UNIVERSITÀ DI PARMA

LiPOVEXA

Nuove strategie per le malattie metaboliche

Istituto Nazionale Biostrutture Biosistemi
XV Convegno Nazionale
10-11 Luglio 2025

Istituto Nazionale Biostrutture Biosistemi
I.N.B.B.
Consorzio Interuniversitario

ABOUT US

At Lipovexa, we are committed to advancing health through clinically validated **therapeutical** and nutraceutical solutions for diabetes management, obesity control, and liver health maintenance, supporting physiological and metabolic well-being.

Our science-driven approach focuses on developing innovative interventions rooted in clinical research, ensuring both efficacy and safety.

By harnessing the power of natural bioactive compounds, we create nutraceuticals and synthetic drugs designed to optimize metabolic processes and promote long-term health benefits.

UNMET NEED

Metabolic disorders like obesity, type 2 diabetes (T2D), and Metabolic dysfunction-associated fatty liver disease (MAFLD) are escalating into a global health crisis, with existing treatments often falling short of providing sustainable, long-term solutions.
Current therapies primarily focus on managing symptoms rather than correcting the underlying metabolic and hormonal imbalances driving these conditions.

There is a critical need for innovative, accessible, and non-invasive solutions that go beyond symptom control to target root causes, enabling early diagnosis and effective intervention.

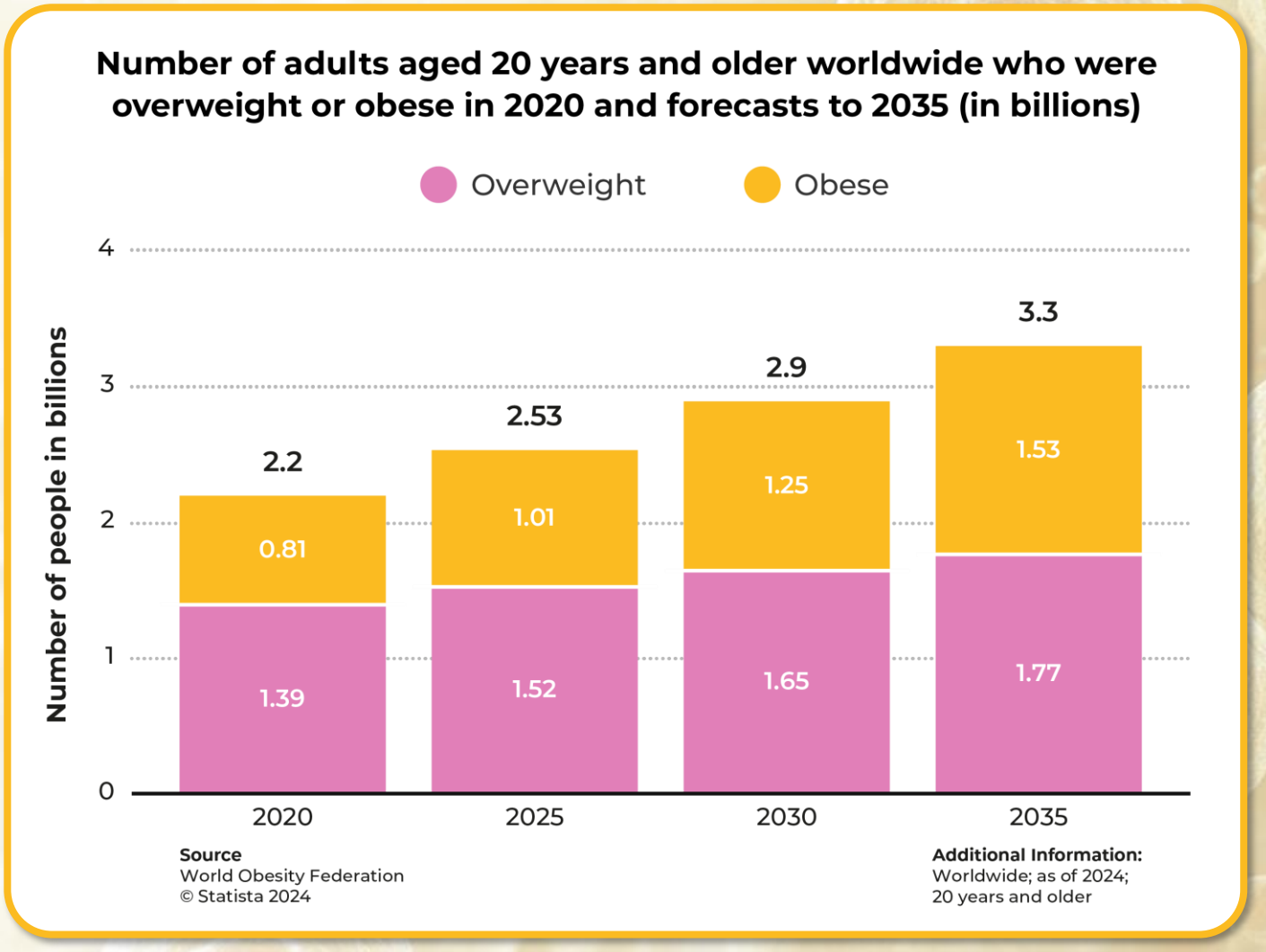
Addressing comorbidities through personalized and sustainable approaches, while enhancing public awareness and preventive healthcare, is essential for a comprehensive, long-term impact on metabolic health.

UNMET NEED – OVERWEIGHT AND OBESITY

In 2020, the total number of overweight and obese individuals was 2.2 billion. This number is projected to reach 2.53 billion in 2025, 2.9 billion in 2030, and 3.3 billion by 2035.

Obesity levels are expected to see a significant increase, from 0.81 billion in 2020 to 1.53 billion in 2035, while the overweight population will grow from 1.39 billion to 1.77 billion in the same period.

These projections underline the urgent need for effective prevention strategies, lifestyle modifications, and healthcare innovations to address the growing obesity epidemic and its associated



MARKET AND COMPETITORS

PHARMACEUTICALS

Need for safer treatments

Drug name	MOA	Side effects (selected)
Orlistat (XENICAL)	Prevents fat absorption	Fecal incontinence
Lorcaserin (BELVIQ)	Appetite suppressant	Carcinogenic, euphoria, hypoglycemia
Phentermine/Topiramate (QSYMIA)	Stimulant/Appetite suppressant	Paraesthesia, increased heart rate, dry mouth, constipation
Bupropion/Naltrexone (CONTRAVE)	Food cravings suppressant	Increased suicide risk, Insomnia, Dizziness
Liraglutide (SAXENDA)	GLP-1R Agonist	Pancreatitis, Nausea, Hypoglycemia

MARKET AND COMPETITORS

THERAPEUTICS

GLP-1 Analogue	Homology with Native GLP-1	Product name	Originator	App. Body Weight-loss
Exenatide	53%	Byetta/ Bydureon	AstraZeneca	3.5 – 5%
Liraglutide	97%	Victoza/ Saxenda	Novo Nordisk	5 – 8%
Dulaglutide	90%	Trulicity	Eli Lilly	2 – 3%
Semaglutide	94%	Ozempic/ Wegovy	Novo Nordisk	10 – 15%

- **Injectables** – Patient discomfort and compliance issues
- **Supraphysiological Concentrations (>10-15 fold)** – GI distress, nausea, vomiting, pancreatitis, depression, gallstones
- **Higher dose regimen when used as anti-obesity vs anti-diabetic** – Dose escalation, high rated occurrence of side effects
- **Economical burden**
- **No oral therapy available** to enhance endogenous GLP-1 production

MARKET AND COMPETITORS

NUTRACEUTICALS

Need for safer treatments

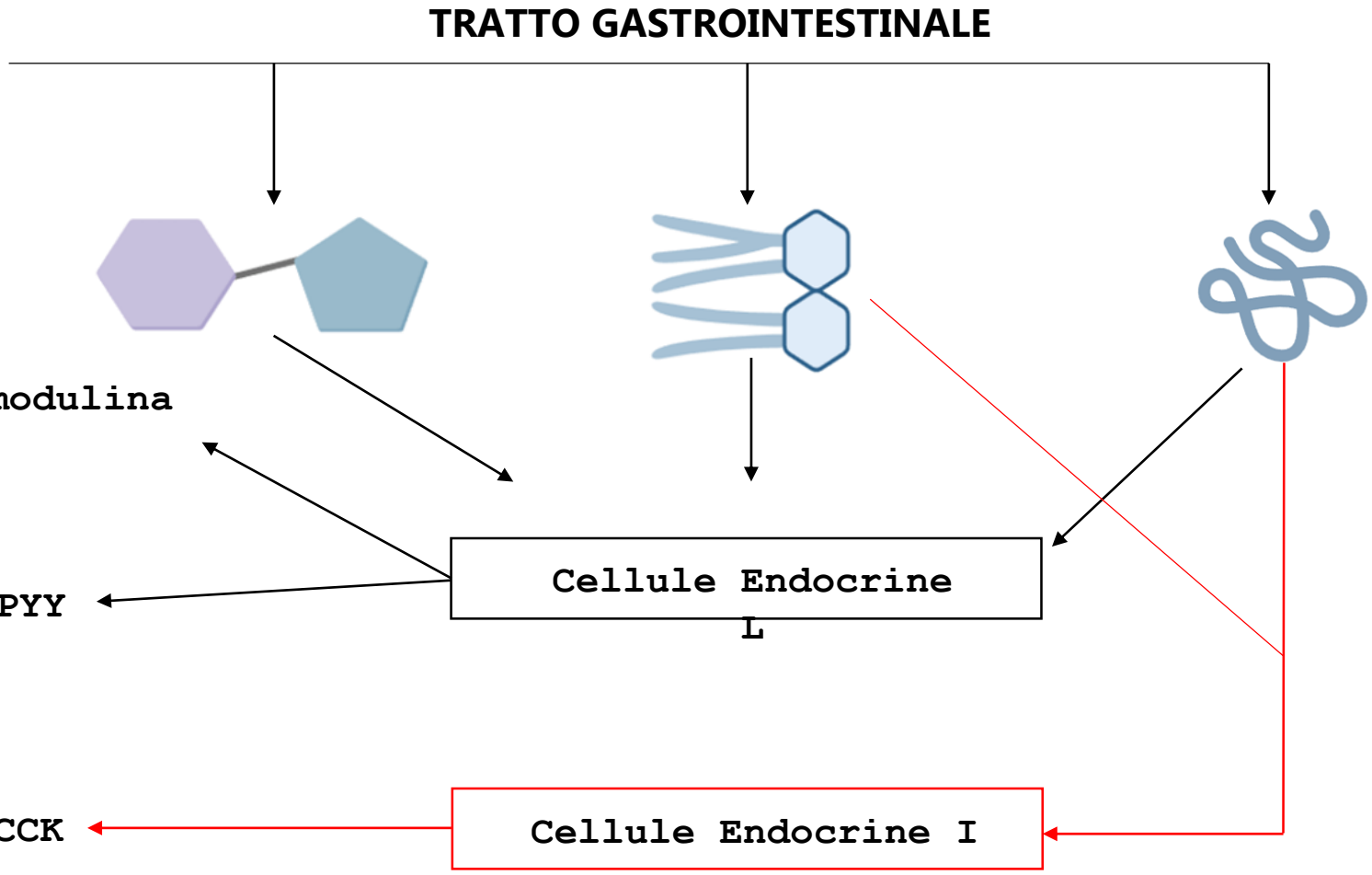
Drug name	MOA	Side effects (selected)
XLS Medical Pro	Reduced fat and carbohydrate absorption	Mild gastrointestinal disorders
Libramed	Reduced fat and carbohydrate absorption	Transient gastrointestinal disorders
Kilocal	Action on glucose metabolism, fluid drainage and intestinal motility	Intestinal disorders
Adiprox Advanced	Supporting basal metabolism and thermogenesis	Possible nervous system stimulation
Akkermansia Gestione Peso	Regulation of lipid metabolism & Gut Health	Mild gastrointestinal disorders

