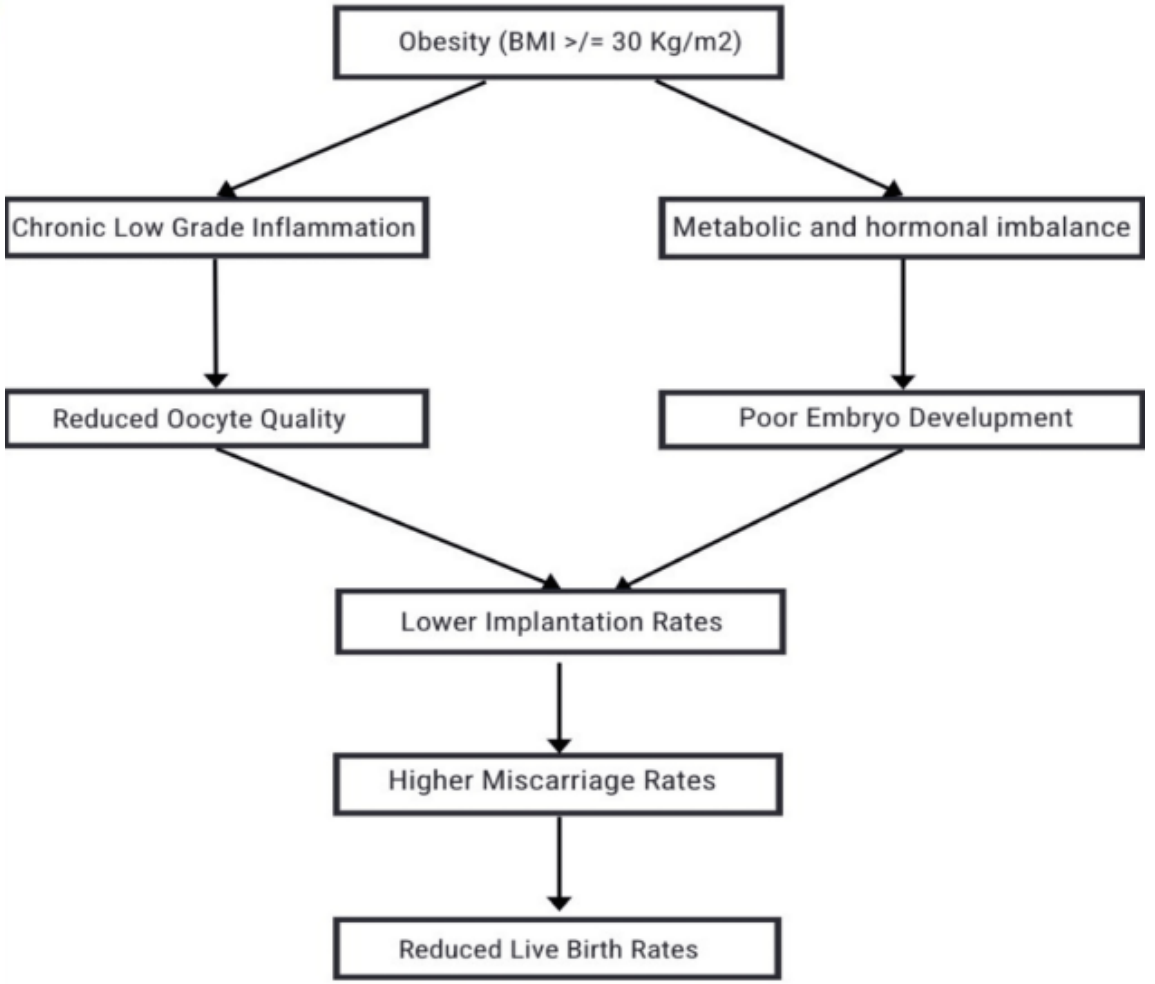
Molecular Basis of Disease 1866 (2020) 165767



Obesity Medicine Volume 54 March 2025, 100585

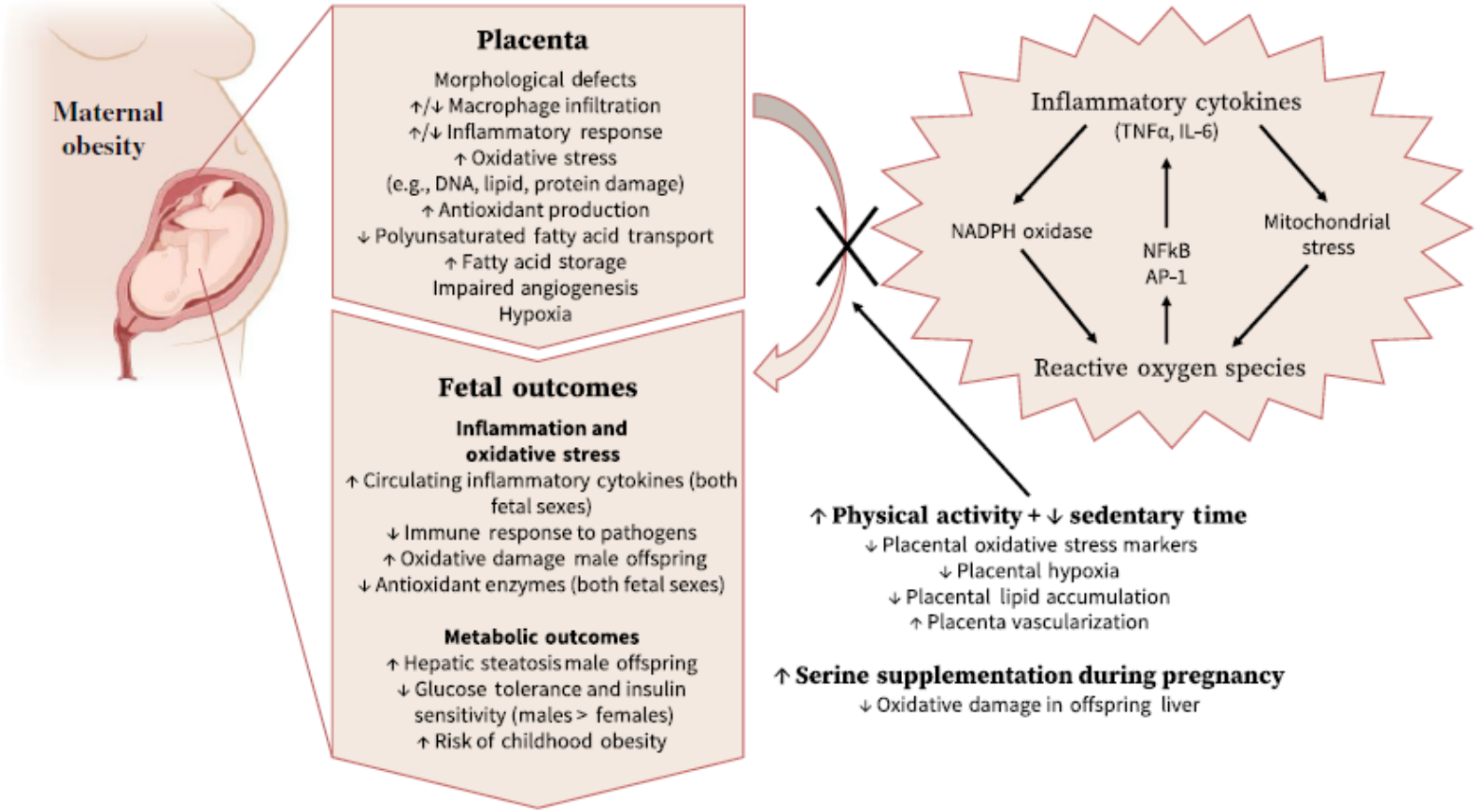
Impact of Obesity on In Vitro Fertilization (IVF) Outcomes: A Systematic Review





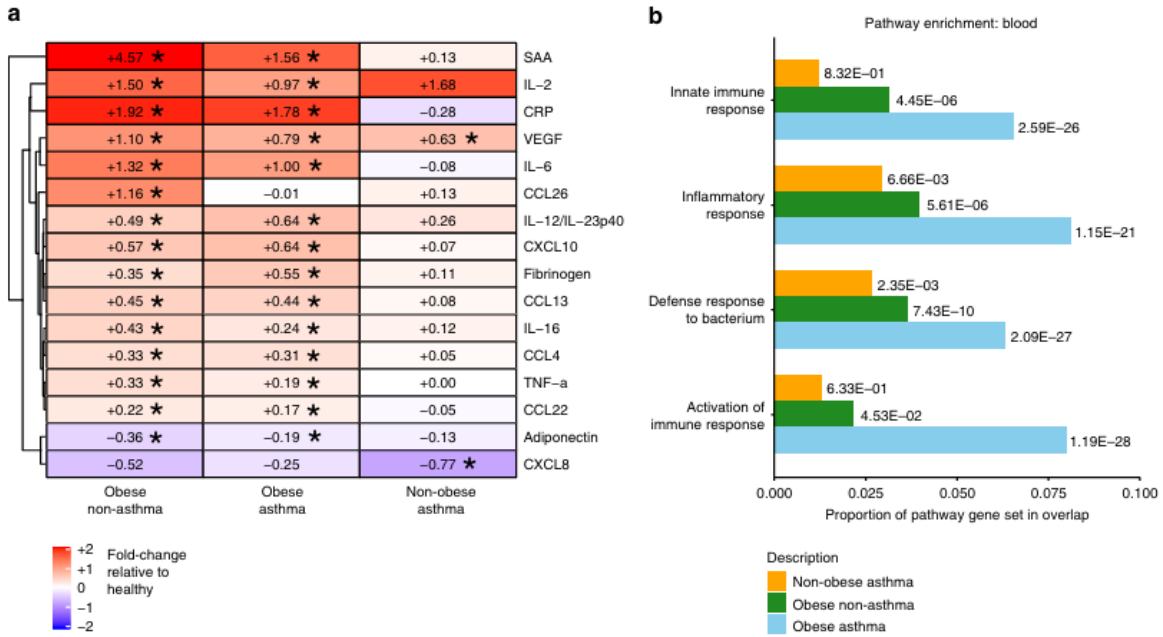
Cureus 17(8): e90695.

Placental inflammation, oxidative stress, and fetal outcomes in maternal obesity

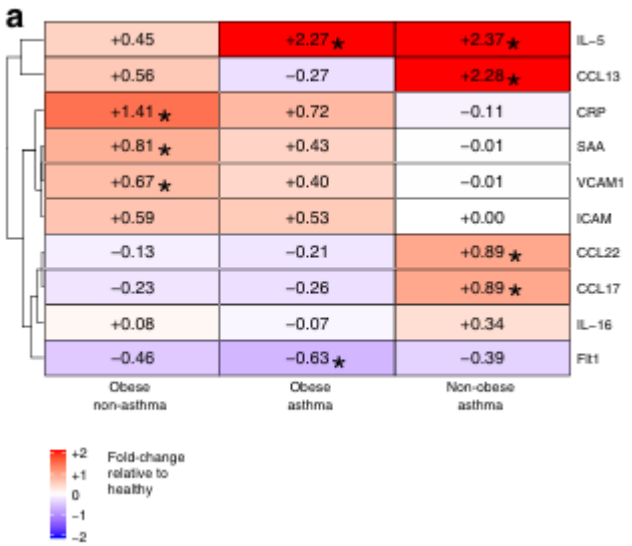


Trends in Endocrinology & Metabolism, July 2024, Vol. 35, No. 7

Obesity and disease severity magnify disturbed microbiome-immune interactions in asthma patients



Blood inflammatory profiles.



Lung inflammatory profiles. Foldchange of cytokine levels in bronchoalveolar lavages (BALs)

Nat Commun. 2019;10(1):5711

Obesity and Cancer Mechanisms: Tumor Microenvironment and Inflammation

Breast white adipose tissue inflammation is detected by the presence of crown-like structures of the breast (CLS-B).