OUR SOLUTIONS

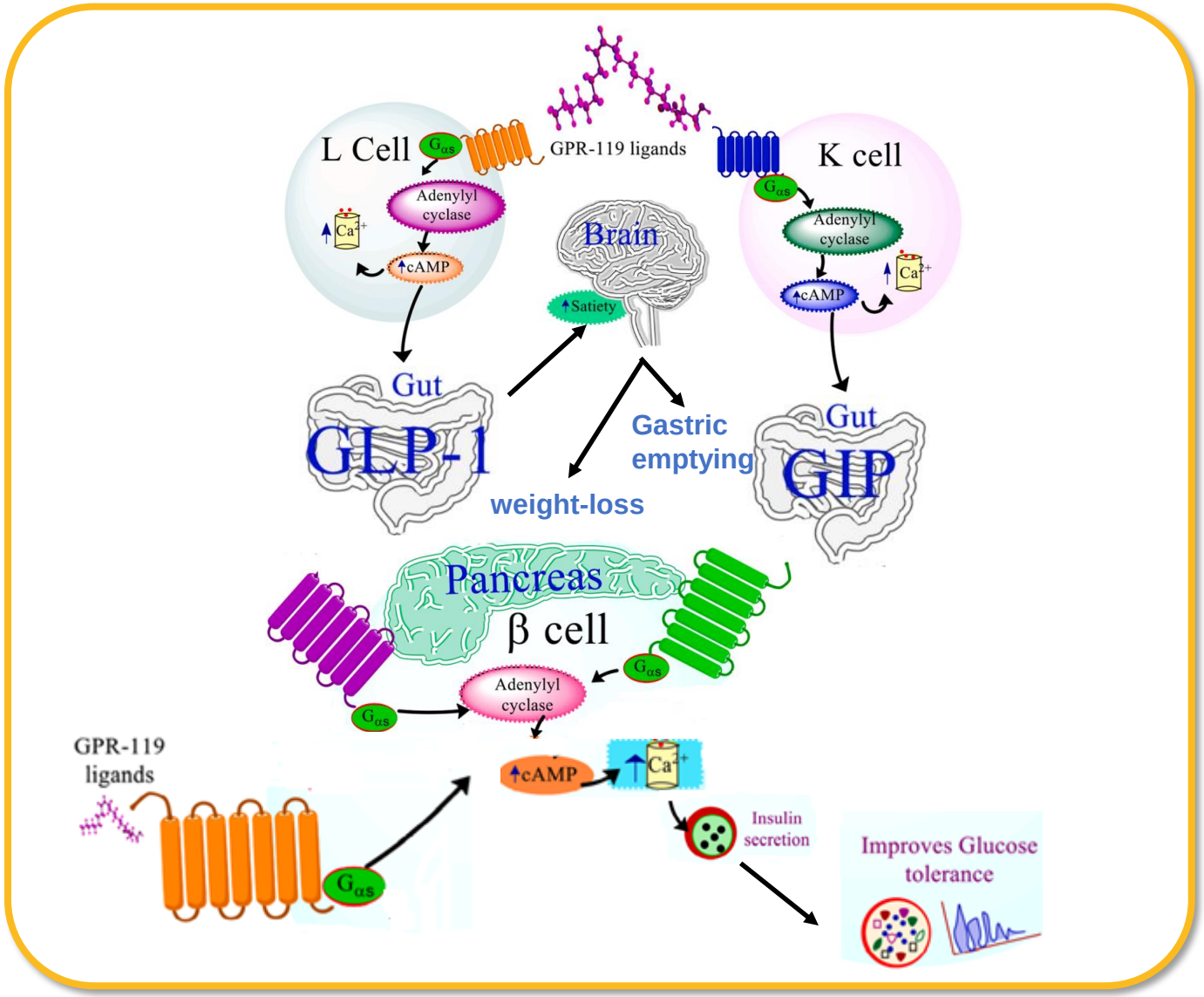
We develop innovative solutions for metabolic disorders by leveraging both **GPR119 therapeutic compounds** and **natural bioactive products** derived from agri-food by-products.

Our approach focuses on **glycaemic control, weight regulation, and metabolic balance** through targeted mechanisms, combination therapies, and optimized pharmacokinetics for better patient outcomes.

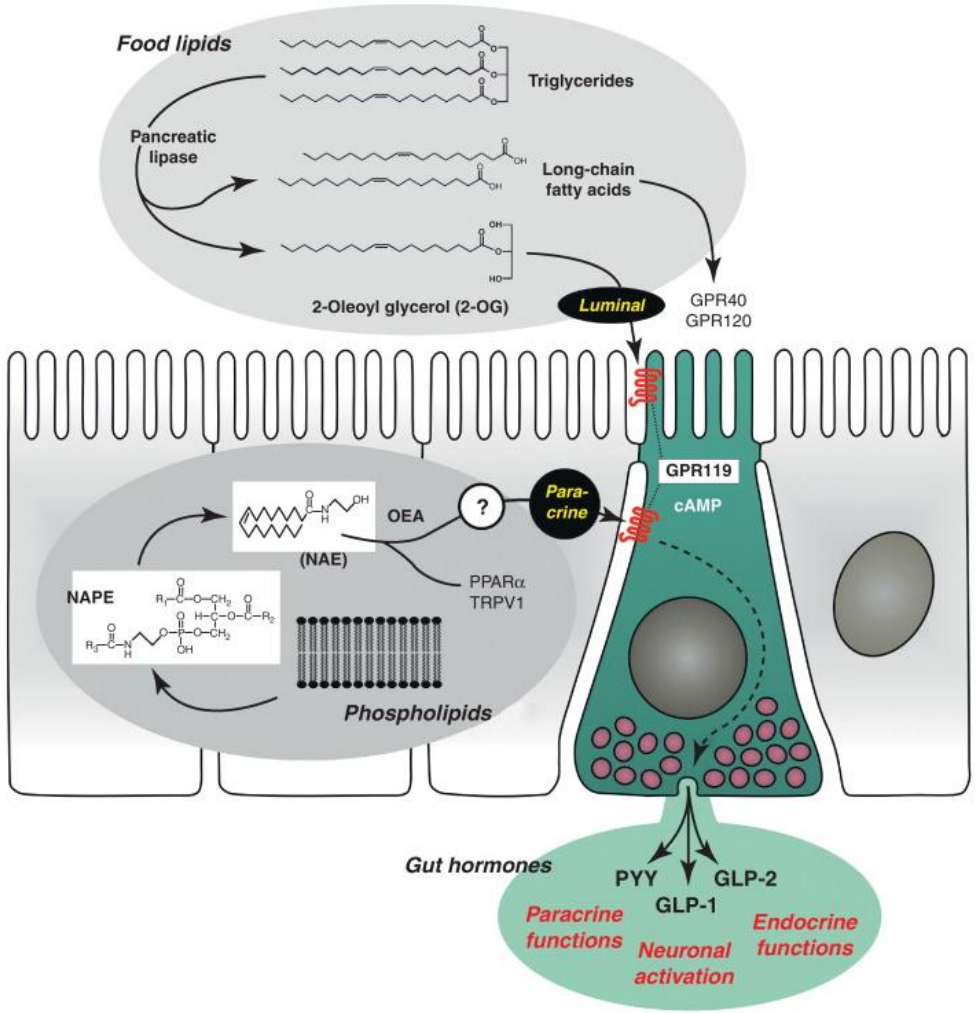
LE CELLULE ENTEROENDOCRINE



GPR119 agonism: a strategy for diabesity

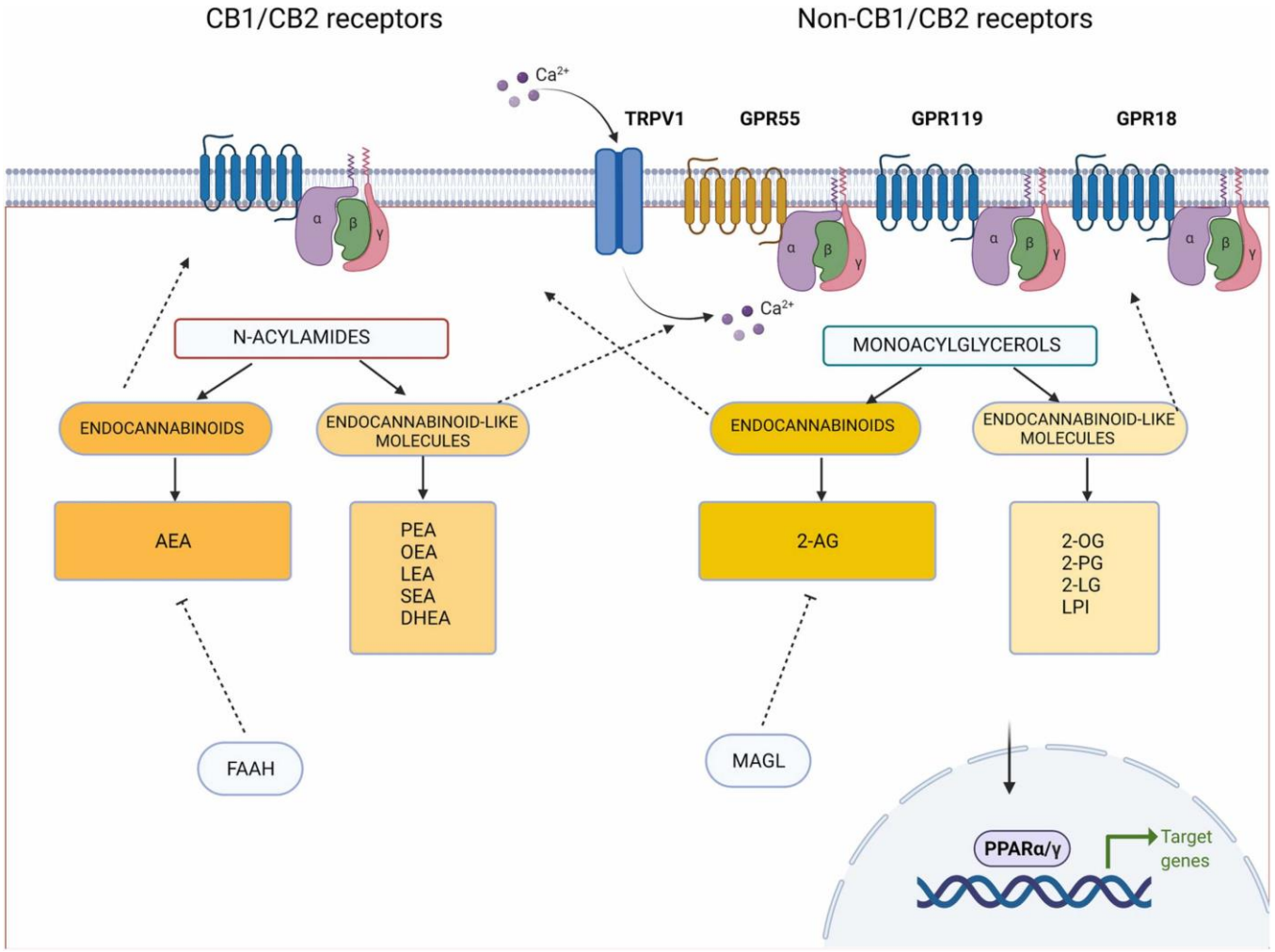


GPR119 IS A FAT SENSOR



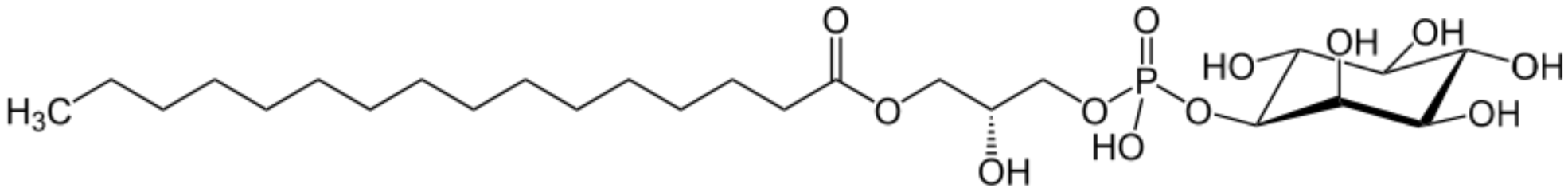
Hansen et al. Trends Pharmacol Sci. 2012

THE ENDOCANNABINOIDOME



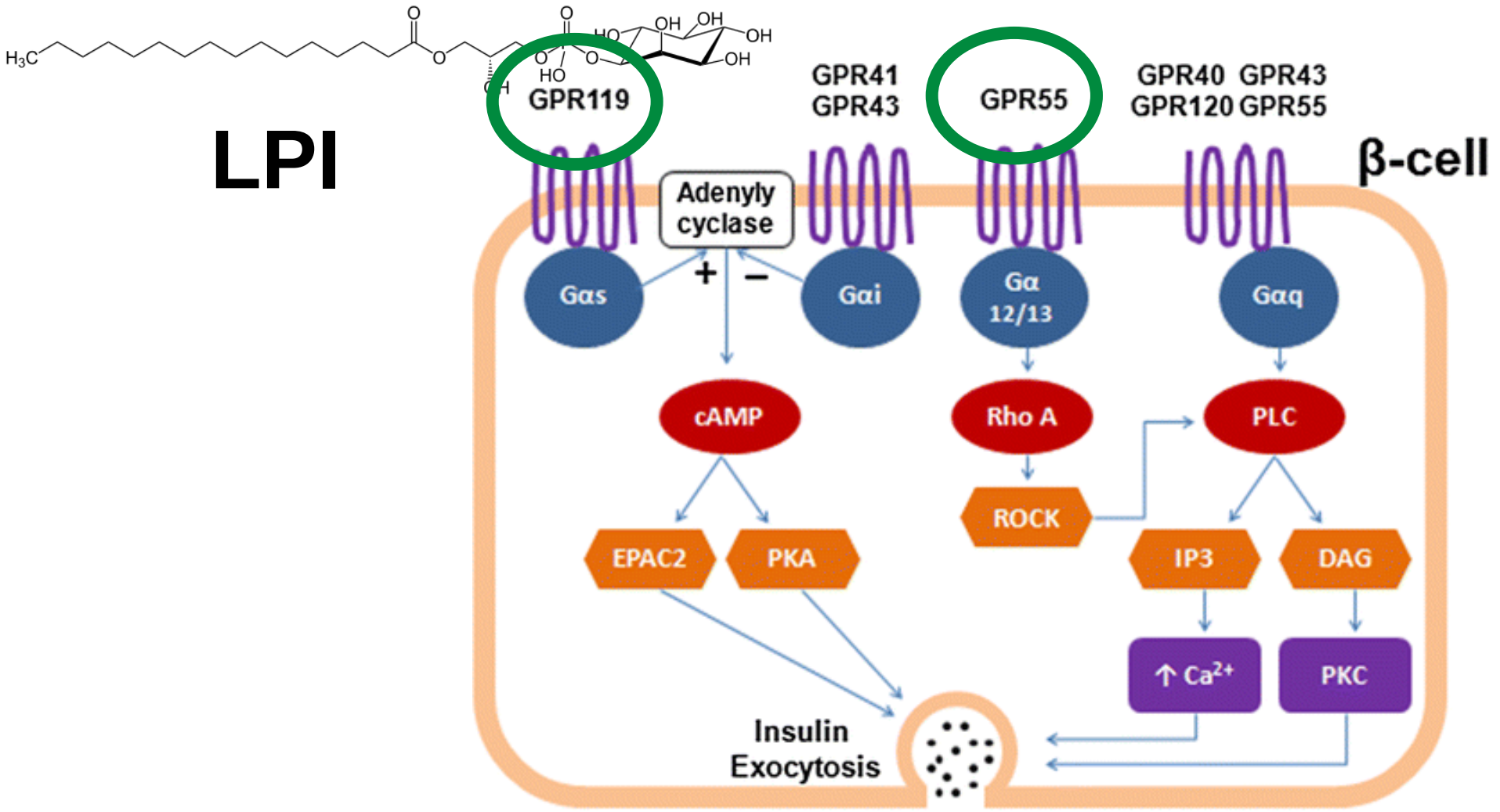
Lian, Casari & Falasca, ***Pharmacological Research*** 2022

LYSOPHOSPHATIDYLINOSITOL

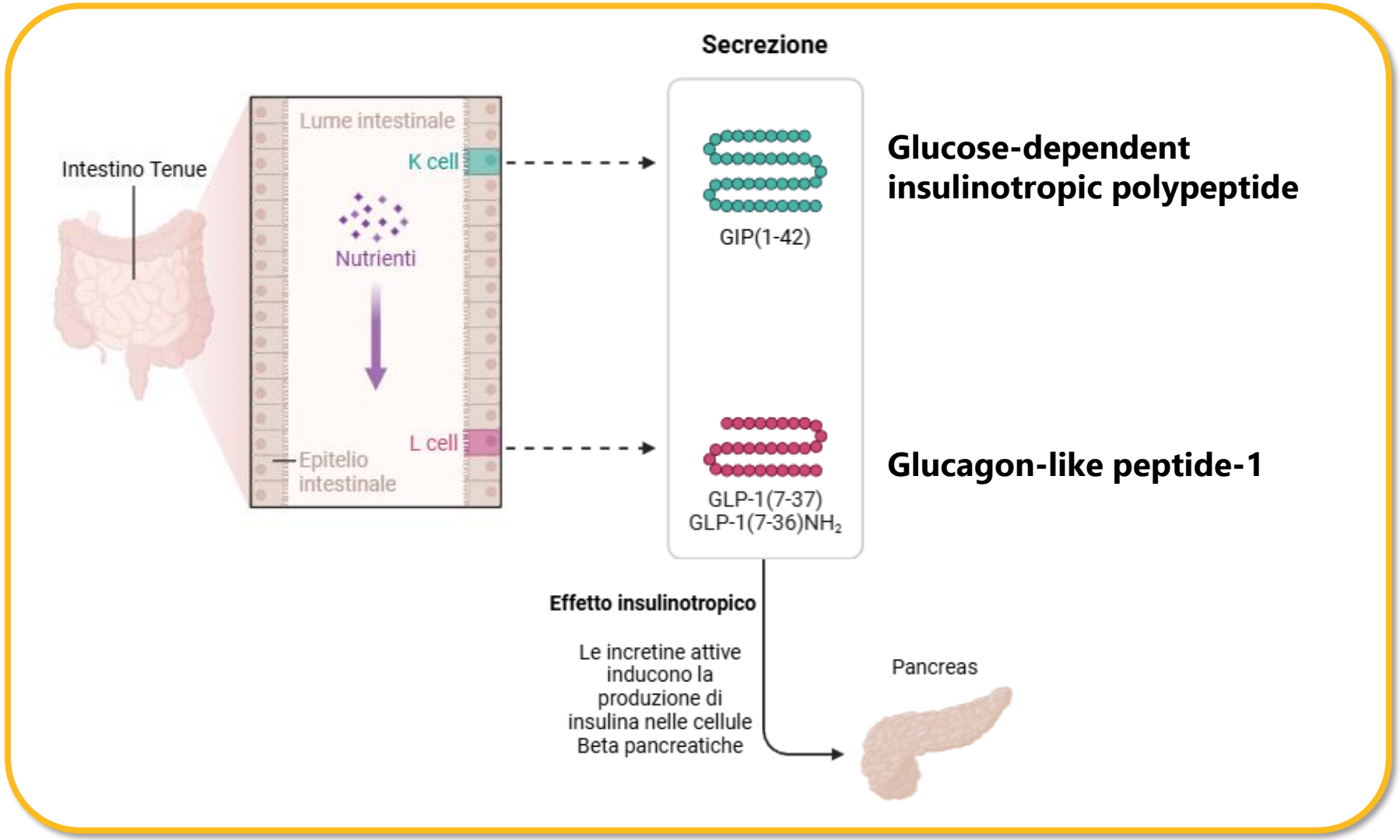


Pineiro & Falasca BBA 2012

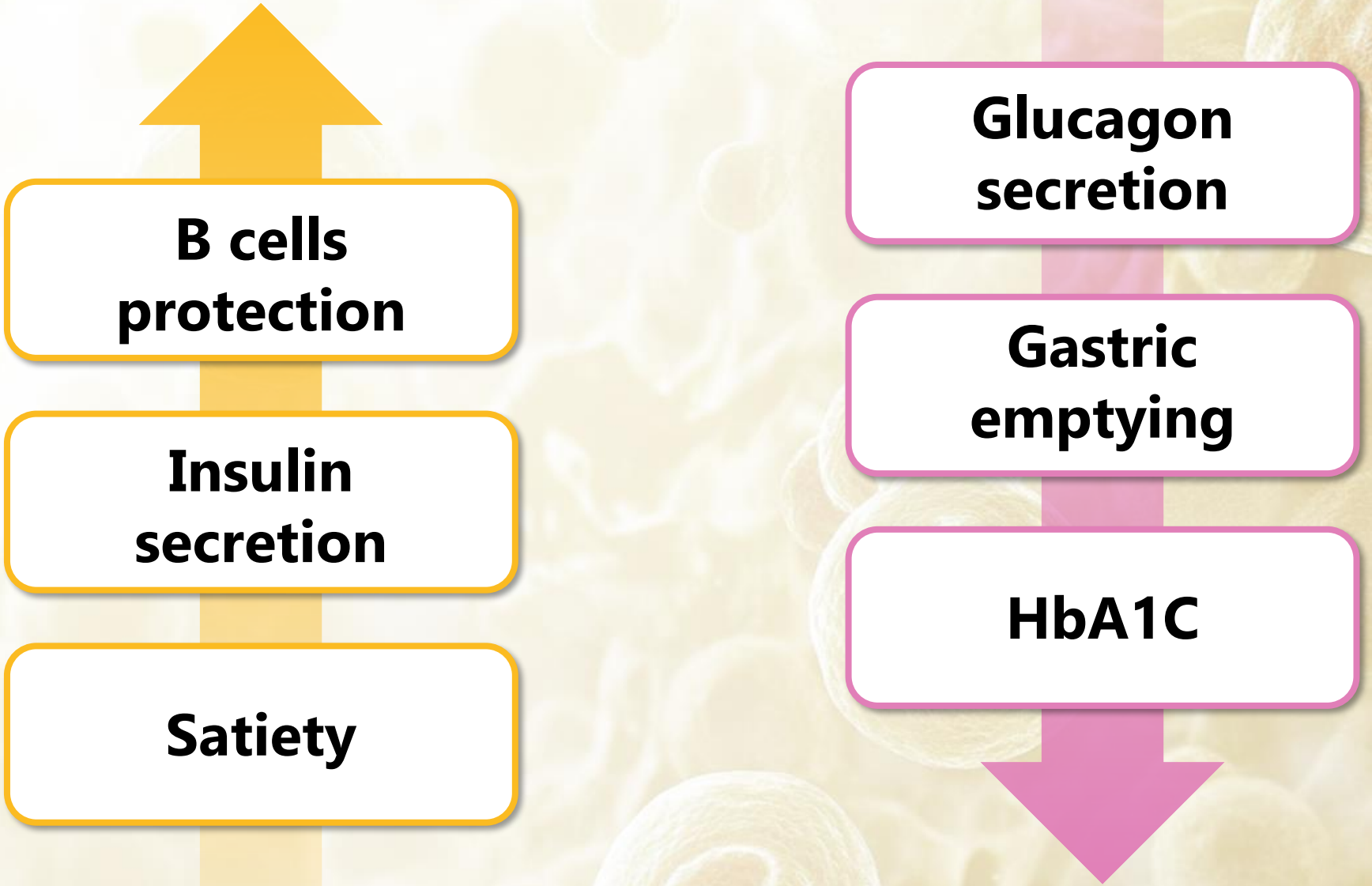
LYSOPHOSPHATIDYLINOSITOL RECEPTORS



GLI ORMONI INCRETINICI



THE IMPORTANCE OF GLP-1



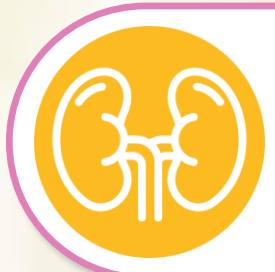
Paternostere & Falasca, Front endocrinology 2018

GLP-1: ORGAN-SPECIFIC PLEIOTROPIC EFFECTS

BRAIN ↓
- Food intake
- Palatability
- Inflammation

GI TRACT
- ↑ Gastric-emptying
- ↓ GI mobility

BONES ↑
- Bone formation
- Bone mass



KIDNEYS ↑
- Diuresis
- Natriuresis

LIVER ↓
- Steatosis

HEART ↑
- Contractility
- Cardiac output
- Vasodilation
- Micocytes survival
- Glucose utilization

MUSCLES ↑
- Insulin sensitivity
- Glucose uptake

PANCREAS ↑
- Insulin secretion
- Insulin sensitivity

Muller TD et al., Glucagon-like peptide (LP-1); Molecular Metabolism; 30 (2019) 72-130

GLI AGONISTI DEL GLP-1

SEMAGLUTIDE

Il semaglutide è un agonista **selettivo** del recettore GLP-1, approvato per il trattamento del diabete di tipo 2 e dell'obesità. Somministrato settimanalmente, ha dimostrato di:

- Migliorare significativamente il controllo glicemico riducendo l'HbA1c.
- Indurre una perdita di peso sostenuta, con una riduzione media del peso corporeo del 15% in pazienti non diabetici.
- Ridurre il rischio cardiovascolare nei pazienti con diabete di tipo 2.