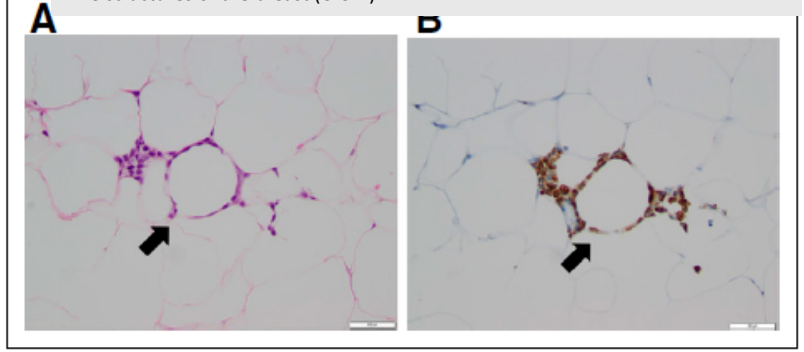
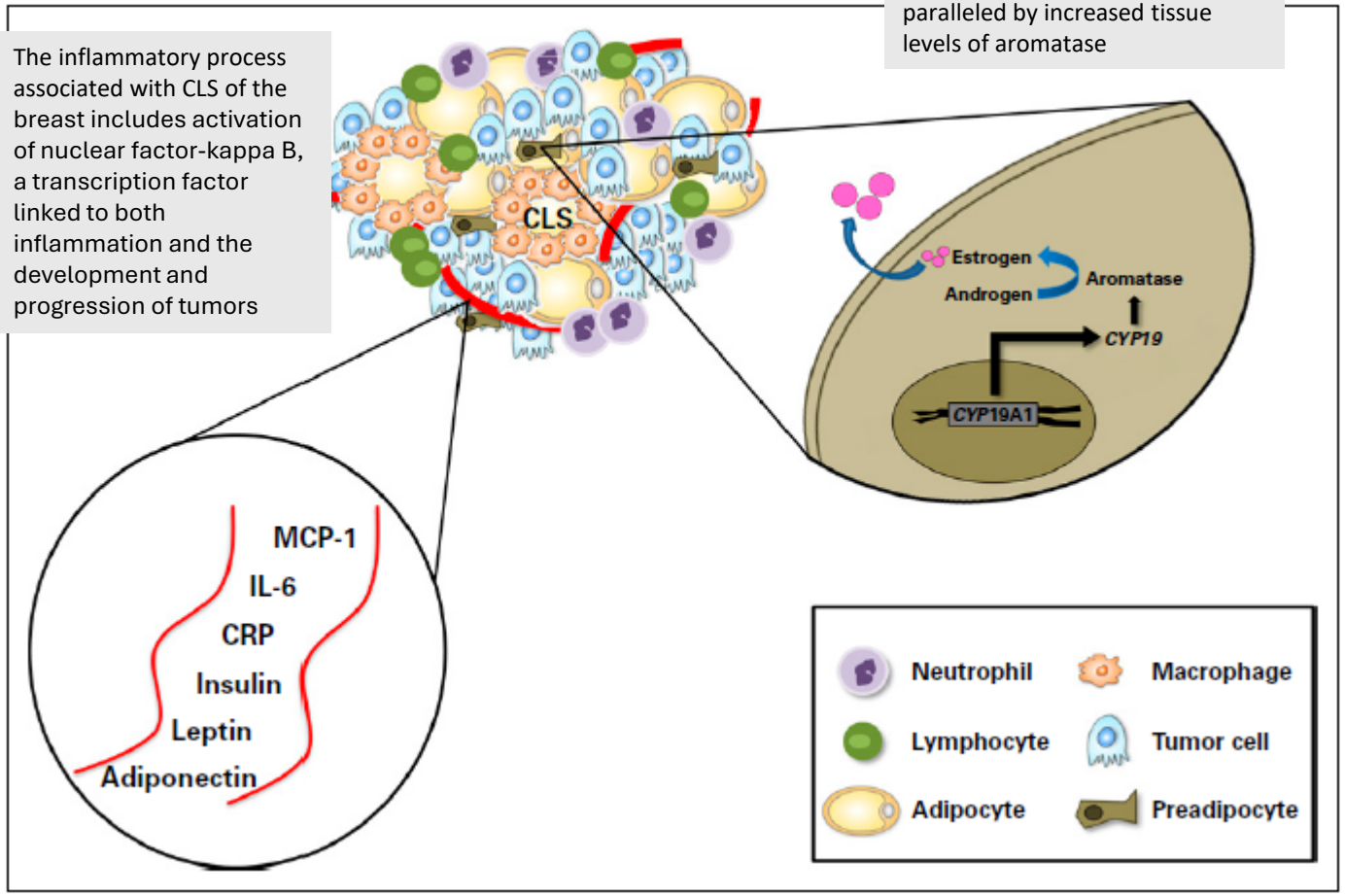


Table 1. Alterations in Circulating Factors in Women With Versus Without White Adipose Tissue Inflammation in the Breast Detected by the Presence of CLS-B[34]

Variable	CLS-B Negative (n = 48)	CLS-B Positive (n = 52)	*P*
Median glucose level, mg/dL (IQR)	72 (67-77)	80 (70-84)	.01
Median insulin level, mU/L (IQR)	4.1 (3.4-5.0)	4.8 (3.7-7.2)	.03
Median total cholesterol level, mg/dL (IQR)	190 (165-213)	199 (176-224)	.15
Median LDL cholesterol level, mg/dL (IQR)	103 (84-128)	114 (97-140)	.06
Median HDL cholesterol level, mg/dL (IQR)	70 (62-81)	59 (50-70)	.003
Median triglyceride level, mg/dL (IQR)	66 (56-79)	93 (68-122)	< .001
Median leptin level, pg/mL (IQR)	7.9 (5.5-15.5)	17.4 (9.6-27.9)	< .001
Median adiponectin level, µg/mL (IQR)	13.3 (10.9-16.3)	9.9 (7.0-12.2)	< .001
Median hsCRP level, ng/mL (IQR)	0.51 (0.32-1.04)	1.06 (0.66-3.04)	< .001
Median IL-6 level, pg/mL (IQR)	0.75 (0.46-1.10)	1.26 (0.72-2.31)	< .001

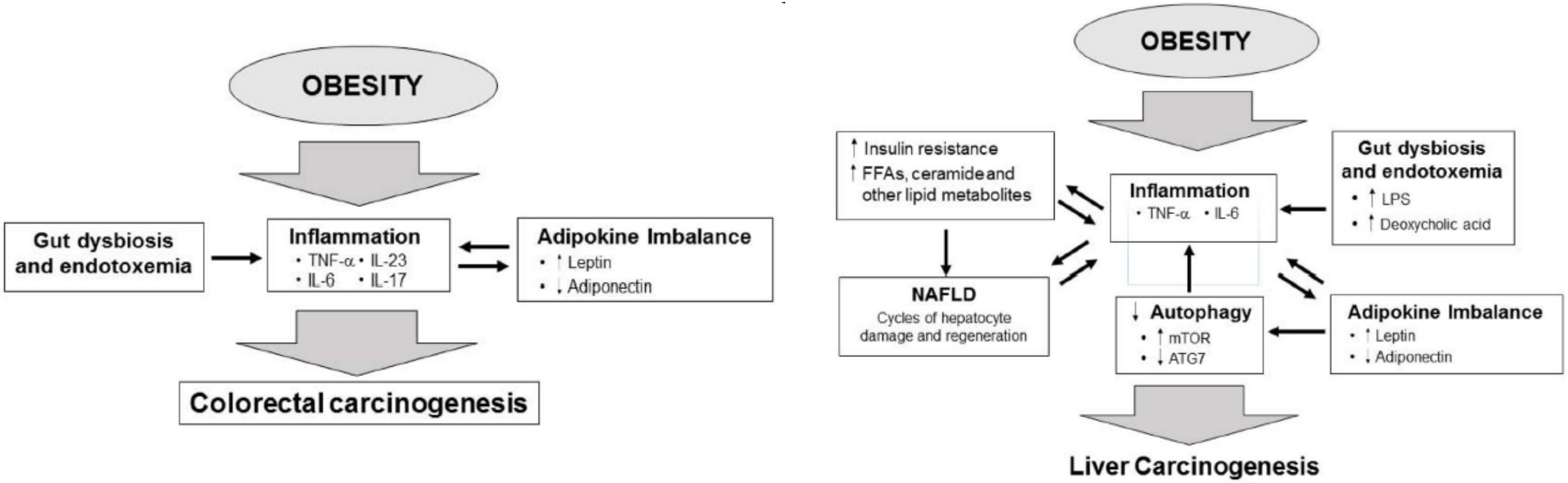
The inflammatory process associated with CLS of the breast includes activation of nuclear factor-kappa B, a transcription factor linked to both inflammation and the development and progression of tumors

Breast WAT inflammation is paralleled by increased tissue levels of aromatase



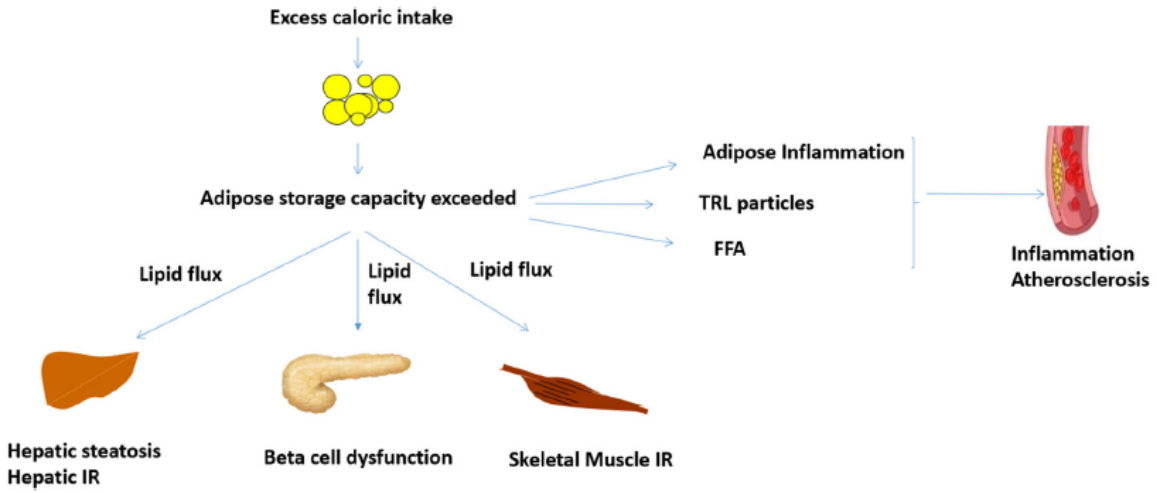
J Clin Oncol 34:4270-4276

Obesity and cancer: inflammation bridges the two



Curr Opin Pharmacol. 2016 August ; 29: 77–89

Obesity and Cardiovascular Disease: The Emerging Role of Inflammation

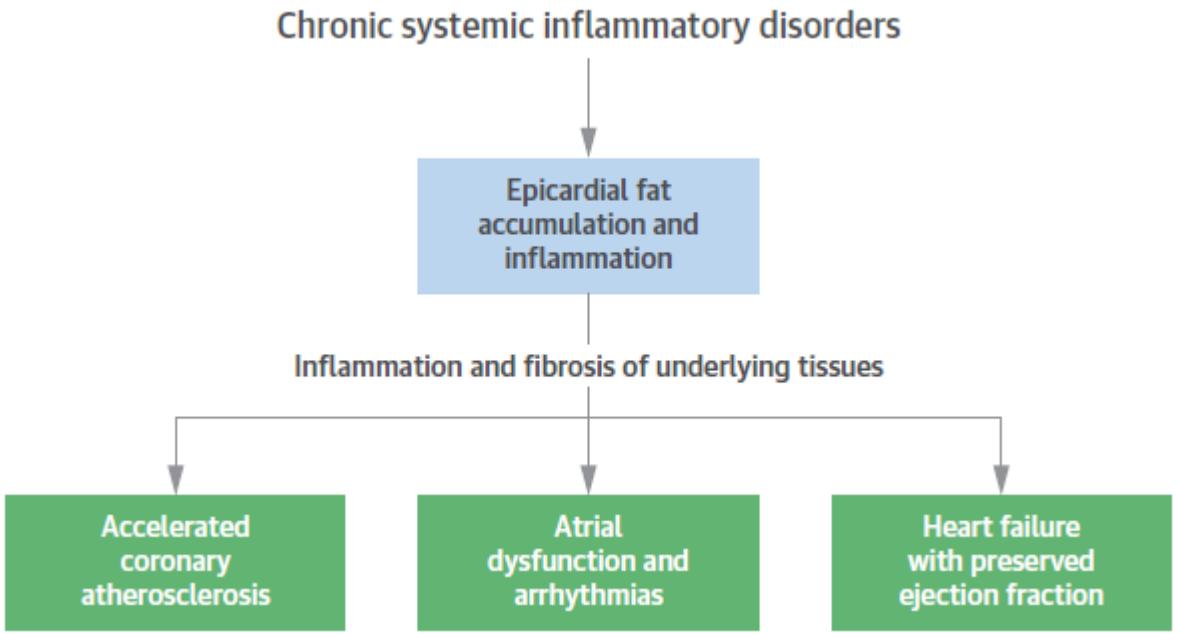


Critical regulators of inflammation in obesity and CVD

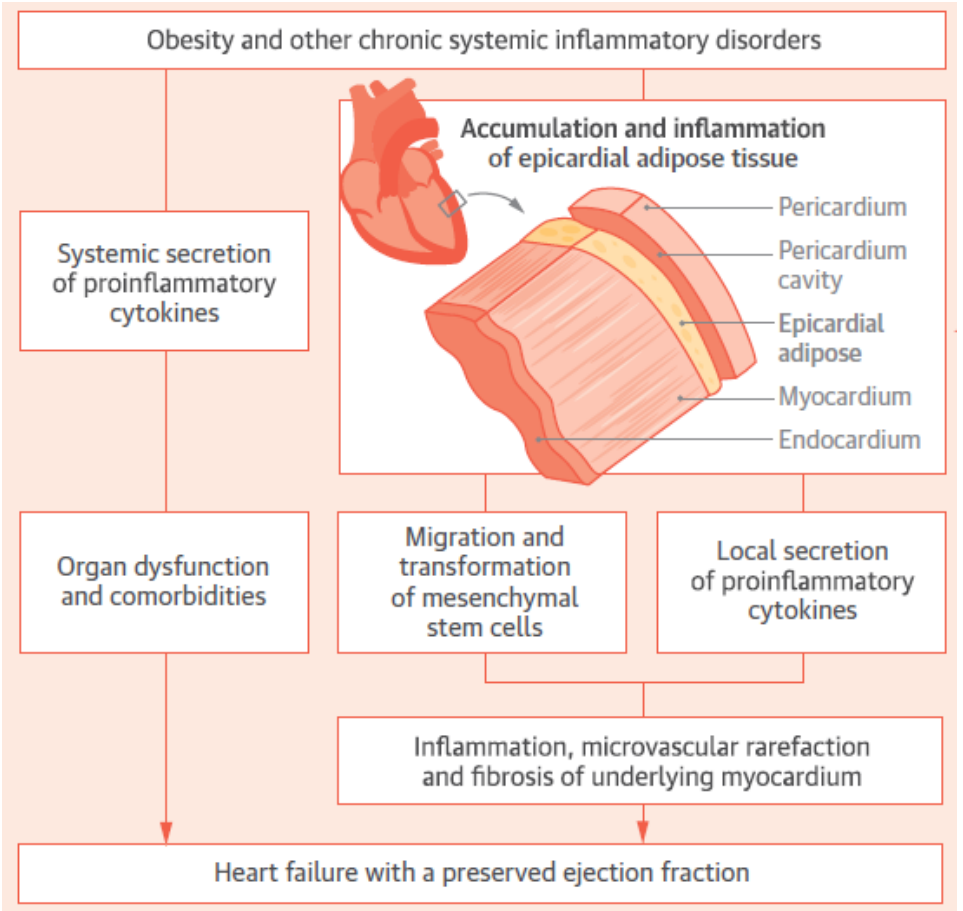
	Impact on metabolic function	Impact on atherosclerosis
Free fatty acid	- Contributes ectopic lipid deposition and insulin resistance and type 2 diabetes	- Activates NLRP3 inflammasome and TLR4 in macrophages
IL-6	- Impairs insulin sensitivity and increases T2D risk in genetic analyses	- Secreted by macrophages to further increase inflammation in atheromas
PAI-1	- FFA increases production - Elevated levels found in individuals with abdominal fat accumulation	- Increases risk of intravascular thrombus and CVD by inhibiting tPA and contributing to fibrinolysis and atherothrombosis
TNF-alpha	- Secreted by macrophages in adipose tissue. Implicated in reduced insulin signaling in animal models	- Secreted by macrophages and inflammatory cells in atheromas to further increase inflammation - Causally implicated in CVD in Mendelian randomization analysis

Front. Cardiovasc. Med. 8:768119.

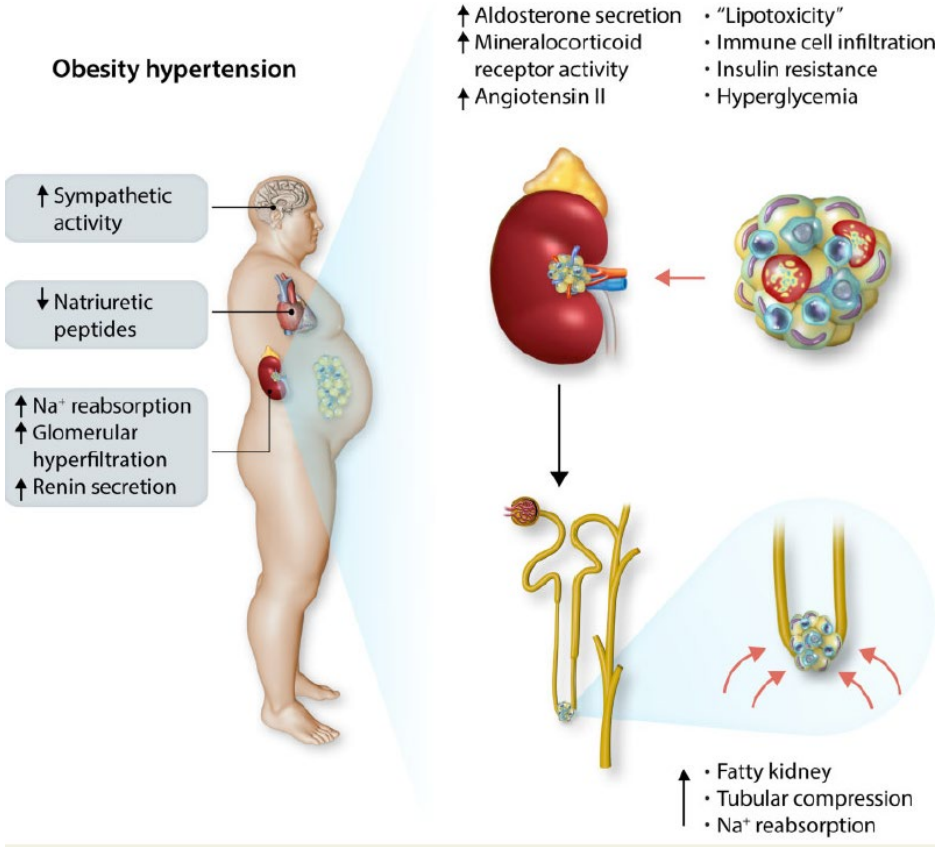
Epicardial Adipose Tissue May Act as the Transducer That Mediates the Effect of Chronic Systemic Inflammatory Disorders to Cause Coronary Atherosclerosis, Atrial Arrhythmias, and Heart Failure With Preserved Ejection Fraction



Potential Role of Epicardial Adipose Tissue in Heart Failure With a Preserved Ejection Fraction

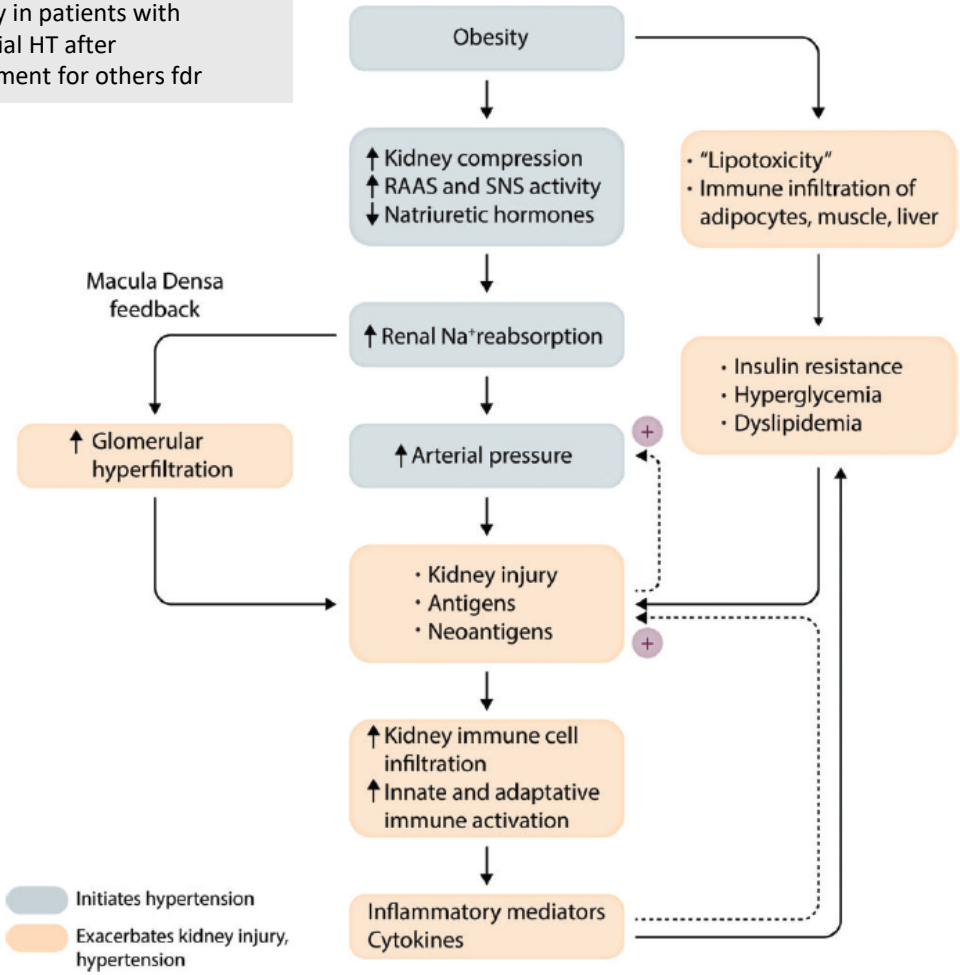


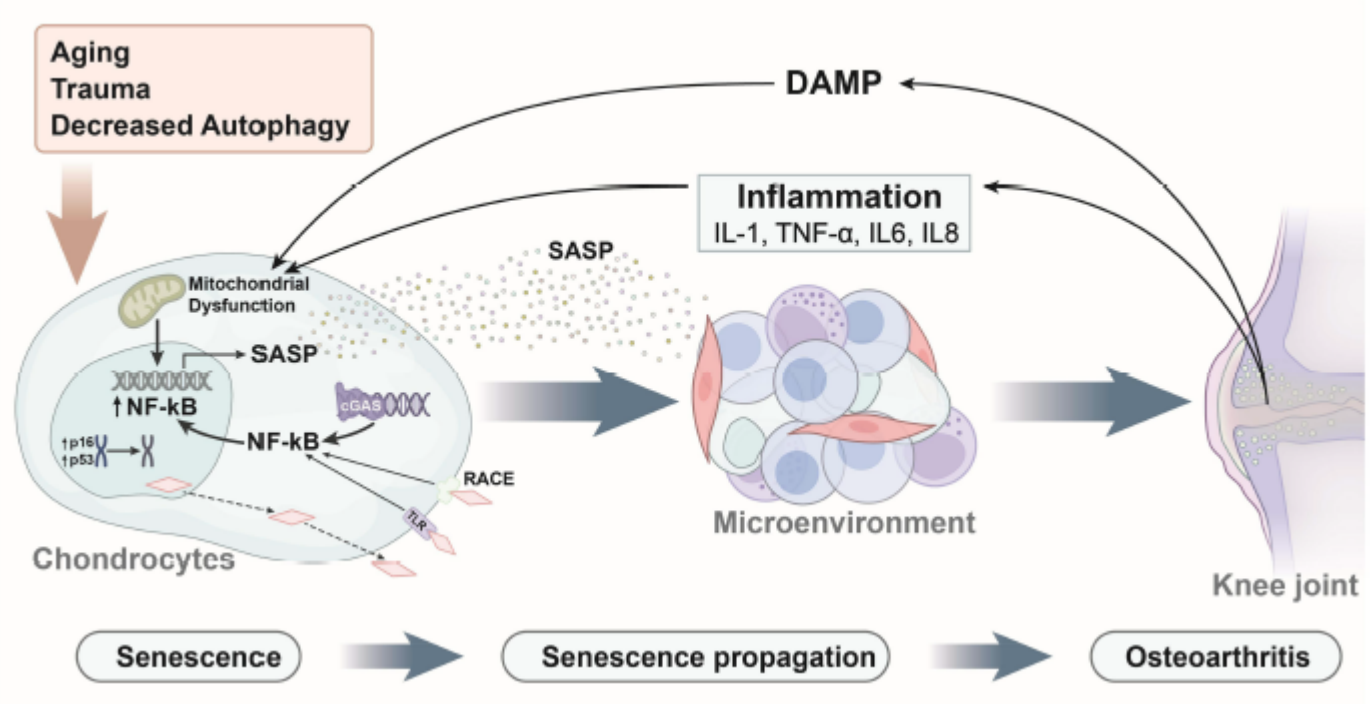
Obesity, kidney dysfunction, and inflammation: interactions in hypertension