TIRZEPATIDE

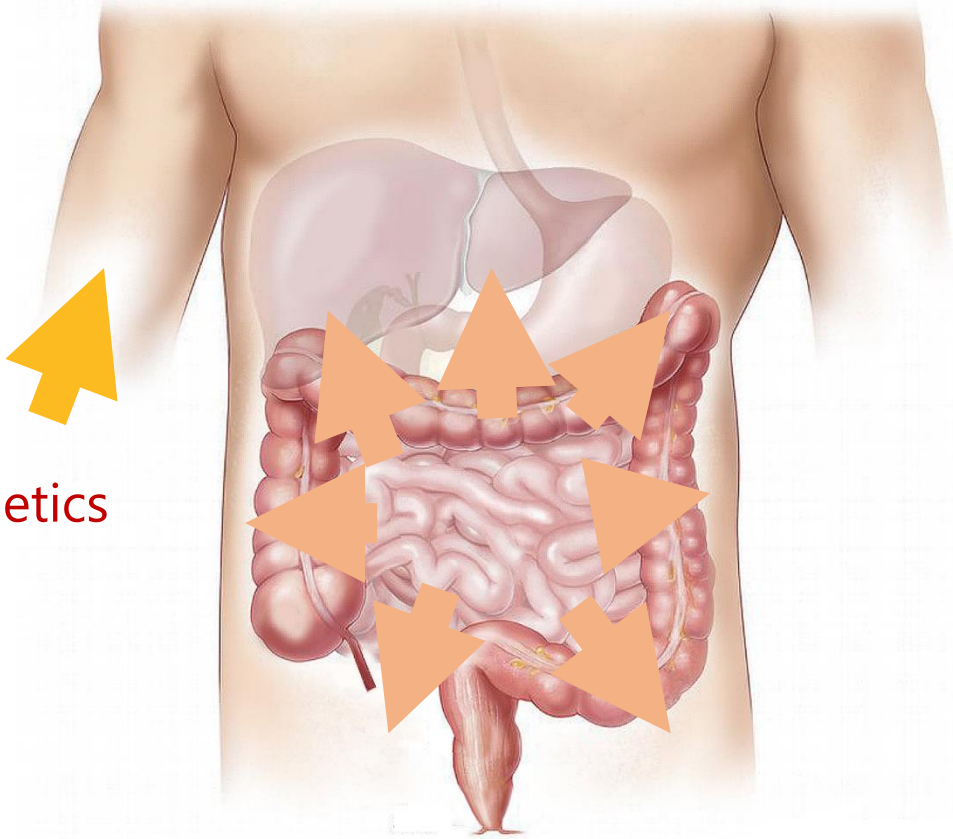
La tirzepatide è un co-agonista **duale** dei recettori GIP e GLP-1, progettato per combinare gli effetti benefici di entrambi gli ormoni incretinici. La tirzepatide agisce:

- Stimolando la secrezione di insulina in modo glucosio-dipendente.
- Riducendo l'appetito e migliorando il metabolismo lipidico.
- Promuovendo una perdita di peso che può superare il 20% del peso corporeo nei pazienti obesi.

Negli studi clinici, è stata dimostrata una riduzione superiore dell'HbA1c e una perdita di peso significativamente maggiore con l'uso della **TIRZEPATIDE** rispetto ai farmaci tradizionali agonisti del GLP-1.

OUR STRATEGY

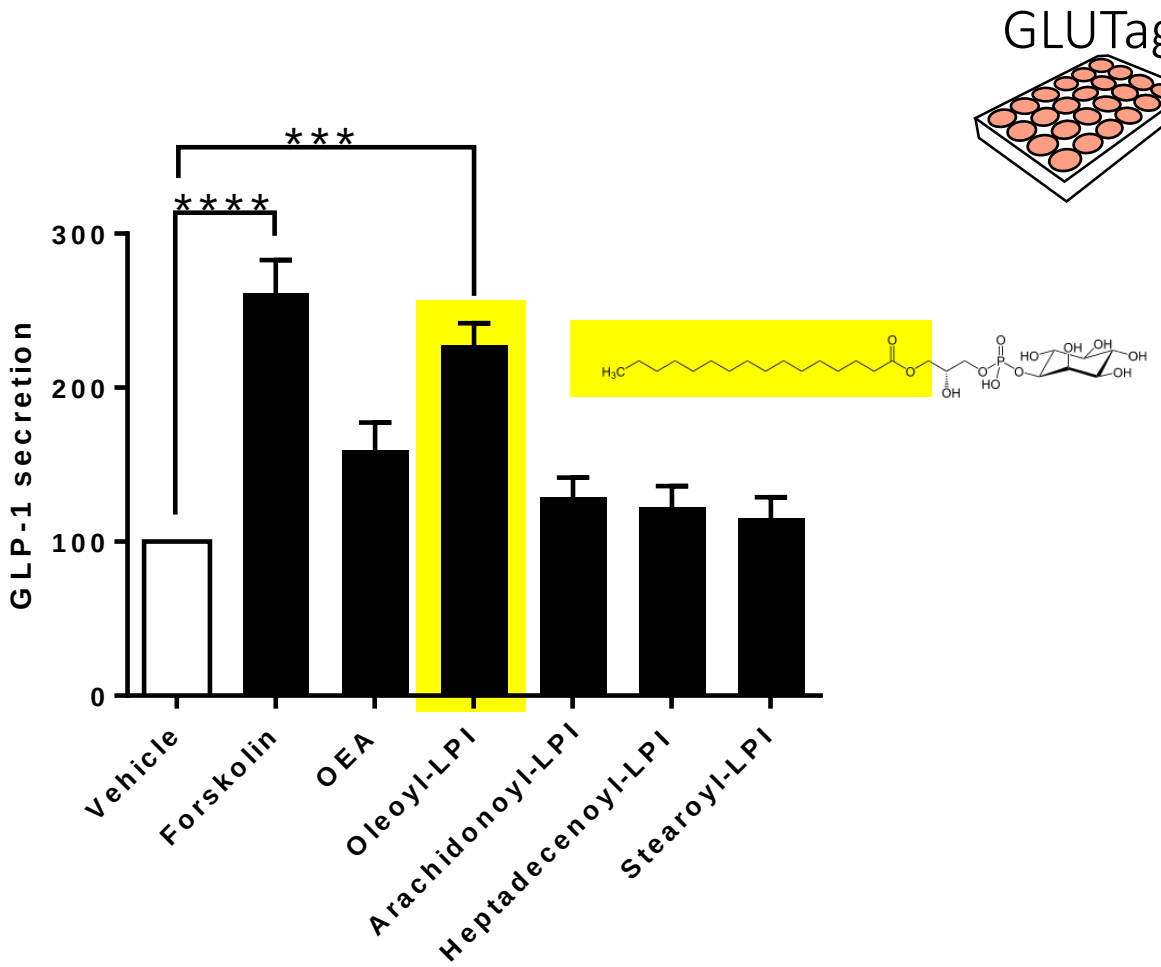
GLP-1 mimetics

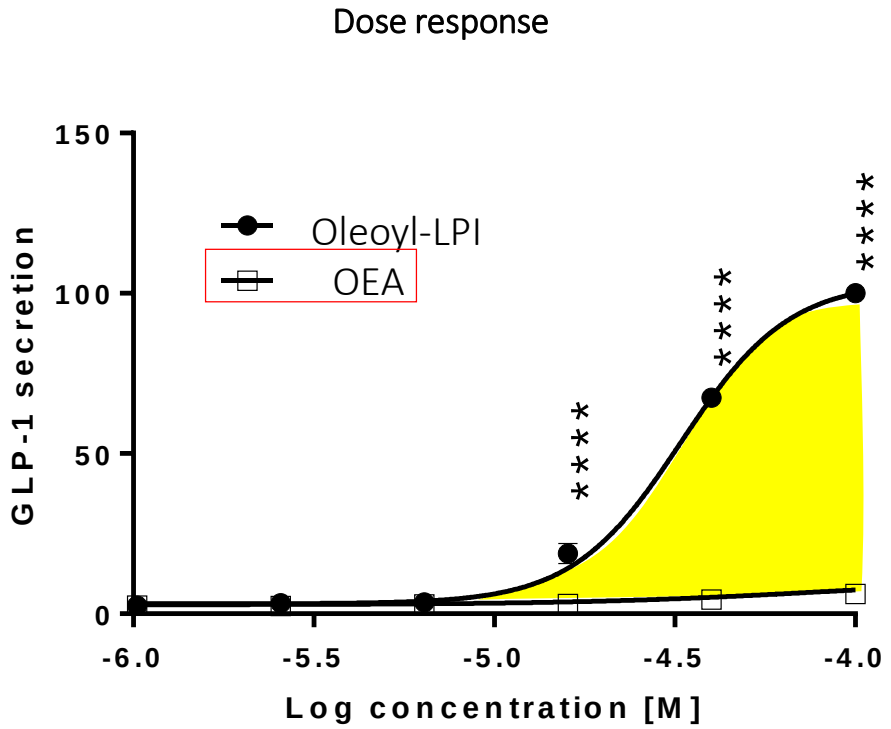


Blood sugar

Satiety

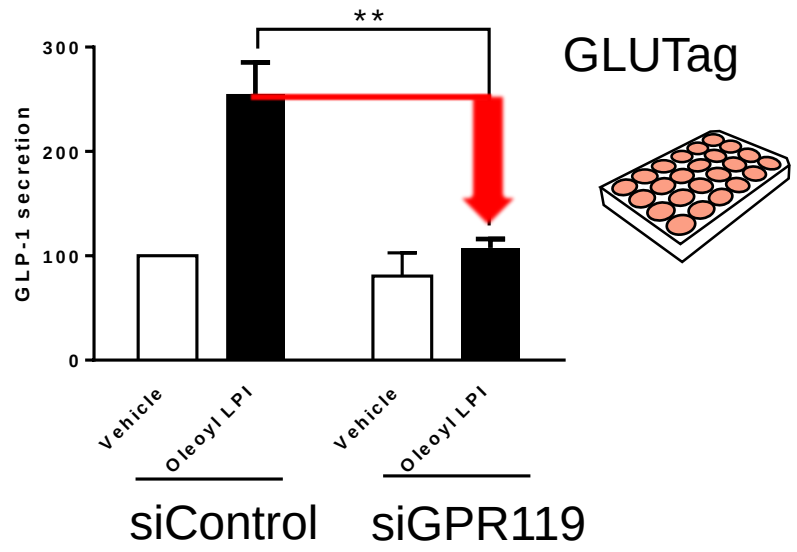
OLEOYL-LPI IS A POTENT GLP-1 SECRETING AGENT



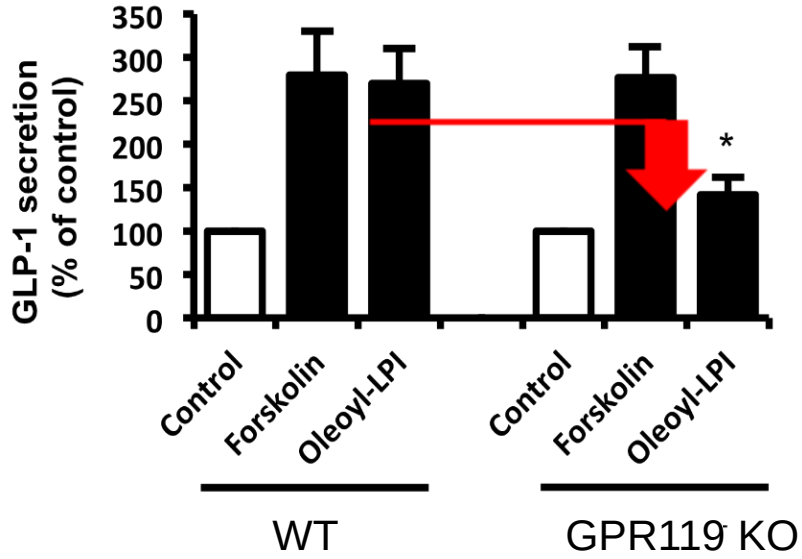


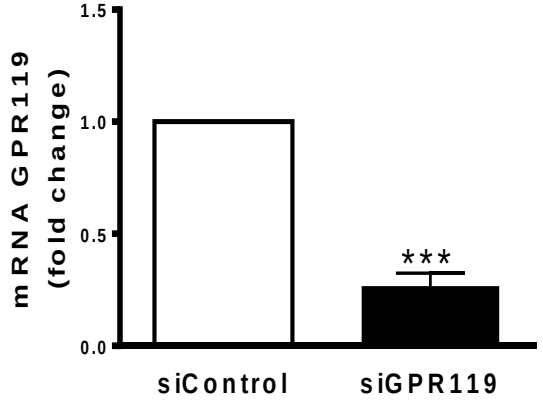
Arifin and Paternoster et al. ***BBA Mol Cell Biol Lipids*** 2018

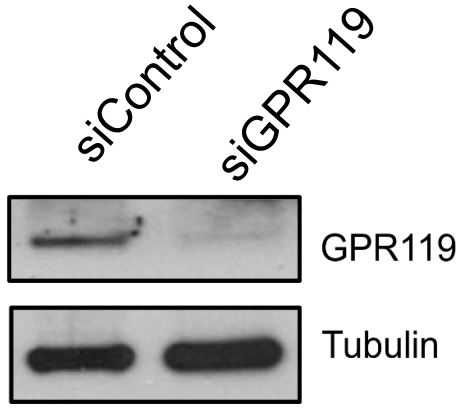
OLEOYL-LPI IS THE ENDOGENOUS LIGAND OF GPR119