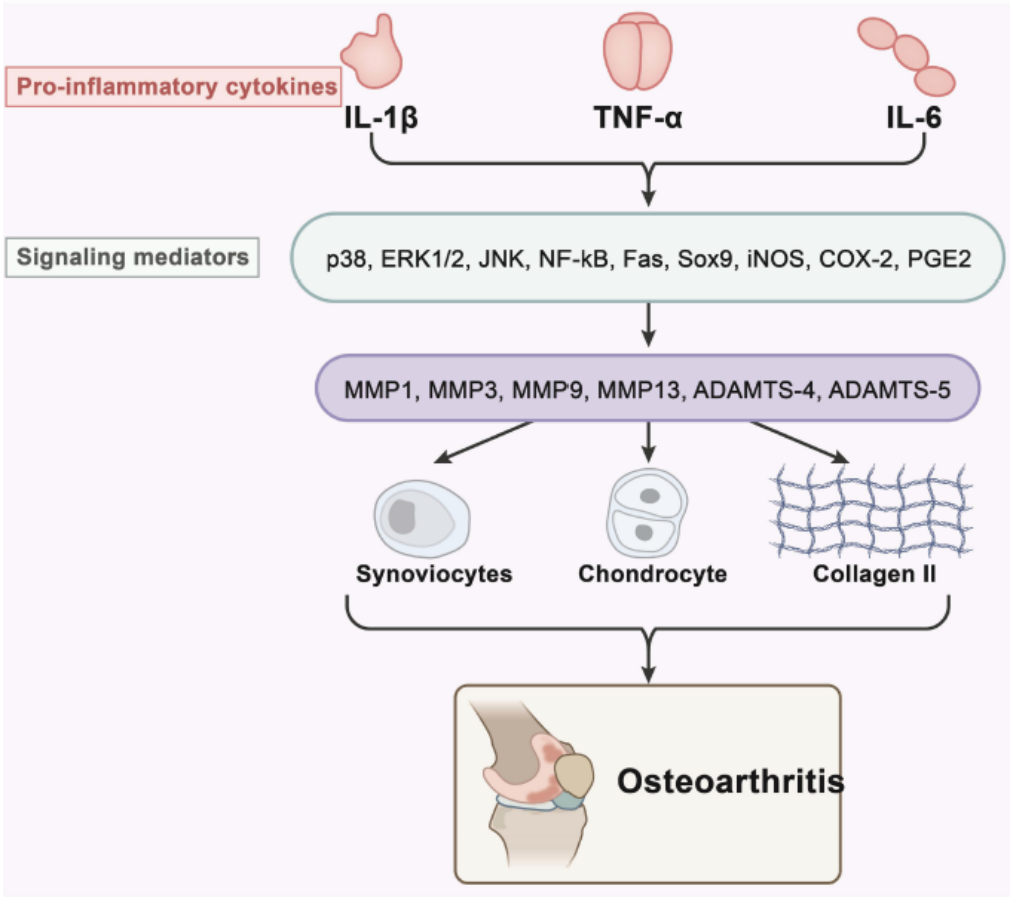


Cardiovascular Research (2021) 117, 1859–1876

higher risk of renal insufficiency was associated with abdominal obesity in patients with essential HT after adjustment for others fdr




Aging
Trauma
Decreased Autophagy
DAMP
Inflammation
IL-1, TNF-α, IL6, IL8
SASP
Mitochondrial Dysfunction
SASP
↑NF-kB
cGAS
↑p16
↑p53
NF-kB
RACE
TLR
Chondrocytes
Microenvironment
Knee joint
Senescence
Senescence propagation
Osteoarthritis


Pro-inflammatory cytokines
IL-1β
TNF-α
IL-6
Signaling mediators
p38, ERK1/2, JNK, NF-kB, Fas, Sox9, iNOS, COX-2, PGE2
MMP1, MMP3, MMP9, MMP13, ADAMTS-4, ADAMTS-5
Synoviocytes
Chondrocyte
Collagen II
Osteoarthritis

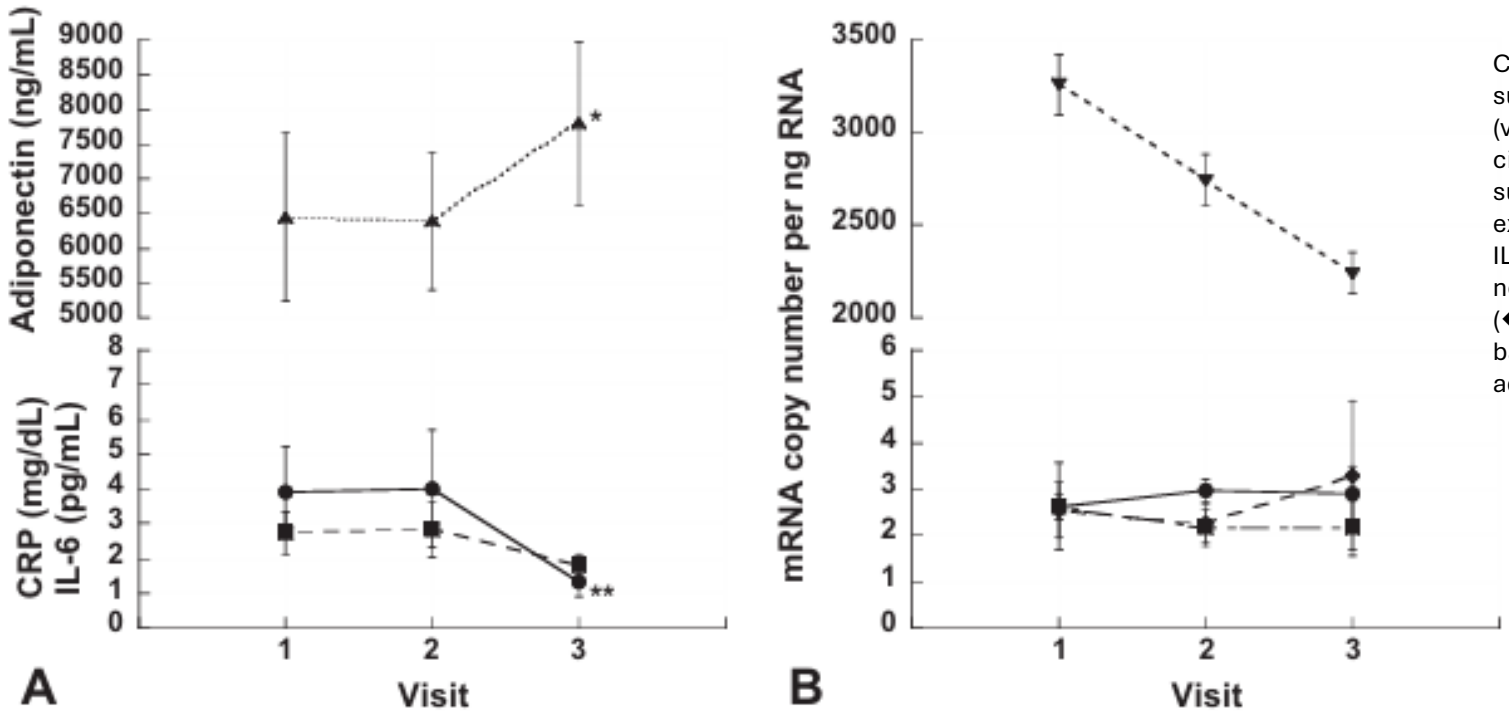
Cell Metabolism

Effects of Moderate and Subsequent Progressive Weight Loss on Metabolic Function and Adipose Tissue Biology in Humans with Obesity

Table 2. Effect of Progressive Weight Loss on Body Composition and Cardiometabolic Risk Factors

	Progressive Weight Loss (n = 9)				Effect of Time
	Baseline	5% Weight Loss	11% Weight Loss	16% Weight Loss	p Value
Weight (kg)†	103.8 ± 16.4	97.9 ± 15.7*	92.5 ± 14.4*	87.0 ± 14.9*	<0.001
BMI (kg/m^2)†	37.7 ± 4.5	35.5 ± 4.3*	33.6 ± 3.9*	31.6 ± 4.1*	<0.001
Body fat (%)†	48.3 ± 4.3	46.3 ± 4.8*	44.2 ± 4.5*	42.2 ± 5.0*	<0.001
Fat mass (kg)†	50.3 ± 10.2	45.4 ± 9.6*	41.1 ± 8.6*	36.9 ± 8.8*	<0.001
Fat-free mass (kg)†	53.0 (46.3, 55.6)	51.5 (45.7, 54.1)*	50.2 (45.2, 53.2)*	49.0 (44.1, 51.4)*	<0.001
Intra-abdominal adipose tissue (cm^3)†	1,656 ± 559	1,501 ± 469	1,277 ± 474*	1,154 ± 457*	<0.001
Intrahepatic triglyceride (%)†‡	8.5 (3.9, 25.9)	7.4 (3.0, 12.5)*	4.1 (1.1, 10.2)*	3.0 (1.1, 5.2)*	<0.001
Free fatty acids, basal (mmol/L)†	0.56 (0.55, 0.65)	0.56 (0.48, 0.64)	0.49 (0.46, 0.58)	0.47 (0.44, 0.55)*	0.050
Glucose, basal (mg/dL)	92.7 ± 8.9	89.4 ± 4.9	89.3 ± 5.7	88.6 ± 2.7	0.288
Insulin, basal (mU/L)†	18.3 ± 7.7	15.5 ± 6.1	12.6 ± 5.5*	9.5 ± 2.8*	<0.001
Triglyceride (mg/dL)†	153 ± 56	130 ± 71	110 ± 59*	97 ± 39*	0.003
HDL cholesterol (mg/dL)	43 ± 10	41 ± 7	42 ± 7	44 ± 7	0.261
LDL cholesterol (mg/dL)	115 (95, 135)	98 (91, 127)	101 (90, 136)	91 (85, 125)	0.162
Alanine transaminase (U/L)†	18.0 (11.5, 25.0)	15.0 (12.0, 16.5)	11.0 (10.0, 16.0)	11.0 (9.5, 14.5)*	0.015
Leptin (ng/mL)†	43.0 ± 13.5	32.8 ± 13.6*	27.1 ± 9.9*	18.6 ± 6.5*	<0.001
Adiponectin (μg/mL)†‡	6.23 ± 2.73	6.34 ± 2.35	6.87 ± 2.63	8.30 ± 3.51*	<0.001
C-reactive protein (mg/L)†‡	4.69 (3.44, 7.84)	4.74 (2.40, 11.24)	5.47 (2.27, 8.30)	3.14 (1.01, 4.43)*	0.019
Interleukin-6 (ng/mL)	2.0 ± 0.6	2.1 ± 0.8	2.1 ± 0.7	2.3 ± 1.0	0.826
MCP-1 (pg/mL)	136 (124, 159)	144 (127, 162)	140 (122, 153)	138 (129, 173)	0.790
WBC count (10^3/mL)	6.8 ± 1.4	7.5 ± 1.5	7.4 ± 1.8	6.8 ± 1.3	0.056

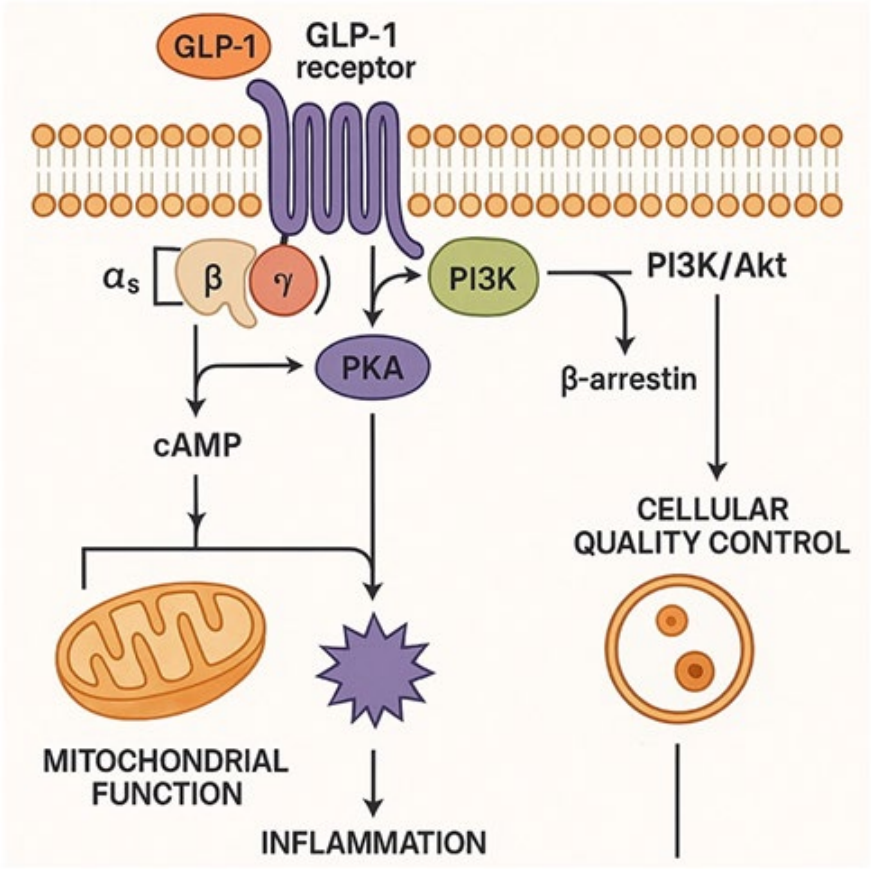
The short-term and long-term effects of bariatric/ metabolic surgery on subcutaneous adipose tissue inflammation in humans



Changesi n circulating plasma markers and mRNAexpression in subcutaneous adipose tissue from baseline (visit 1) to one (visit 2) and 12 (visit 3) months after bariatric/metabolic surgery. (A) No change in circulating CRP (●), IL-6 (■), and adiponectin (▲) within the first month of surgery. By 12 months,relative to baseline levels, circulating adiponectin exhibited a marked increase (*p = 0.003), while CRP (**p = 0.002) but not IL-6 (p = 0.183) concentrations were significantly reduced. (B) There were no significant changes in mRNA expression patterns for TNFα (●), IL-1β (◆), IL-6 (■) and adiponectin (▼)in subcutaneous adipose tissue from baseline out to 12 months post-surgery, except for a downward trend in adiponectin expression (p = 0.069).