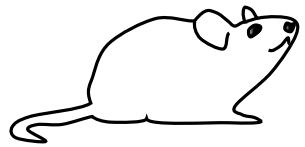
GLUTag

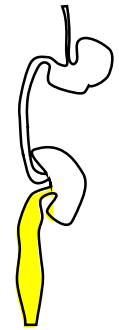






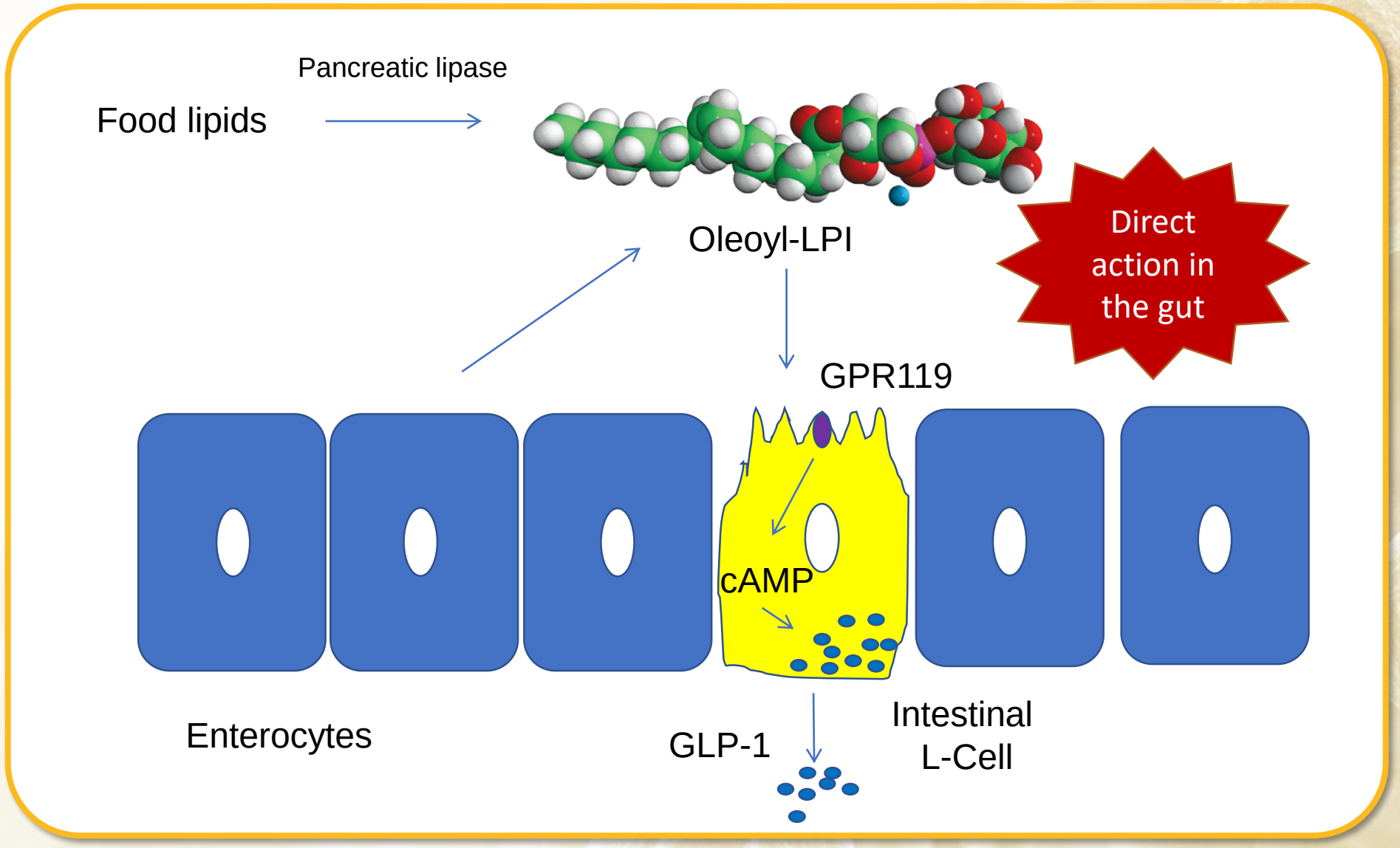
Ex-vivo
Colon preparations





Arifin et al. ***BBA Mol Cell Biol Lipids*** 2018

MECHANISM OF ACTION



DISCOVERY OF GUT-ORIENTED GPR119 AGONISTS

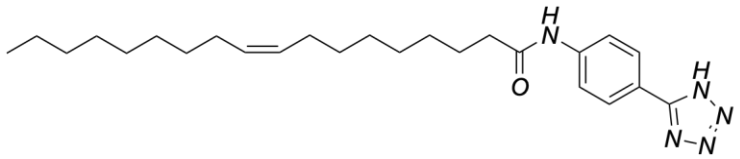
ELSEVIER

Pharmacological Research

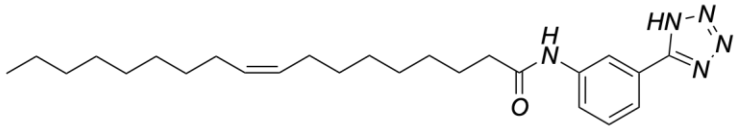
Volume 172, October 2021, 105822

Pharmacological and structure-activity relationship studies of oleoyl-lysophosphatidylinositol synthetic mimetics

Silvano Paternoster [a], Peter V. Simpson [b], Elena Kokh [a], Hüsün Sheyma Kizilkaya [c], Mette Marie Rosenkilde [c], Ricardo L. Mancera [a], Damien J. Keating [d], Massimiliano Massi [b], Marco Falasca [a]



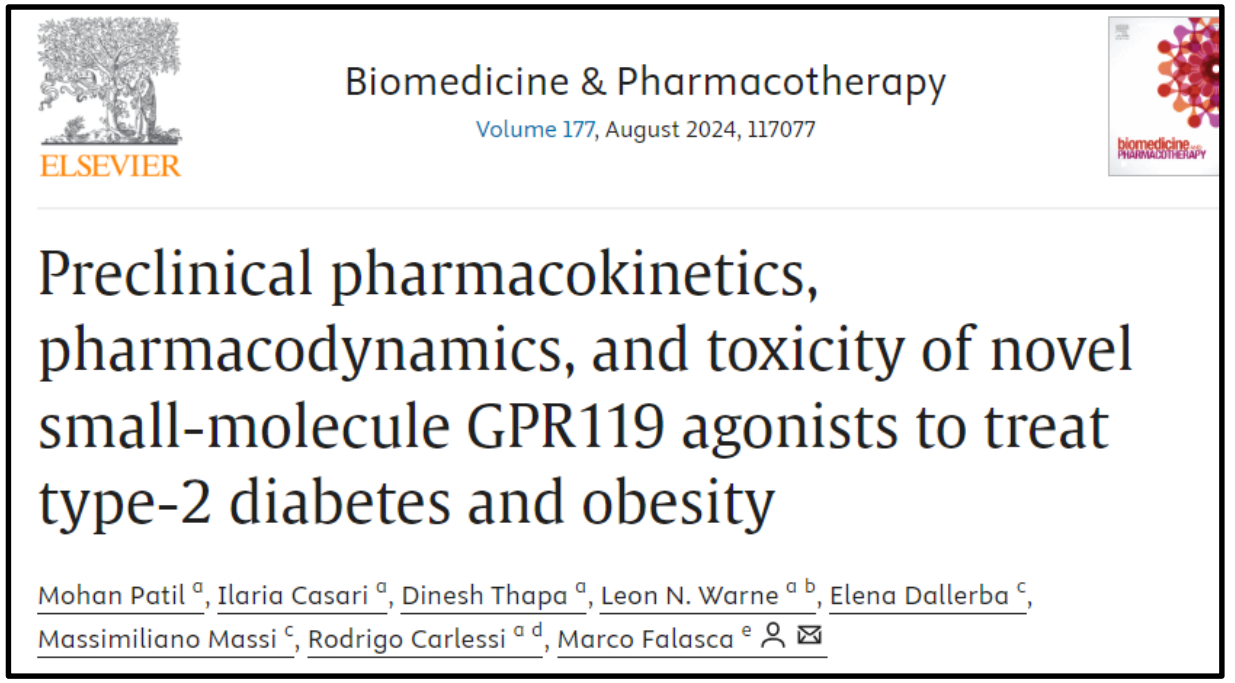
ps297



ps318

Compounds ps297 and ps318 are novel small-molecule, gut-oriented GPR119 agonists

ACUTE SAFETY, EFFICACY AND PHARMACOKINETICS



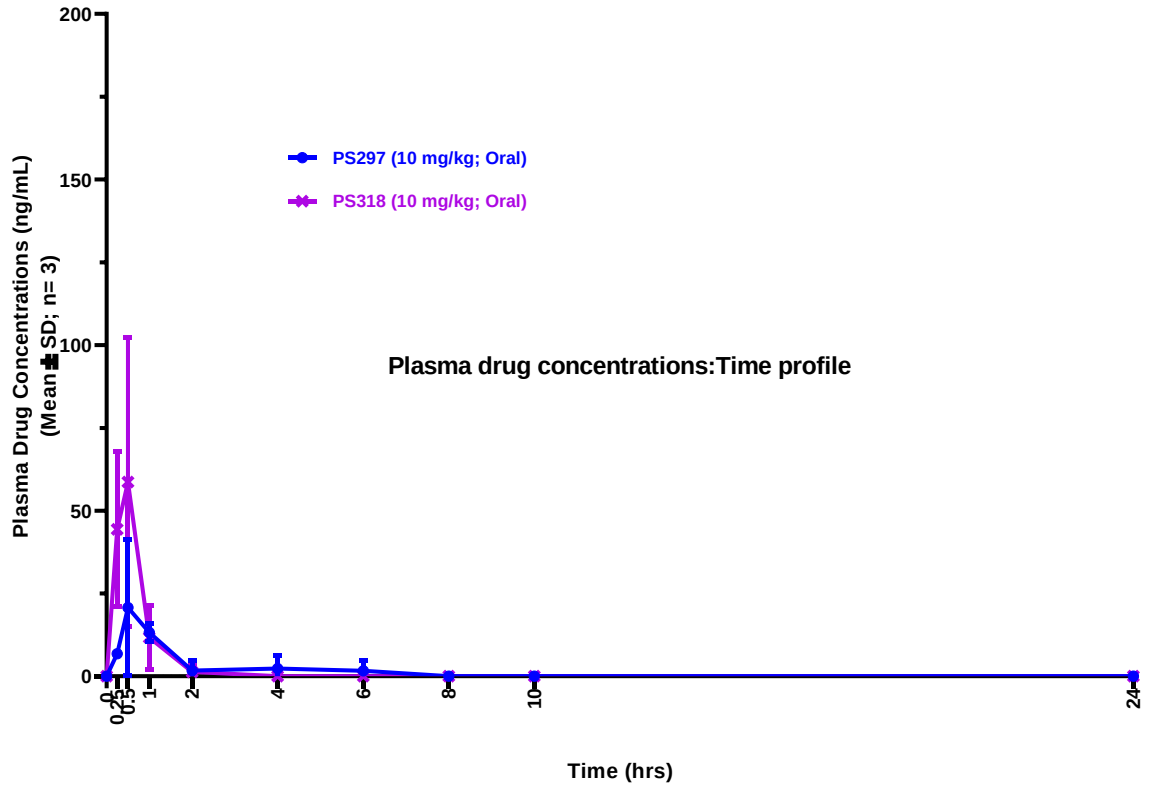
Biomedicine & Pharmacotherapy
Volume 177, August 2024, 117077

Preclinical pharmacokinetics, pharmacodynamics, and toxicity of novel small-molecule GPR119 agonists to treat type-2 diabetes and obesity

Mohan Patil [a], Ilaria Casari [a], Dinesh Thapa [a], Leon N. Warne [a b], Elena Dallerba [c], Massimiliano Massi [c], Rodrigo Carlessi [a d], Marco Falasca [e]

- **Compounds ps297 and ps318 act as GLP-1 secretagogues**
- **Exhibits poor gut permeability *in-vitro* and restricted oral bioavailability *in-vivo***
- **Safe and tolerable in healthy mice model**

SINGLE ORAL DOSE PHARMACOKINETICS



Calculated PK measures

	ps297	ps318
Cmax (ng/mL)	23 ± 19	75 ± 22
Tmax Range (hr)	0.5 – 1	0.25 – 0.5
AUCinf (h*ng/mL)	19.6±21	35±23
t 1/2	NC	NC
% Recovery in Urine	0.0006 ±0.0001	0.00064 ±0.0006
% Recover in Faeces	25 ± 23	5 ± 2.4