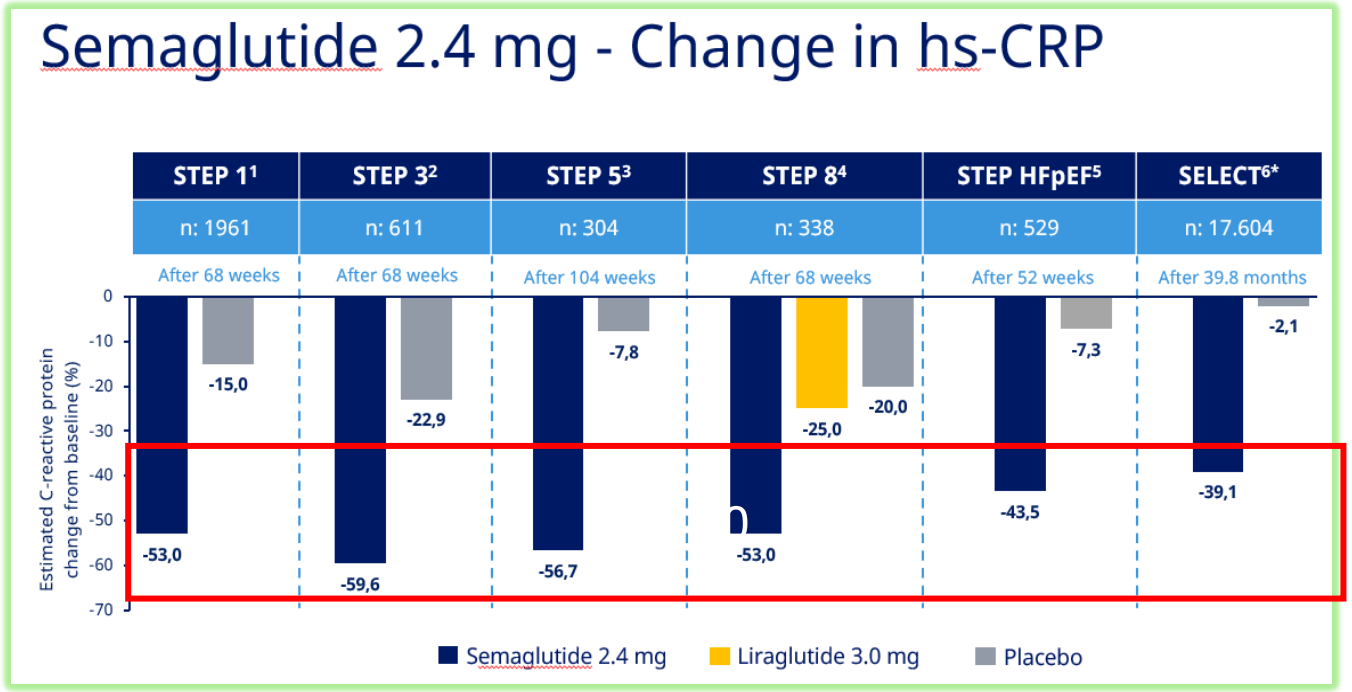
Metabolism 70: 12– 22, 2017.

Emerging Frontiers in GLP-1 Therapeutics:



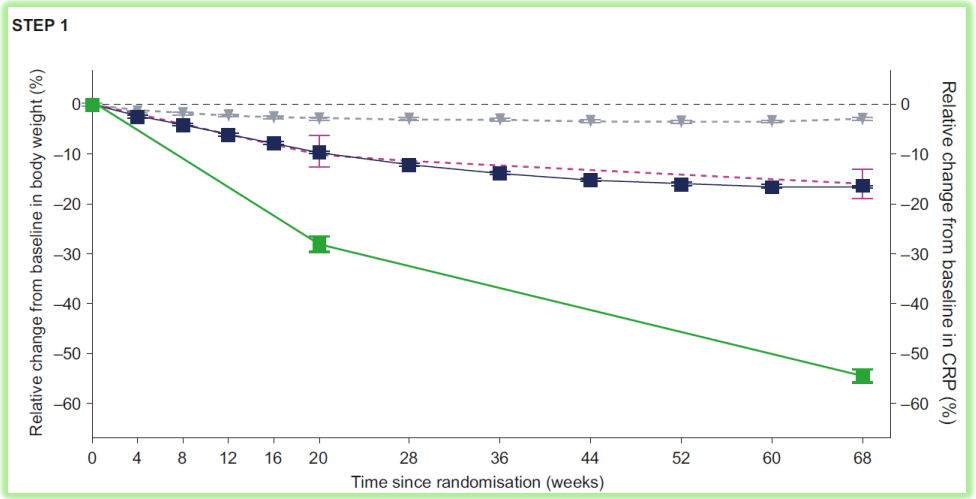
- GLP-1 receptor activation potently inhibits nuclear factor kappa B **(NF-κB),** the master transcriptional regulator of inflammation.
- The **inflammasome**, particularly the NLRP3 complex, represents another critical target. GLP-1 RAs suppress NLRP3 inflammasome activation through multiple mechanisms: inhibition of priming signals via reduced NF-κB activity, attenuation of reactive oxygen species generation through enhanced mitochondrial function, induction of autophagy that removes damaged mitochondria serving as inflammasome triggers, and direct interference with NLRP3-ASC interaction through PKA-mediated phosphorylation .
- Direct immunomodulatory effects occur through GLP-1 receptors expressed on mul tiple immune cell populations. In **macrophages**, GLP-1 signaling promotes polarization from the pro-inflammatory M1 to the anti-inflammatory M2 phenotype through STAT6 activation and metabolic reprogramming .

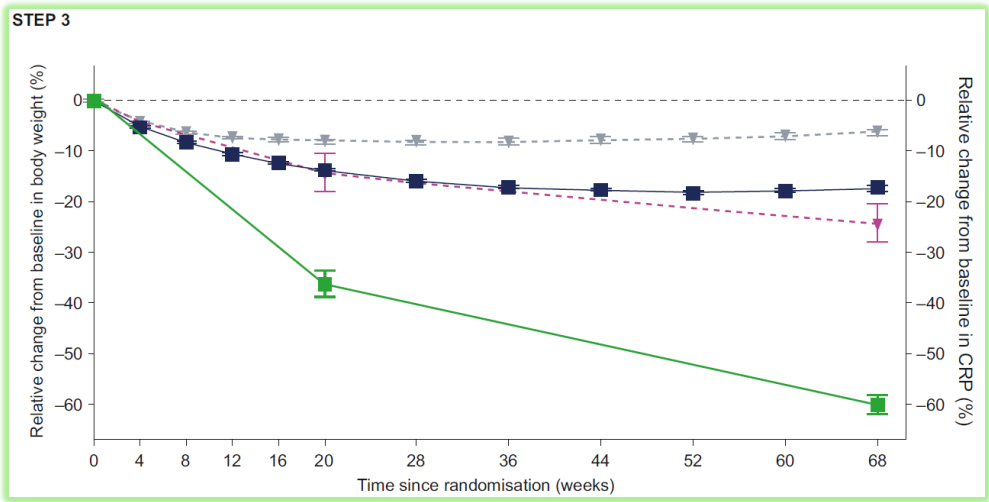
Anti-inflammatory effects of semaglutide 2.4 mg



*Estimated change from baseline for treatment policy estimand. *Relative changes from baseline (log-transformed before analysis) to week 104, estimated using ANCOVA with treatment as factor and the baseline value as covariate. CIs have not been adjusted for multiplicity.*
ANCOVA, analysis of covariance; hsCRP, high-sensitivity C-reactive protein.

Adapted from 1. Wilding et al. N Engl J Med 2021; doi:10.1056/NEJMoa2032183; 2. Wadden et al. JAMA. doi:10.1001/jama.2021.1831; 3. Garvey et al. Nat Med 28, 2083–2091 (2022); 4. Rubino et al. JAMA 2022; 327(2): 138-150; 5. Kosiborod MN, et al. N Engl J Med. 2023;389(12):1069-1084. 6. Lincoff AM, et al. N Engl J Med. 2023;389(24):2221-2232.





Semaglutide 2.4 mg - Body weight, relative change from baseline (%)
Semaglutide 2.4 mg - CRP, relative change from baseline (%)
Placebo - Body weight, relative change from baseline (%)
Placebo - CRP, relative change from baseline (%)

Adapted from Verma S, et al. EClinicalMedicine. 2022 Nov 29;55:101737.

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

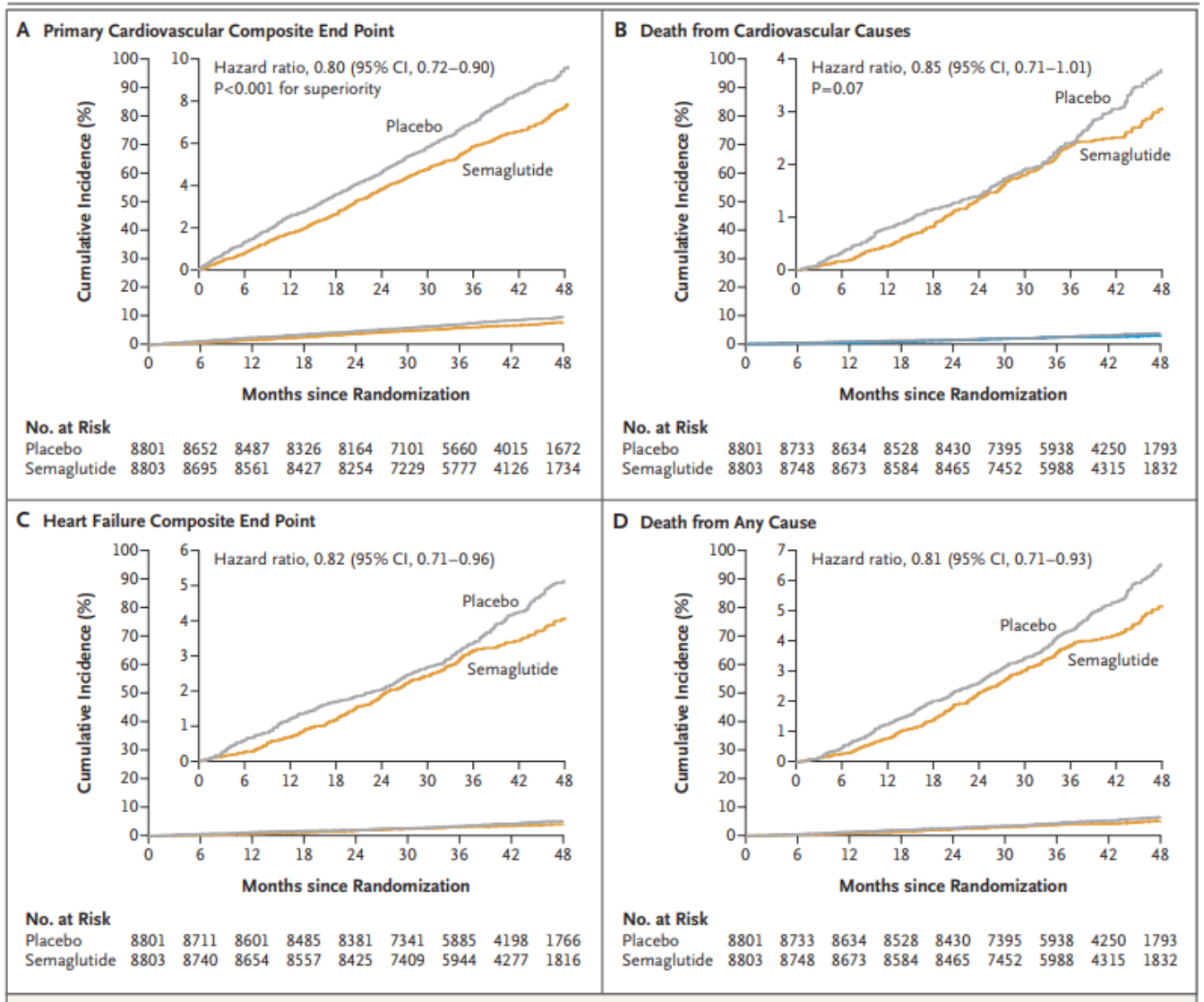


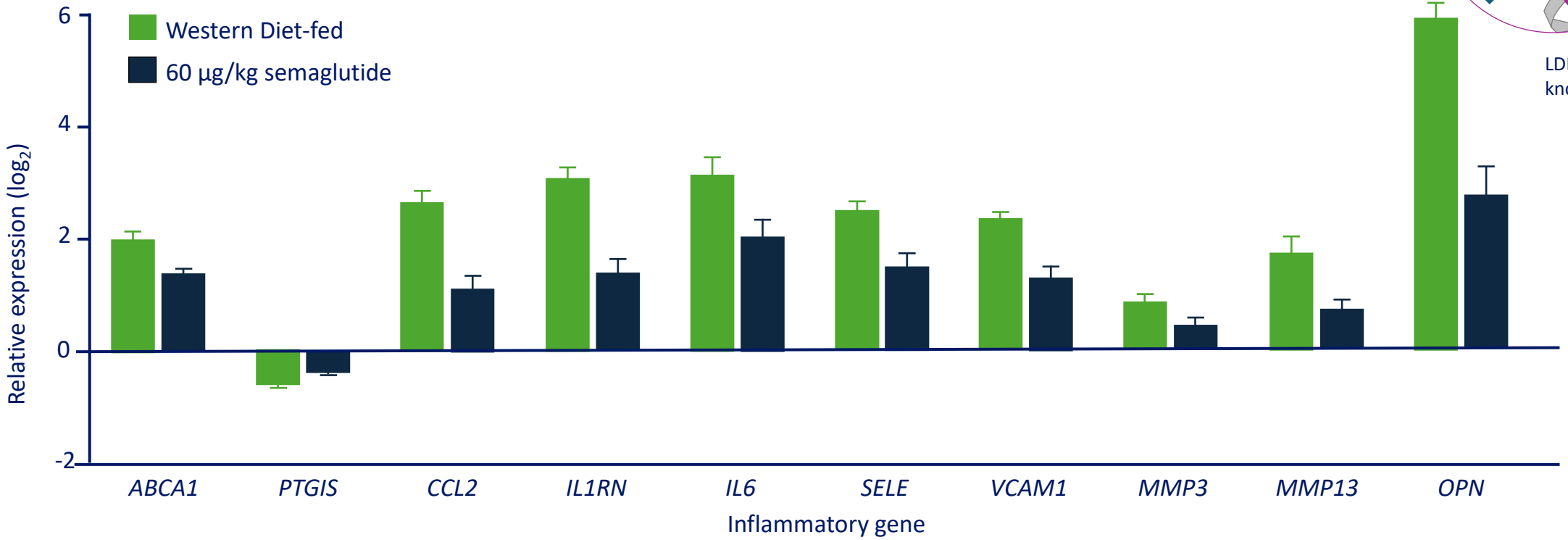
Figure 1. Time-to-First-Event Analysis for Primary and Confirmatory Secondary Efficacy End Points.