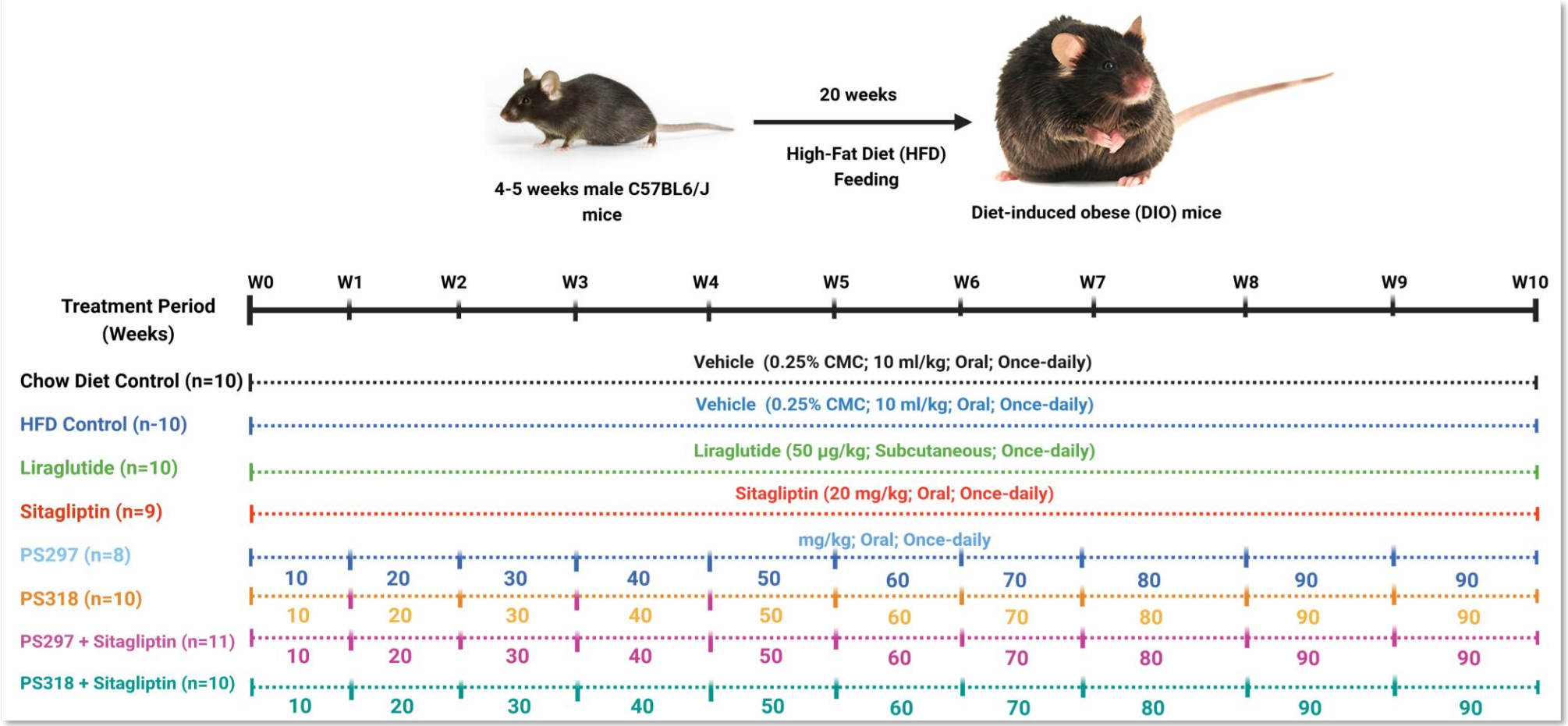
Values expressed as MEAN±SD

Low oral absorption of both the agents resulted poor oral pharmacokinetics in mice

Patil…& Falasca, *Biomed Pharmacoter* 2024

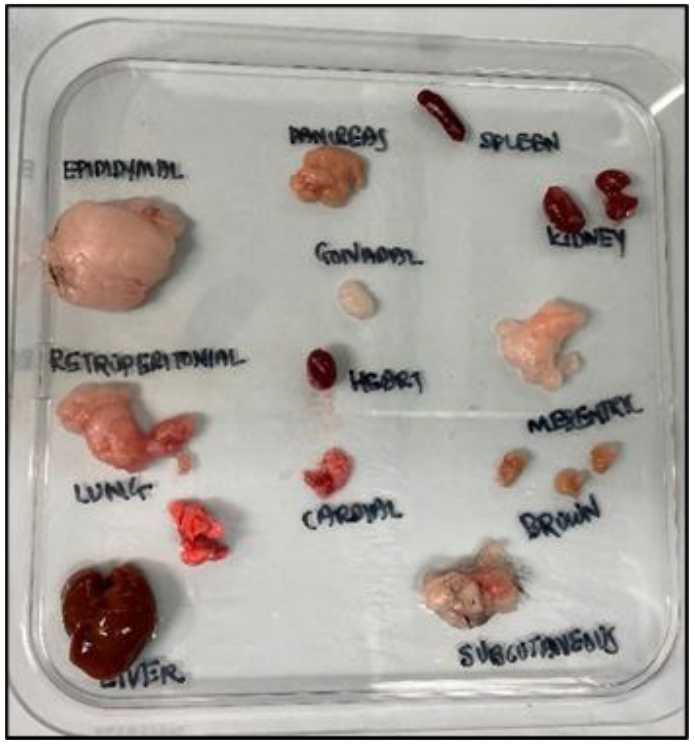
CHRONIC EFFECT ON DIET-INDUCED OBESE MICE

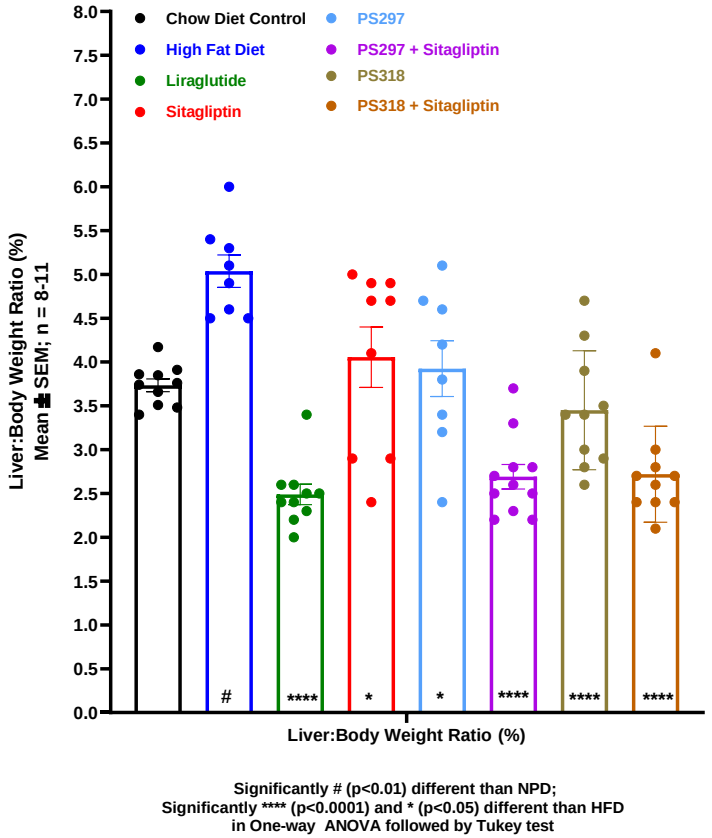
STUDY DESIGN



Animal ethics approval ARE-2022-12

EFFECT ON LIVER WEIGHTS



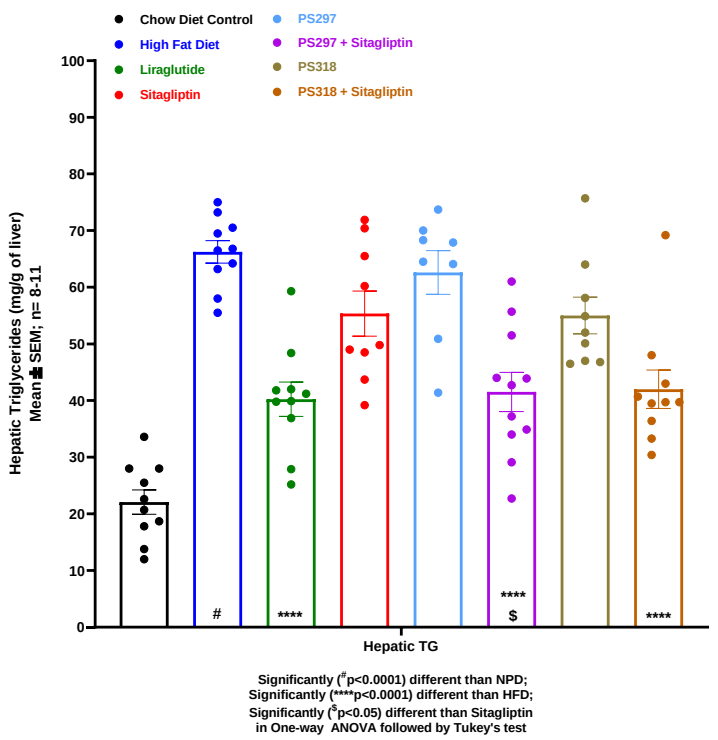


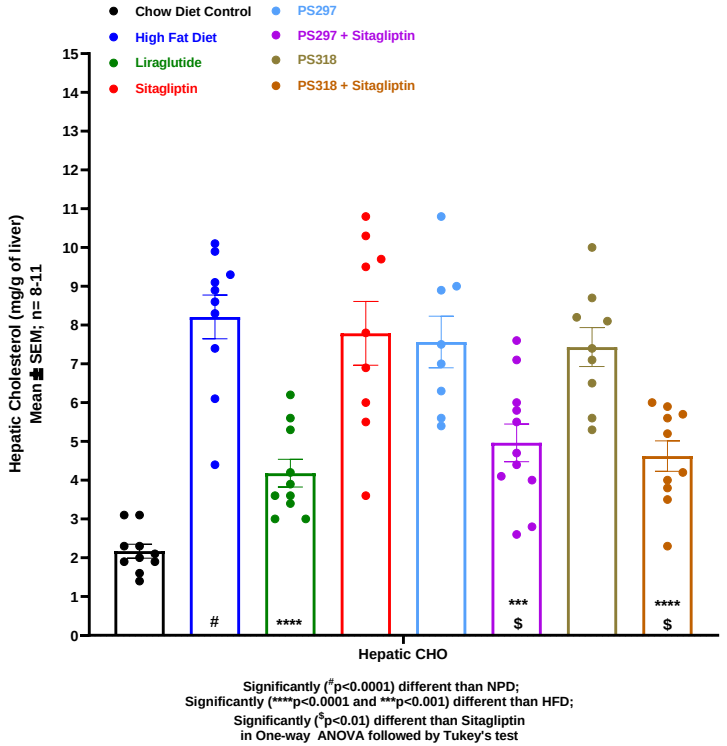
Significantly # ($p<0.01$) different than NPD;
Significantly **** ($p<0.0001$) and * ($p<0.05$) different than HFD
in One-way ANOVA followed by Tukey test

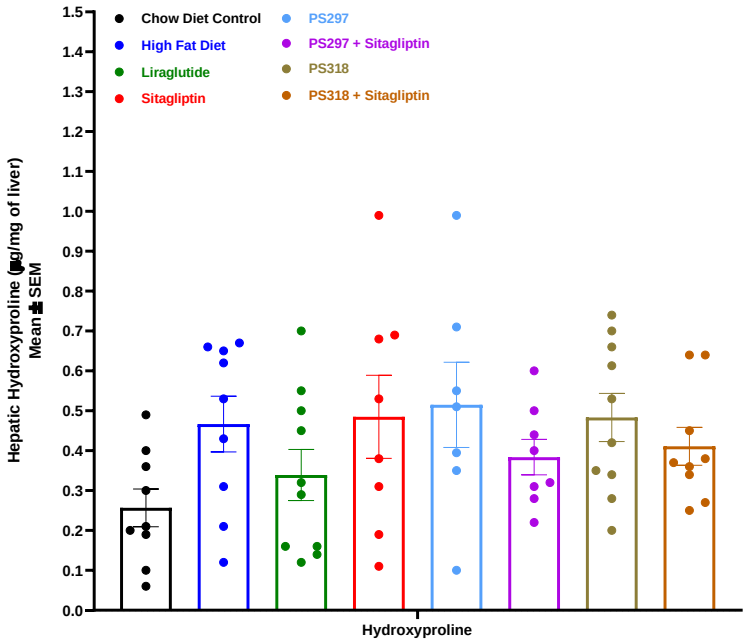
Treatment with ps297 and ps318 alone and in combinations with sitagliptin significantly reduced liver weights

Patil...& Falasca, *Biomed Pharmacoter* 2024

LIVER TRIGLYCERIDES, CHOLESTEROL AND HYDROXYPROLINE LEVELS

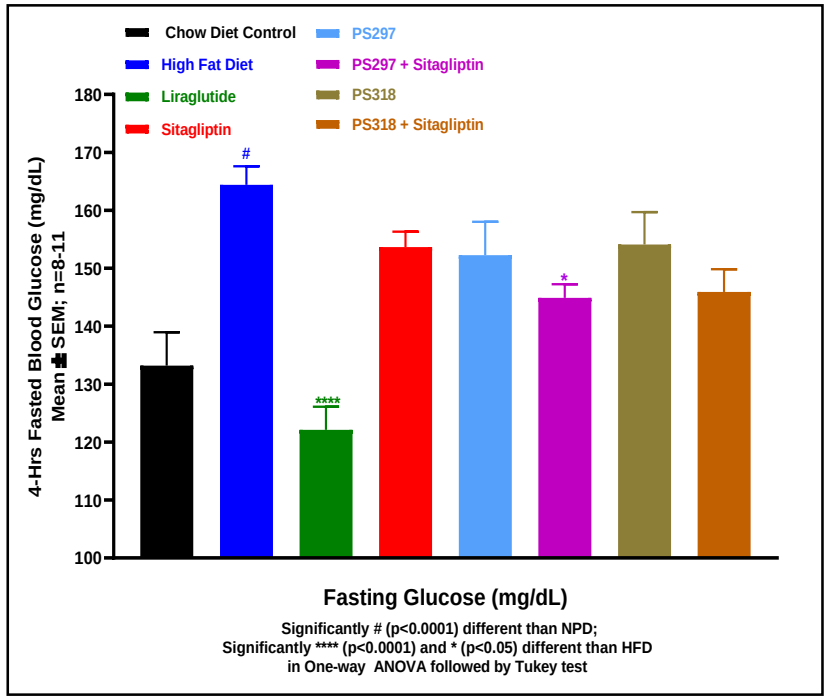


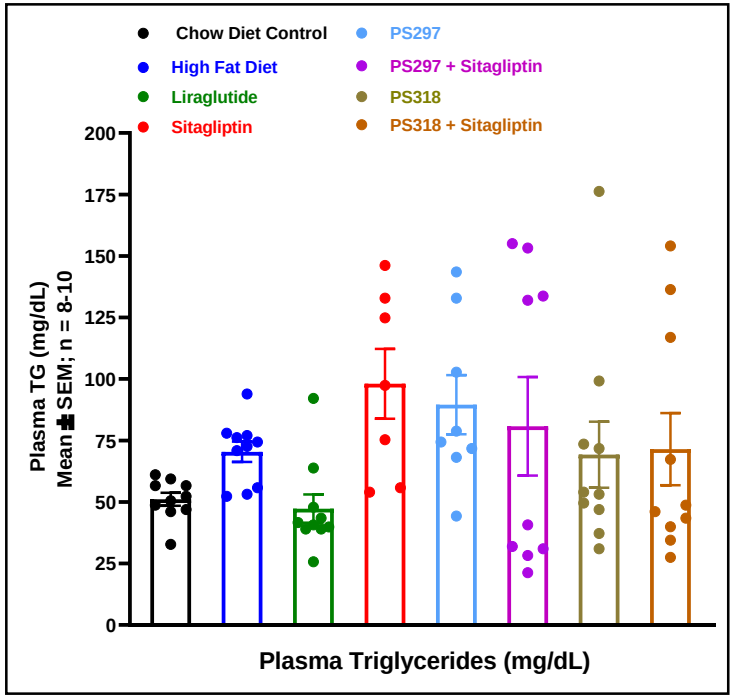


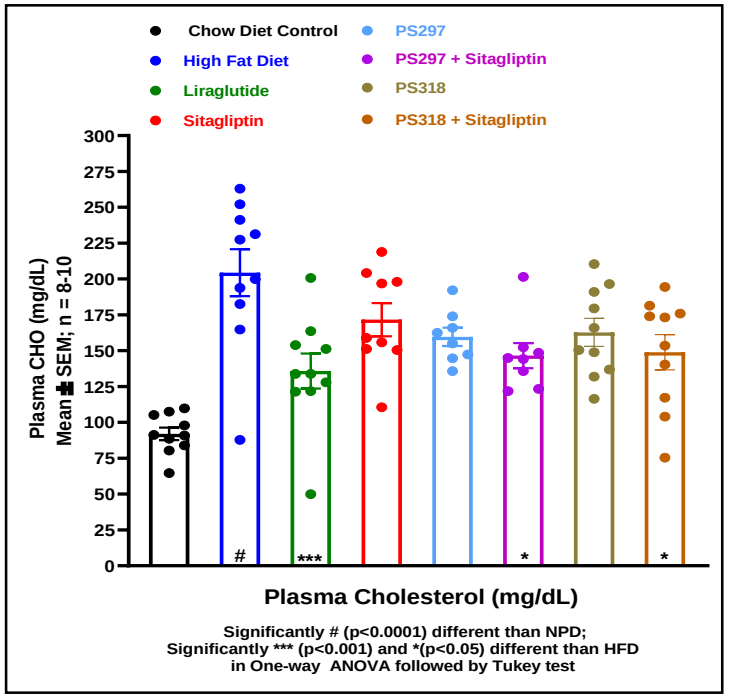


Patil...& Falasca, *Biomed Pharmacoter* 2024

EFFECT ON PLASMA BIOCHEMISTRY



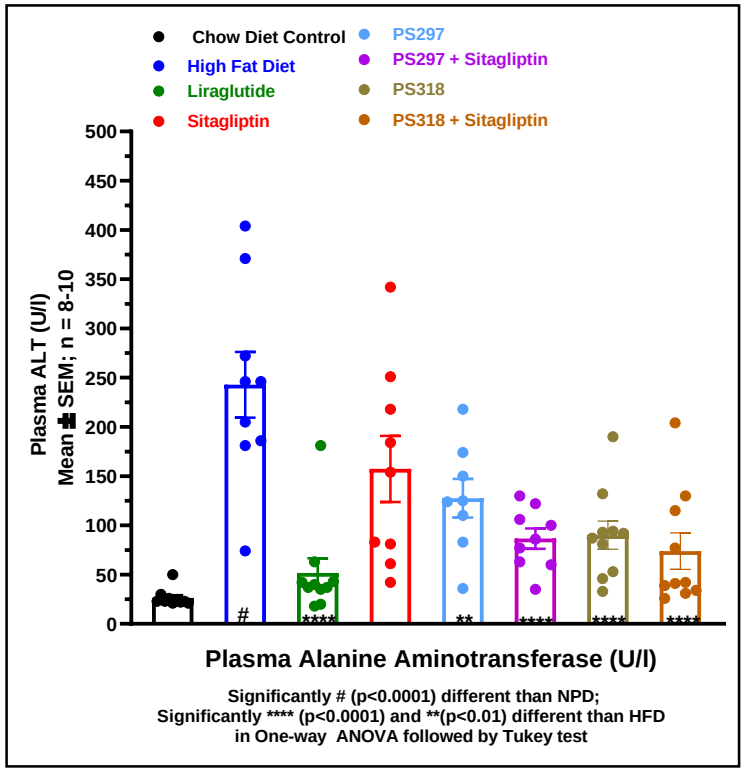


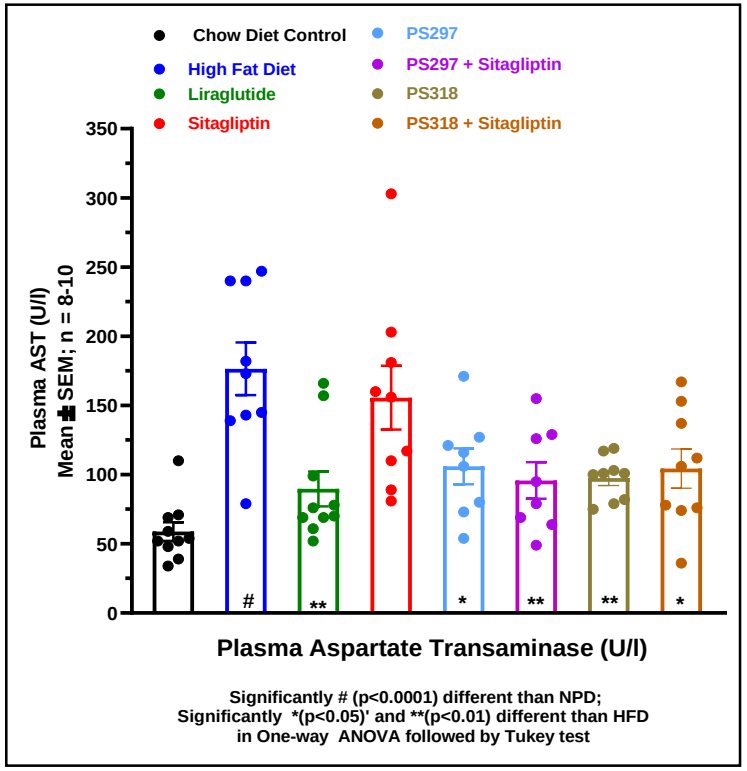


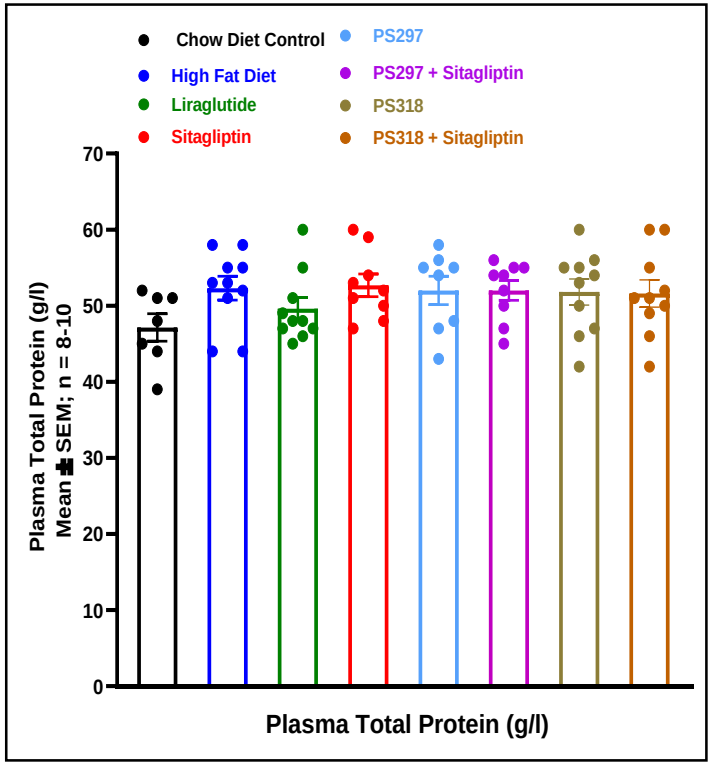
- **ps297 combination with sitagliptin significantly reduced fasted plasma glucose**
- **Both the investigational agents in combinations with sitagliptin reduced plasma cholesterol levels in obese mice**

Patil…& Falasca, *Biomed Pharmacoter* 2024

EFFECT ON PLASMA BIOCHEMISTRY







Both the investigational agents alone and in combinations with sitagliptin reduced liver enzymes in obese mice