N Engl J Med. 2023 Dec 14;389(24

Semaglutide downregulates expression of inflammatory genes

Expression of inflammatory genes is lower in mice treated with semaglutide

LDL receptor knockout mice

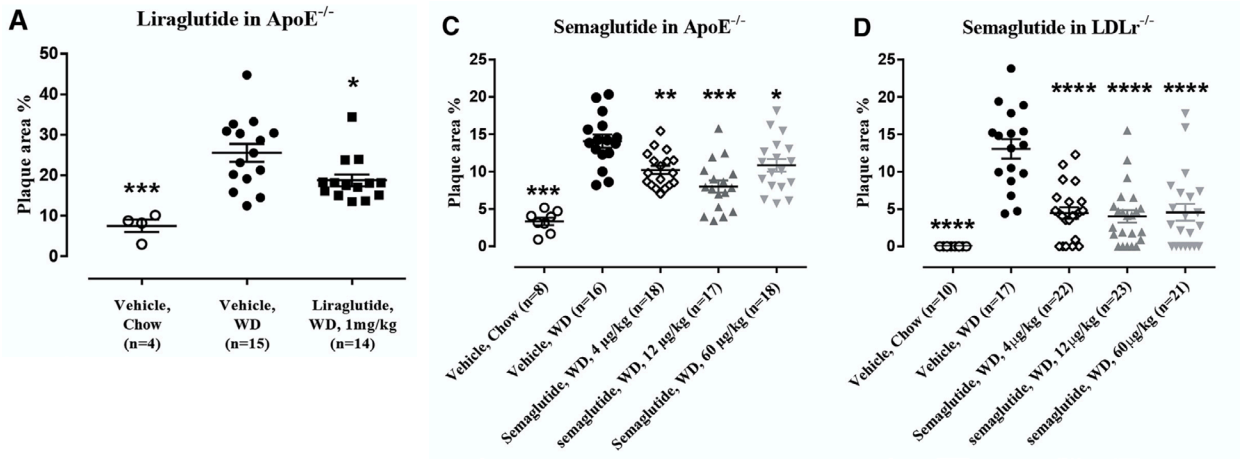


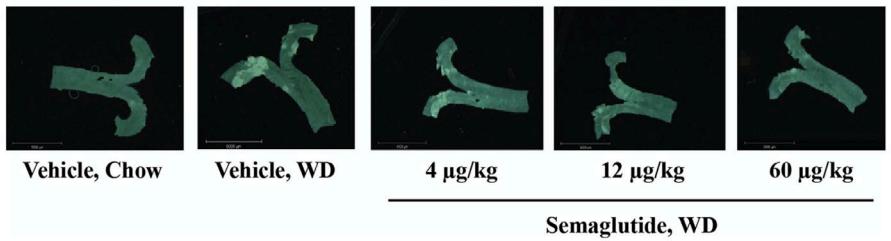
ABCA1, ATP-binding cassette transporter; CCL2, chemokine ligand 2; IL1RN, interleukin-1 receptor antagonist; IL6, interleukin-6; LDL, low density lipoprotein; MMP, matrix metalloproteinase; OPN, osteopontin; PTGIS, prostaglandin I2 synthase; SELE, selectin E; VCAM, vascular cell adhesion molecule.

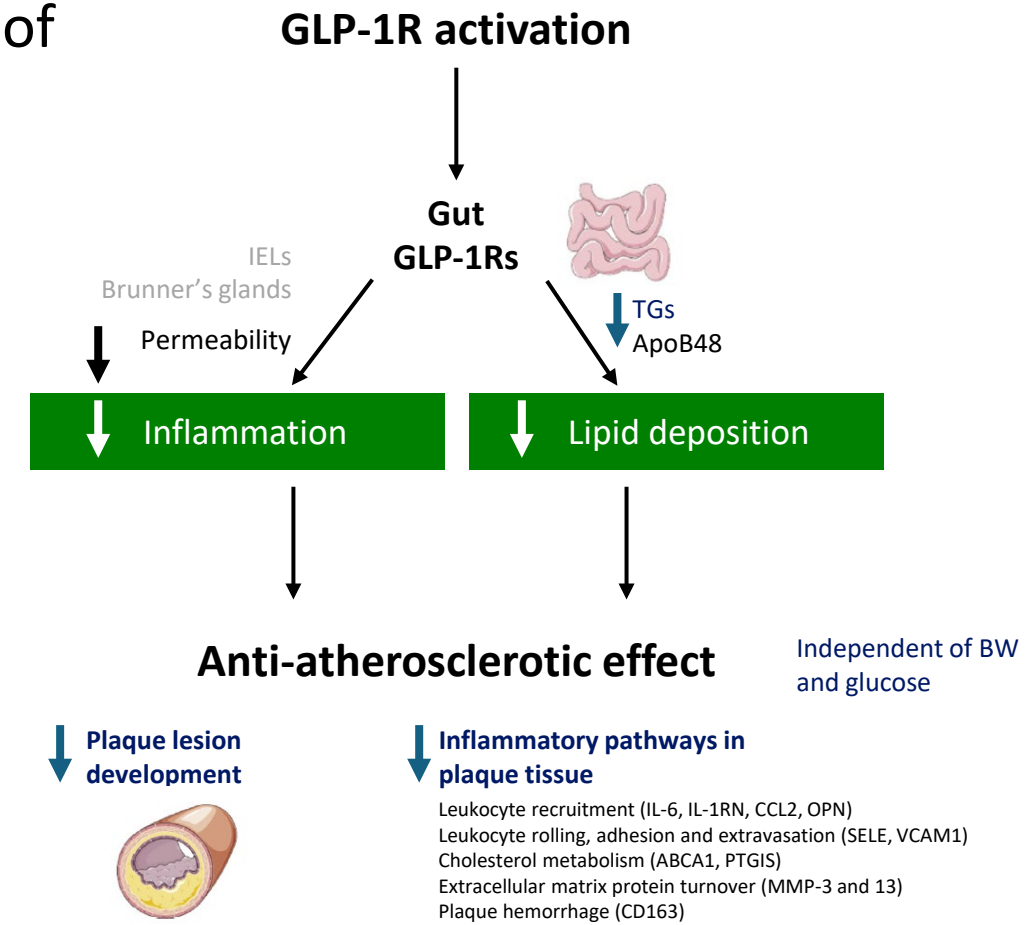
Rakipovski et al. JACC Basic Transl Sci 2018;3:844–57.

Semaglutide has anti-atherosclerotic effects

Attenuation of plaque lesion area in mouse models of atherosclerosis is independent of dose

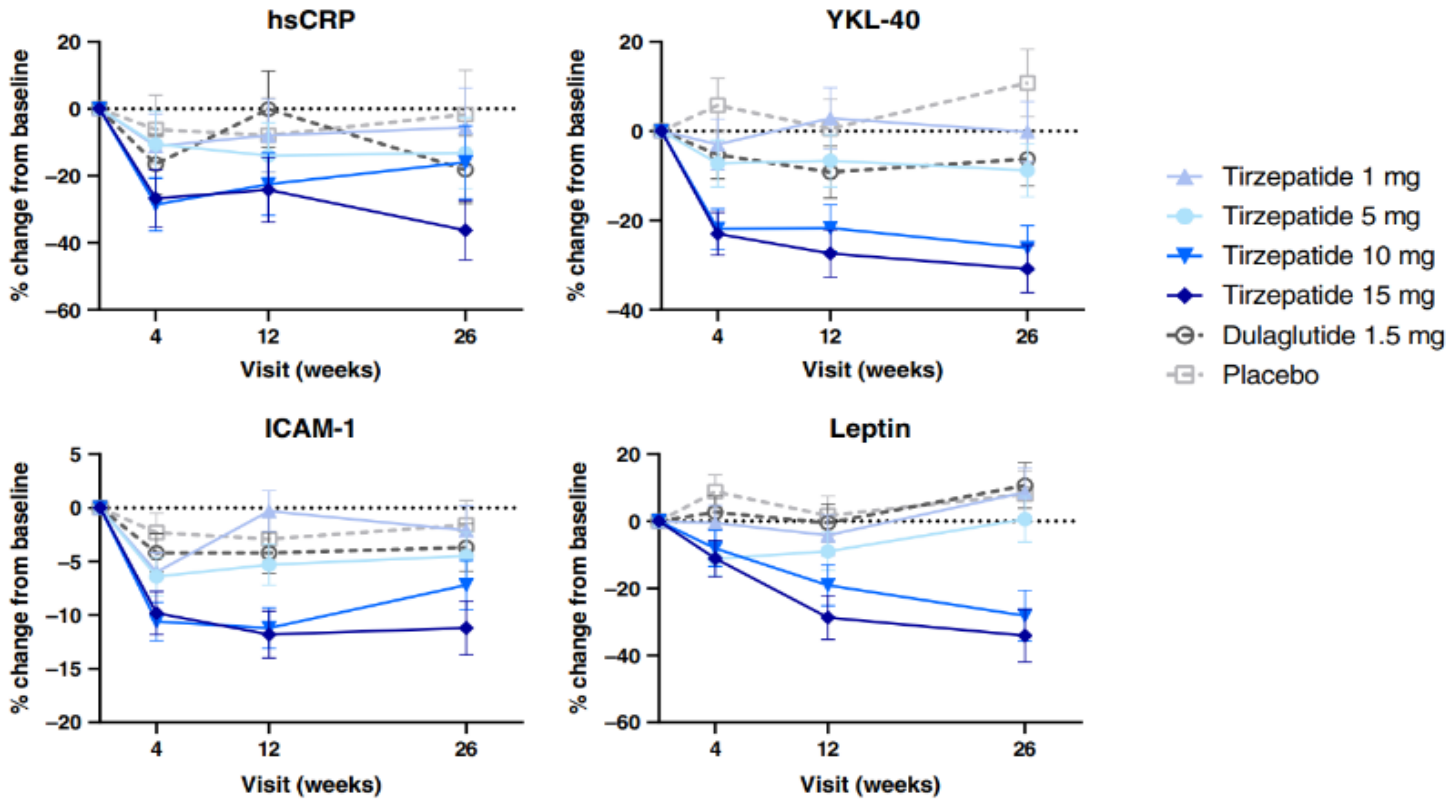






JACC Basic Trans Science. 2018;3(6):844–57.

Tirzepatide decreased several biomarkers that have been associated with cardiovascular risk



*P<.05 vs. baseline; #P<.05 vs. placebo; †P<.05 vs. Dulaglutide. **P<.001 vs. baseline; ##P<.001 vs. placebo; ††P<.001 vs. Dulaglutide.
CV=Cardiovascular; DU=Dulaglutide; hsCRP=High-Sensitivity C-Reactive Protein; ICAM-1=Intercellular Adhesion Molecule-1; TZP=Tirzepatide; YKL-40=Chitinase-3 Like-Protein-1

Wilson JM, et al. *Diabetes Obes Metab*. 2022;24(1):148-153.


THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity

Milton Packer, M.D., Michael R. Zile, M.D., Christopher M. Kramer, M.D., Seth J. Baum, M.D., Sheldon E. Litwin, M.D., Venu Menon, M.D., Junbo Ge, M.D., Govinda J. Weerakkody, Ph.D., Yang Ou, Ph.D., Mathijs C. Bunck, M.D., Karla C. Hurt, B.S.N., Masahiro Murakami, M.D., and Barry A. Borlaug, M.D., for the SUMMIT Trial Study Group*

SUMMIT: efficacy on co-primary and secondary endpoint

6-Minute Walk Distance (α protected)

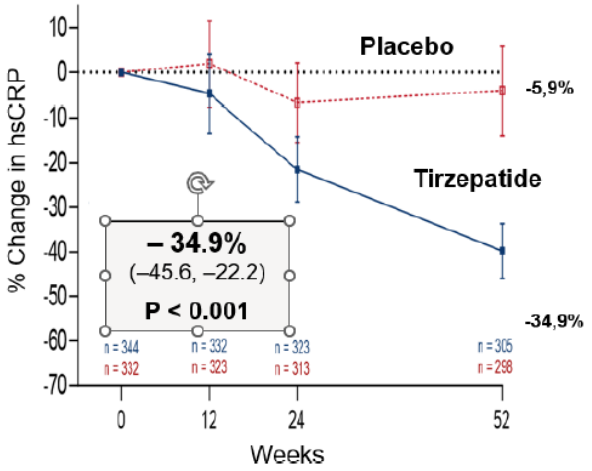
+ 26 m in TZP group
+ 10 m in placebo group

+ 18.3 meters (9.9, 26.7)

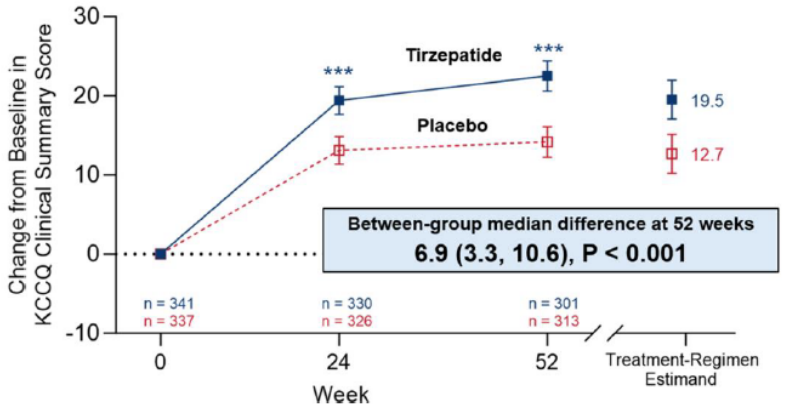
at 52 weeks BGD

P < 0.001

HS C-Reactive Protein (α Protected)



Health Status (KCCQ-CSS) (α =0.01)



Packer et al. *NEJM* 2024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Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity

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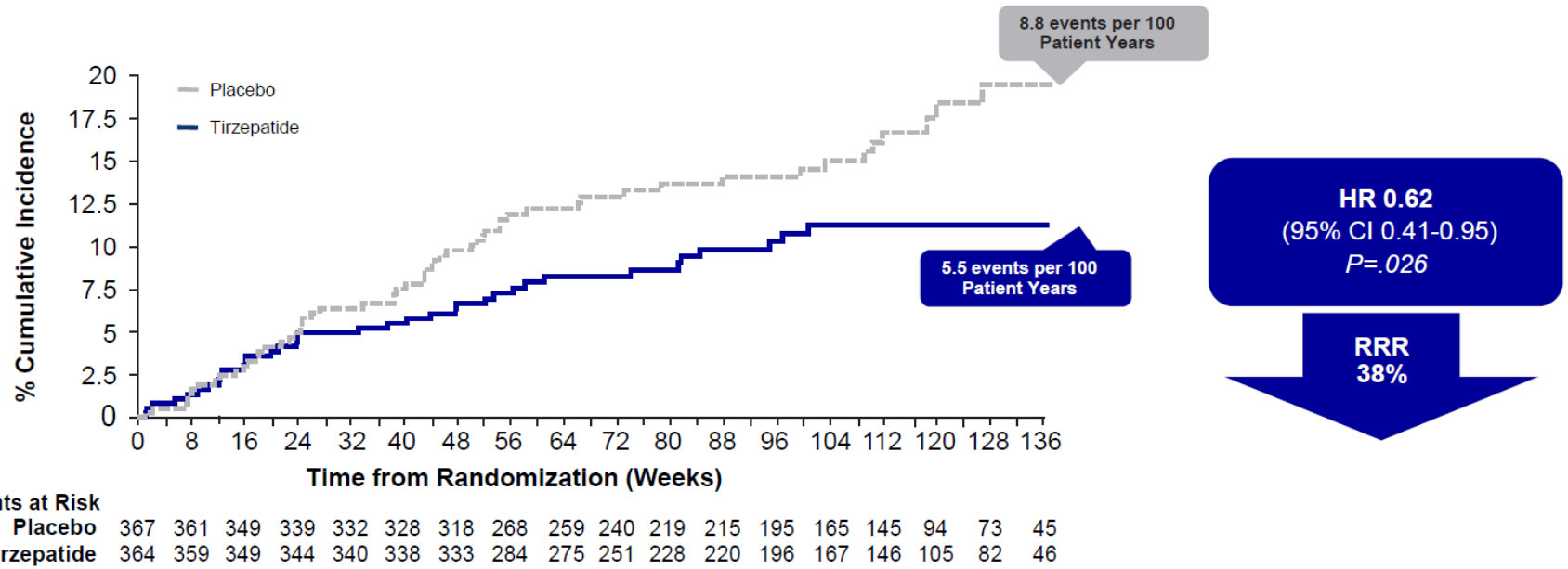
SUMMIT Study: Primary Endpoint: Time to First Event for CV Death or Worsening HF Event[a]

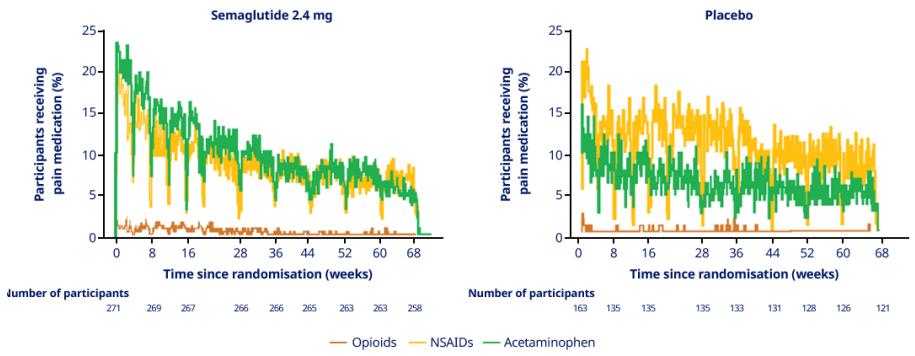


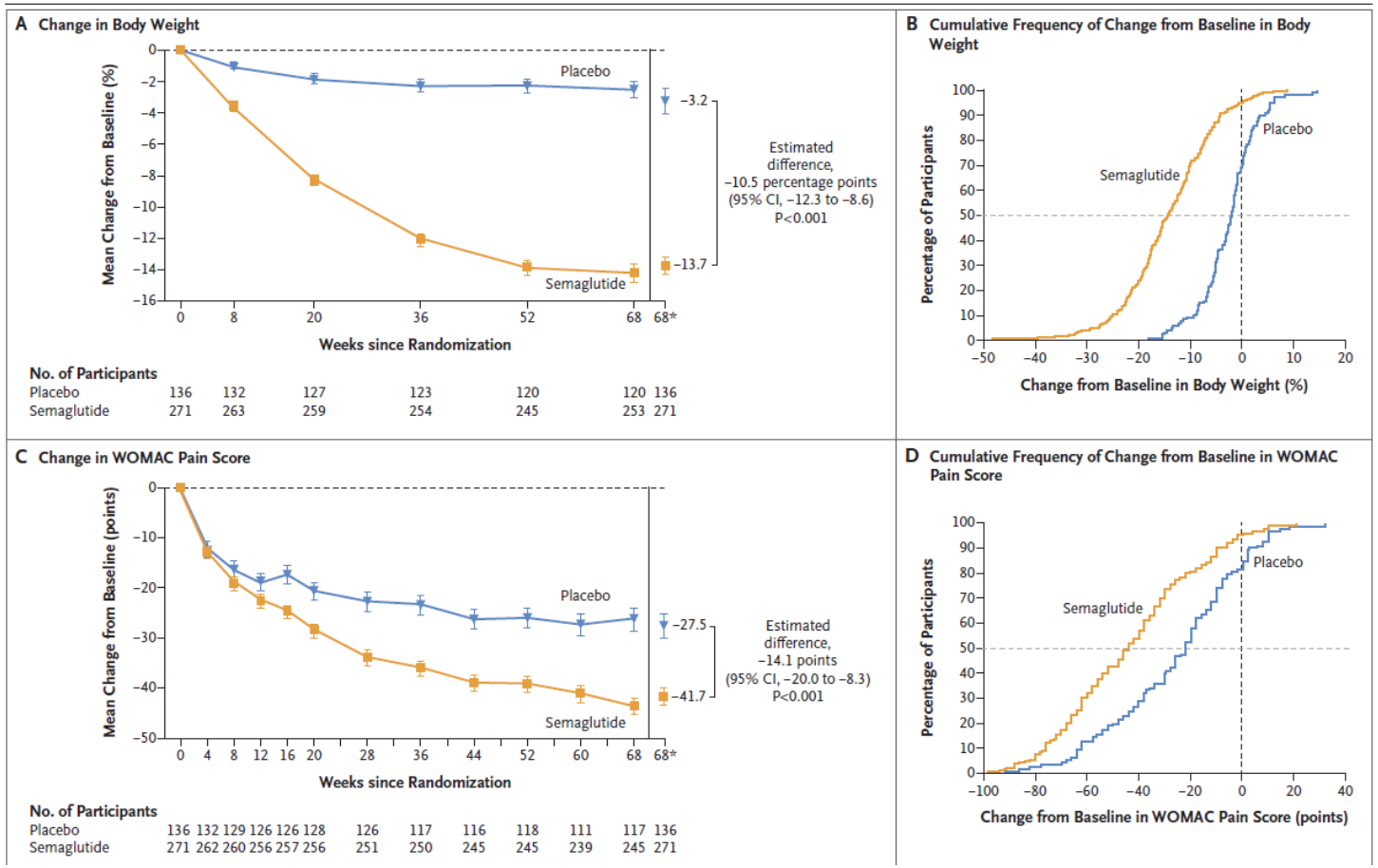
Participants at Risk																		
Placebo	367	361	349	339	332	328	318	268	259	240	219	215	195	165	145	94	73	45
Tirzepatide	364	359	349	344	340	338	333	284	275	251	228	220	196	167	146	105	82	46

[a]Worsening HF event was defined as heart failure symptoms requiring hospitalization, intravenous drugs for HF in an urgent care setting or intensification of oral diuretics. Changes in oral diuretics without worsening HF was not designated as an event.
CI=Confidence Interval; CV=Cardiovascular; HF=Heart Failure; HR=Hazard Ratio; RRR=Relative Risk Reduction.
Packer M, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2410027 (Ahead of print).

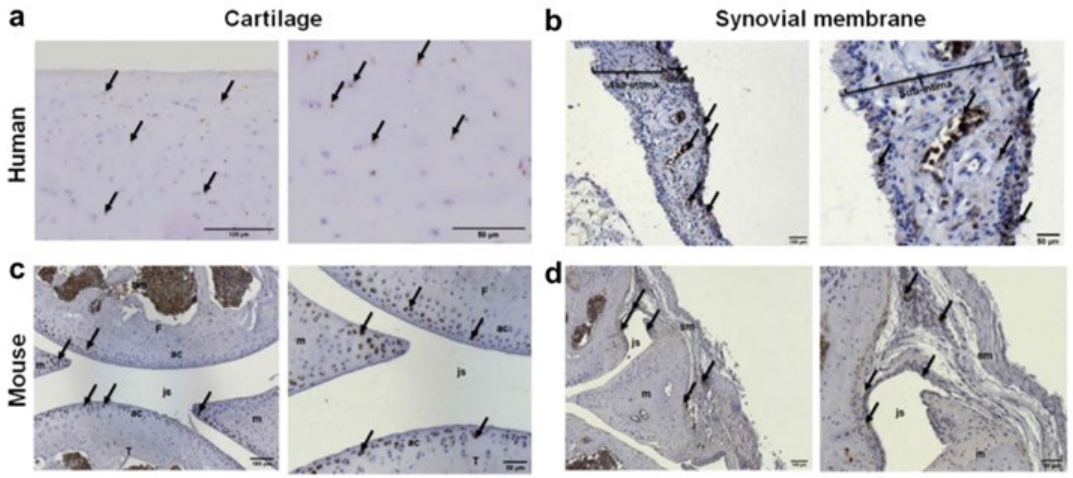
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 OCTOBER 31, 2024 VOL. 391 NO. 17

Once-Weekly Semaglutide in Persons with Obesity and Knee Osteoarthritis

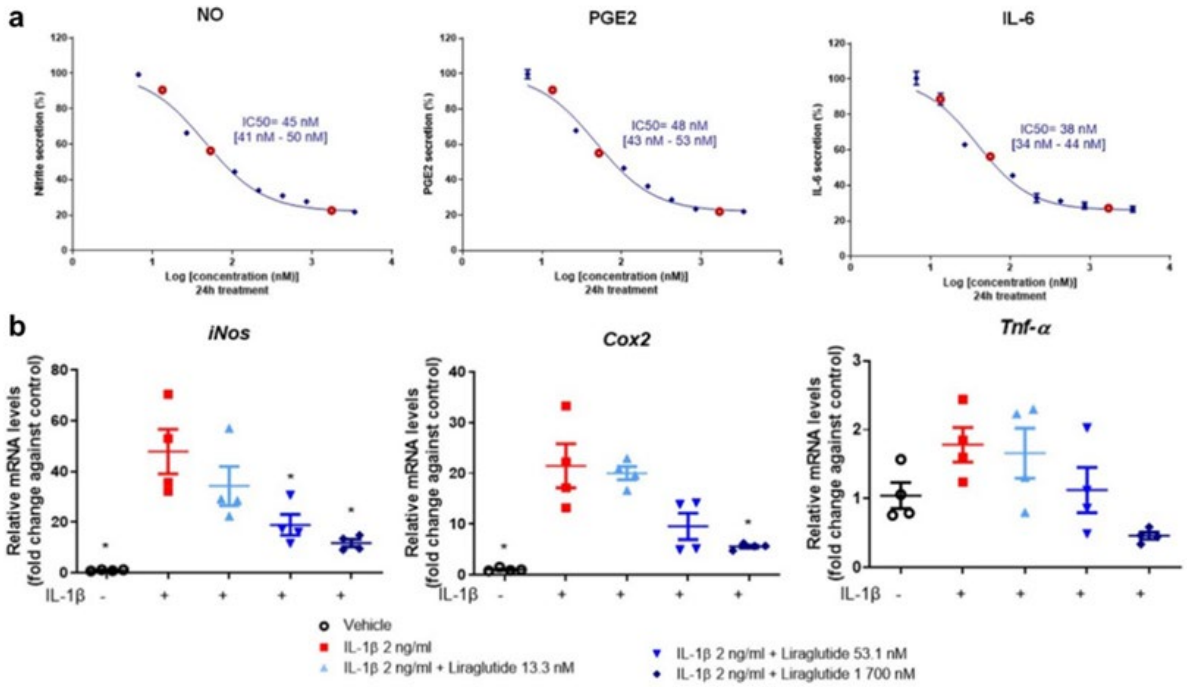




Liraglutide, a glucagon-like peptide 1 receptor agonist, exerts analgesic, anti-inflammatory and anti-degradative actions in osteoarthritis



Expression of GLP-1 receptor in OA human and non-OA mouse knee joint

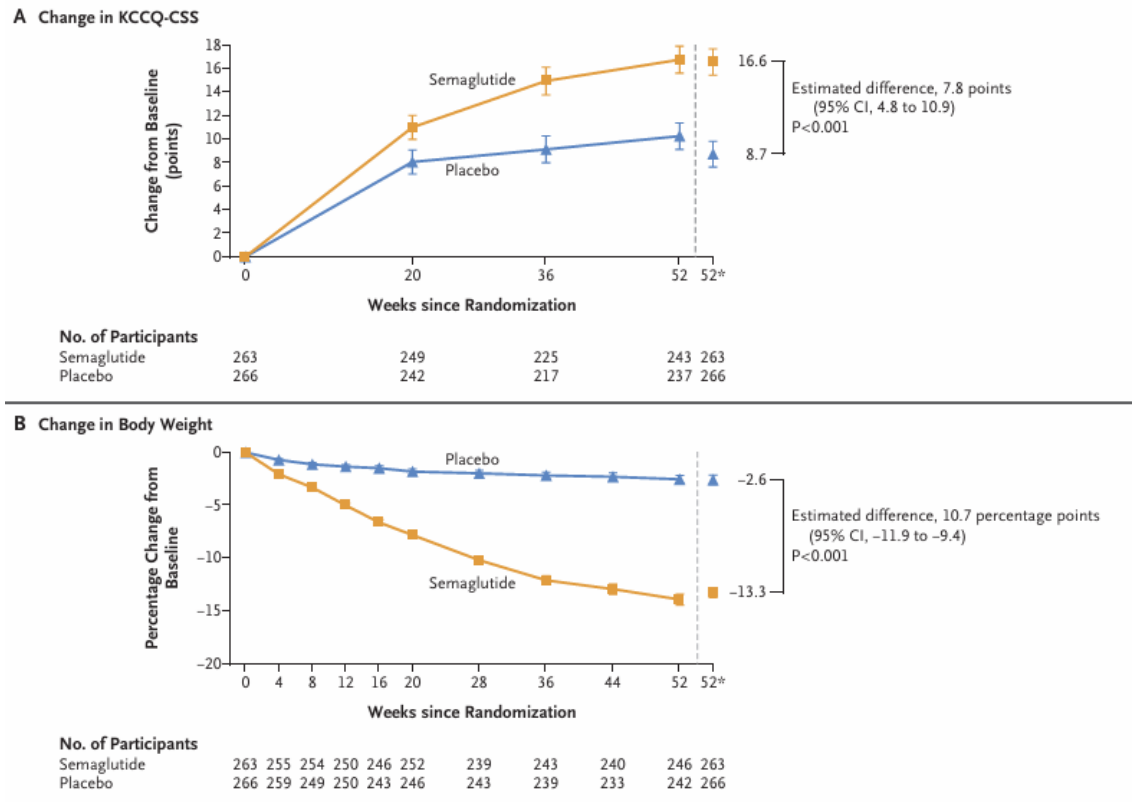


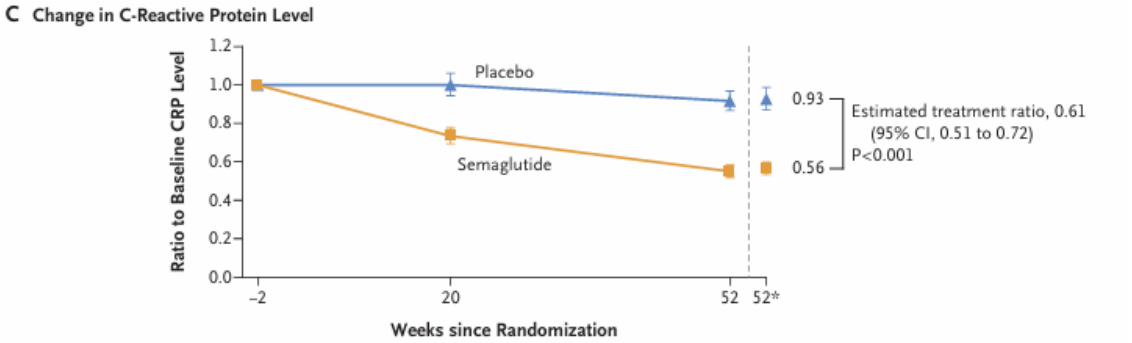
Anti-inflammatory effects of liraglutide in murine primary chondrocytes.

Sci Rep 2022; 12: 1567.

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 SEPTEMBER 21, 2023 VOL. 389 NO. 12

Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity



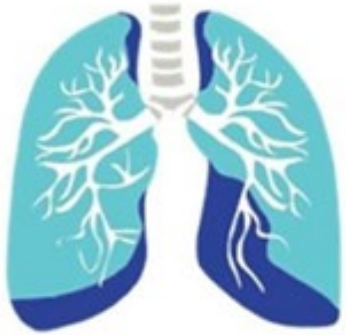


Visual abstract

The relationship between the use of GLP-1 receptor agonists and the incidence of respiratory illness: a meta-analysis of randomized controlled trials

Background :

GLP-1RAs are novel anti-hyperglycemic agents commonly used. In addition to cardiovascular benefits, emerging evidence suggests that such drugs may also be associated with respiratory benefits. Currently, the relationship between GLP-1RAs and respiratory diseases is unclear.



Study design Meta-analysis

Data sources 28studies 77,485 participants

Conclusion

In conclusion, using GLP-1RAs was linked to a lower risk of overall respiratory diseases, especially Pulmonary edema and Bronchitis.

A comprehensive meta-analysis of 28 randomized controlled trials involving 77,485 participants demonstrated that GLP-1 RAs were associated with a 14% lower risk of respiratory disease

Condition	Effect	Risk Reduction	Population
General Respiratory Disease	Overall protection	14% (RR 0.86)	77,485 participants
COPD Exacerbations	Reduced exacerbations	18% (HR 0.82)	T2DM + COPD patients
Asthma Exacerbations	Fewer exacerbations	Significant reduction	T2DM + asthma patients
Pneumonia	Prevention	28% (HR 0.72)	COPD patients

A comprehensive meta-analysis of 28 randomized controlled trials involving 77,485 participants demonstrated that GLP-1 RAs were associated with a 14% lower risk of respiratory disease

Condition	Agent	Study	Primary Finding	Status
Alzheimer's Disease	Liraglutide	ELAD	50% less brain volume loss	Completed
Parkinson's Disease	Oral Semaglutide	EVOKE/EVOKE+	CDR-Sum of Boxes	Ongoing
	Exenatide	EXENATIDE-PD3	No disease modification	Completed
	Lixisenatide	LixiPark	Slower motor progression	Completed
	Semaglutide	Oslo University	Motor symptoms	Ongoing

A comprehensive meta-analysis of 28 randomized controlled trials involving 77,485 participants demonstrated that GLP-1 RAs were associated with a 14% lower risk of respiratory disease

Pharmaceutics 2025, 17, 1036

‘Ozempic babies’: Reports of surprise pregnancies raise new questions about weight loss drugs

By Mira Cheng and Meg Tirrell, CNN
9 minute read · Updated 2:00 PM EDT, Wed May 8, 2024

Catera Bentley and her husband tried for more than two years to have a child. She became pregnant after taking Mounjaro. Catera Bentley

‘Ozempic babies’

Bentley is far from alone. Numerous women have shared stories of “Ozempic babies” on social media. But the joy some experience in discovering pregnancies may come with anxiety about the unknowns, as these medicines haven’t been studied in people who are pregnant.

“We don’t know the effect of early exposure ... on the fetus,” said Dr. Jody Dushay, a physician focused on endocrinology and metabolism at Beth Israel Deaconess Medical Center and an assistant professor at Harvard Medical School.

Dushay said she recommends that women stop taking these drugs two months before trying to get pregnant, as directed in their prescribing information.

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Cite this as: *BMJ* 2025;388:q2440
http://doi.org/10.1136/bmj.q2440
Published: 29 January 2025

FACT CHECK

Ozempic babies: are weight loss drugs leading to unintended pregnancies?

Posts about unexpected pregnancies while using drugs such as Ozempic for weight loss are trend on social media. Does any scientific evidence back this up? **Sangeetha Nadarajah** reports

Amid the rising popularity of glucagon-like peptide-1 (GLP-1) receptor agonists for weight loss such as semaglutide (Ozempic/Wegovy) and tirzepatide (Mounjaro/Zepbound), anecdotal reports of unintended pregnancies, even in people using oral birth control or with existing fertility challenges, have begun trending on social media. But despite the media attention and the popularity of the hashtag #ozempicbabies, experts have told *The BMJ* that these cases may be less common than portrayed.

Mechanisms and warnings

Mounjaro's manufacturer, Eli Lilly, advises patients using oral hormonal contraceptives to switch to a non-oral contraceptive or to add a barrier method of contraception for four weeks after initiating Mounjaro and for four weeks after each dose escalation. This is due to the potential reduction in absorption of oral contraceptives caused by delayed gastric emptying.[2] Ozempic/Wegovy also carries a warning that all oral medicines may be absorbed less effectively because of delayed gastric emptying.

Non-oral contraceptive methods, such as intrauterine devices, implants, patches, and vaginal rings, are unaffected by GLP-1 receptor agonists, since they're not absorbed in the gastrointestinal tract. Healthcare providers are advised to recommend back-up contraception such as condoms to avoid unintended pregnancies, as well as offering preconception counselling for women starting GLP-1 receptor agonists.

The drug companies Novo Nordisk (which makes Ozempic/Wegovy) and Eli Lilly, along with regulatory agencies including the US Food and Drug Administration and the European Medicines Agency, have issued guidelines on GLP-1 receptor agonists and pregnancy. Both Novo Nordisk and Eli Lilly recommend discontinuing these medicines (Ozempic/Wegovy; Mounjaro) at least two months before attempting to conceive. These recommendations were formalised in 2022 for Ozempic/Wegovy and in 2023 for Mounjaro. In 2022 the European Medicines Agency advised women to stop taking GLP-1 drugs at least two months before conception. The US Food and Drug Administration echoed these concerns in 2023, citing limited human data on pregnancy outcomes.

Sharma says, "I have not had patients conceive spontaneously while taking GLP-1 agonists, and currently the available data on humans is limited. However, animal data showed some increased risks of fetal malformations and obstetric complications, hence the warning to be off these medications when trying to conceive or when pregnant."

IL
PESO DELLA GLICEMIA

DIABETE E OBESITÀ TRA RISCHIO
CARDIO-RENALE, EPATICO E NEUROLOGICO

DIABETE E OBESITÀ TRA RISCHIO
CARDIO-RENALE, EPATICO E NEUROLOGICO

Sesto San Giovanni (MI)
IRCCS MultiMedica

SID
Società Italiana
di Diabetologia

Grazie per l'attenzione!

Paola S. A. Morpurgo

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