Patil...& Falasca, *Biomed Pharmacoter* 2024

EFFECT ON HAEMATOLOGY

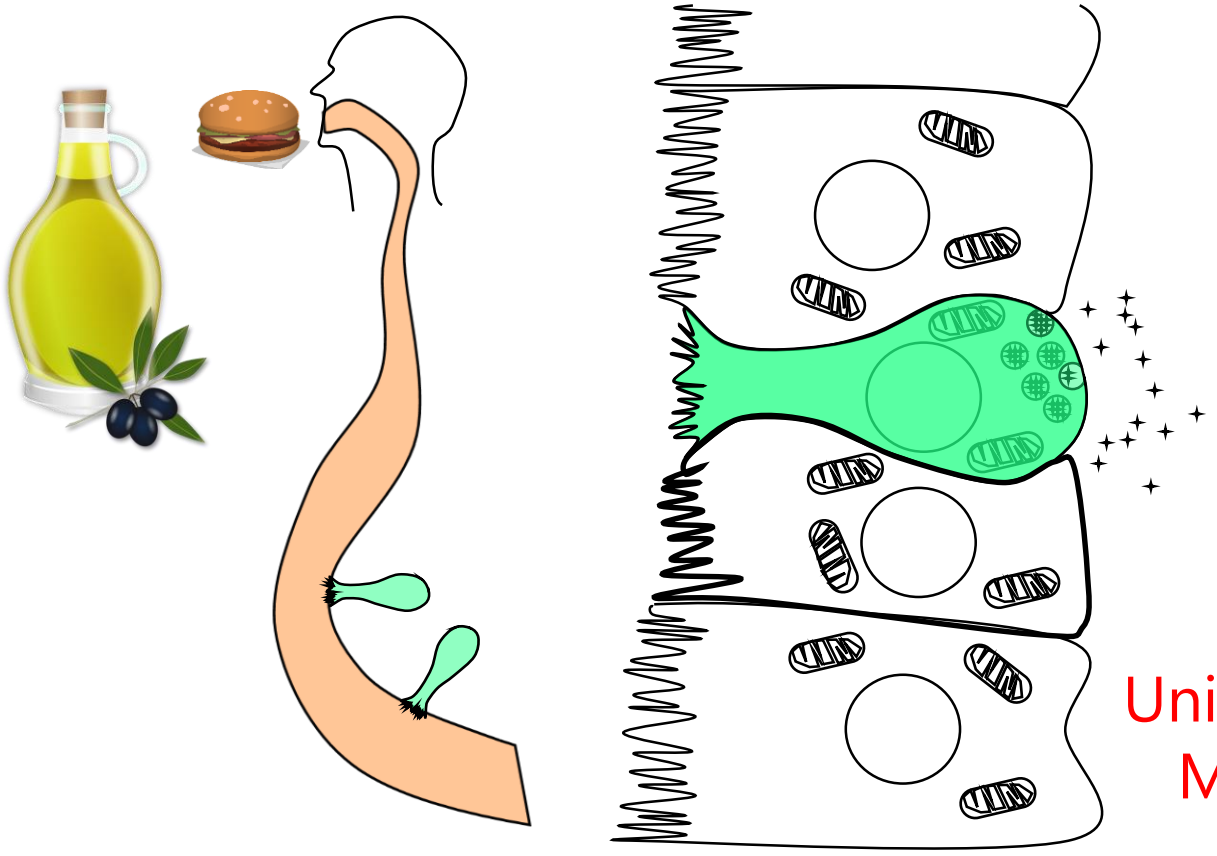
Haematology															
Treatment Groups	WBC (10^9/L)	Lymphocytes (10^9/L)	Monocytes (10^9/L)	Granulocytes (10^9/L)	RBC (10^{12}/L)	Haemoglobin (g/L)	Haematocrit (%)	Mean corpuscular volume (fL)	Mean corpuscular hemoglobin (pg)	Mean corpuscular hemoglobin concentration (g/L)	Red cell distribution width (%)	Platelets (10^9/L)	Mean platelet volume (fL)	Platelet distribution width	Procalcitonin (%)
NPD Control	4.8 ± 0.4	2.2 ± 0.9	0.60 ± 0.1	3.1 ± 0.5	8.2 ± 0.1	108.0 ± 2.2	35.5 ± 0.5	43.5 ± 0.4	13.2 ± 0.1	303.9 ± 2.9	15.5 ± 0.30	1327 ± 51	4.6 ± 0.1	16.0 ± 0.1	0.61 ± 0.02
HFD Control	6.2 ± 1.1	4.0 ± 1.0	0.44 ± 0.1	1.3 ± 0.2	8.7 ± 0.2	116.9 ± 3.1	38.8 ± 1.0	44.7 ± 0.2	13.4 ± 0.1	301.0 ± 1.5	15.5 ± 0.20	1062 ± 48#	4.7 ± 0.2	15.8 ± 0.04	0.45 ± 0.03
Liraglutide	5.8 ± 0.8	2.6 ± 0.9	0.49 ± 0.1	2.7 ± 0.5	8.2 ± 0.1	109.6 ± 1.2	35.3 ± 0.3	43.4 ± 0.4	13.4 ± 0.2	309.7 ± 1.6*	14.4 ± 0.20*	1199 ± 34	4.3 ± 0.1	15.7 ± 0.03	0.51 ± 0.02
Sitagliptin	4.9 ± 0.8	3.2 ± 0.7	0.36 ± 0.1	1.7 ± 0.4	7.8 ± 0.3	105.8 ± 4.4	34.4 ± 1.4	44.4 ± 0.2	13.6 ± 0.1	306.6 ± 1.7	15.6 ± 0.08	980 ± 36	4.9 ± 0.2	16.4 ± 0.2*	0.35 ± 0.07
PS297	5.6 ± 0.5	2.0 ± 0.8	0.37 ± 0.1	3.2 ± 0.9	8.3 ± 0.4	110.7 ± 5.8	37.3 ± 1.6	45.2 ± 0.4	13.3 ± 0.2	295.7 ± 3.7	15.9 ± 0.13	1160 ± 89	4.7 ± 0.1	15.9 ± 0.07	0.49 ± 0.06
PS297 + Sitagliptin	3.6 ± 0.6	2.3 ± 0.4	0.25 ± 0.1	1.1 ± 0.3	8.1 ± 0.3	109.0 ± 3.6	35.7 ± 1.2	44.3 ± 0.3	13.3 ± 0.1	301.4 ± 1.6	15.3 ± 0.23	919 ± 70	4.5 ± 0.1	16.02 ± 0.08	0.39 ± 0.04
PS318	6.2 ± 0.8	4.0 ± 0.8	0.28 ± 0.1	1.2 ± 0.4	8.6 ± 0.2	116.5 ± 2.7	38.8 ± 0.8	44.9 ± 0.4	13.4 ± 0.1	299.7 ± 1.4	15.6 ± 0.21	917 ± 93	4.7 ± 0.1	16.2 ± 0.1	0.34 ± 0.04
PS318 + Sitagliptin	6.2 ± 0.9	4.2 ± 0.9	0.4 ± 0.1	2.8 ± 0.7	8.3 ± 0.2	109.8 ± 3.7	36.7 ± 1.2	44.1 ± 0.4	13.1 ± 0.1	298.3 ± 1.4	15.6 ± 0.27	978 ± 36	4.6 ± 0.2	15.8 ± 0.1	0.38 ± 0.04

*All Values are expressed as MEAN ± SEM; Significantly #(p<0.05) different than NPD and *(p<0.05) than HFD in One-way ANOVA followed by Tukey test*

Long-term treatment with both the investigational agents showed no clinically relevant changes in blood hemogram

Patil…& Falasca, *Biomed Pharmacoter* 2024

HARNESSING NATURE TO FIGHT OBESITY



Blood sugar

Satiety

Unique, and safer
Mechanism of action

Arifin et al. *BBA Mol Cell Biol Lipids* 2018; Paternoster et al. *Pharm Res* 2021.

INTELLECTUAL PROPERTY

SYNTHETIC DERIVATIVES OF OLEOYL-LYSOPHOSPHATIDYLINOSITOL (OLEOLYL-LPI) AND USES THEREOF

The invention relates to oleoyl-lysophosphatidylinositol(oleoyl-LPI) and new synthetic derivatives thereof and uses thereof, and to pharmaceutical compositions comprising such compounds. The invention provides activators and/or up-regulators of glucoregulatory hormones such as glucagon like peptide-1 (GLP-1), and more specifically to agonists, partial agonists and reverse antagonists of GPR119 or activators of GLP-1 activity and/or synthesis and/or secretion, and pharmaceutical compositions comprising same, uses thereof in therapy of diabetes, obesity and other metabolic disorders.

2018226396 - Australia (granted).
ZL201880070700.4 - China (granted).
EP18851286.7 - Europe (pending).
762161 - New Zealand (pending).
16/643,165 - USA (pending).

LIPOVEXA TEAM

Marco Falasca, Ph.D.

Principal Investigator & Co-founder

- Professor of Metabolism at Curtin University (Australia); past roles at Queen Mary University of London, University College London, and Consorzio Mario Negri Sud.
- Research experience includes NYU Medical Center.
- Leads the Laboratory of Metabolism and Cellular Bio-signaling at University of Parma.
- Scientific coordinator of EU-funded PoliBioSan project.
- 200+ publications and several international patents.

Mohan Patil, Ph.D.

PhD Biomedicine M.Pharm (pharmacology) B.Pharm

- Pharmaceutical researcher at Curtin University (Australia) with 15+ years of industrial drug development and academic experience.
- Formerly Senior Research Scientist at Wockhardt and Piramal Enterprises.
- Skilled in laboratory techniques (biochemistry, in-vitro, animal models), pharmacology, pre-clinical studies.

LIPOVEXA TEAM

Filippo Surace, MD
Non-executive Chairman

- Serial entrepreneur and innovator with 30+ years of experience
in the medical field with extensive expertise in leading healthcare organizations and strategic investments.
- Founder & Chief Executive Officer of Gruppo Surace and of Cube Labs S.p.A.
- Former President of the Pharmaceutical and Healthcare Division
of Confindustria Lecce.
- Former Associate Professor at Temple University Center for Biotechnology College of Science and Technology, Philadelphia US.

Stefano Di Marco, Ph.D.
Project Manager

- Master's degree in Cellular and Molecular Biology and Doctorate in Cancer Biology at University of Zurich.
- Post-doctorate at Center for Epigenetics & Metabolism at UC Irvine.
- Postdoctoral fellowship at the Department of Bioengineering at UC Berkeley.

Riccardo Muscatello
Project Manager

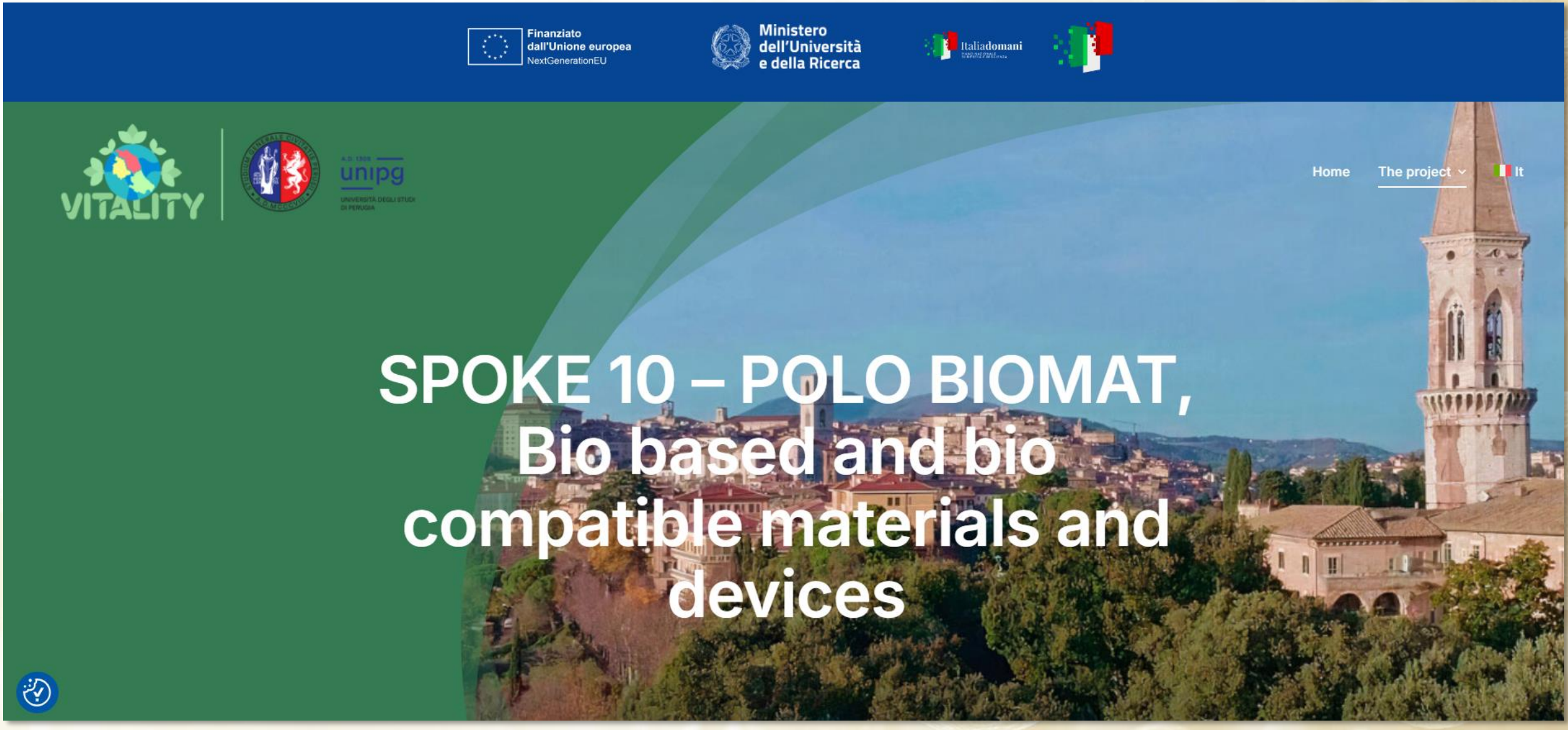
- Nutritionist and expert focused on the study of nutraceutical compounds in the prevention of cardiovascular and metabolic disease.
- Master's degree in Human Nutrition, now attending a Master
in Nutraceutical Compounds.

METABOLIC SIGNALLING LAB

Department of Medicine & Surgery, Università di Parma

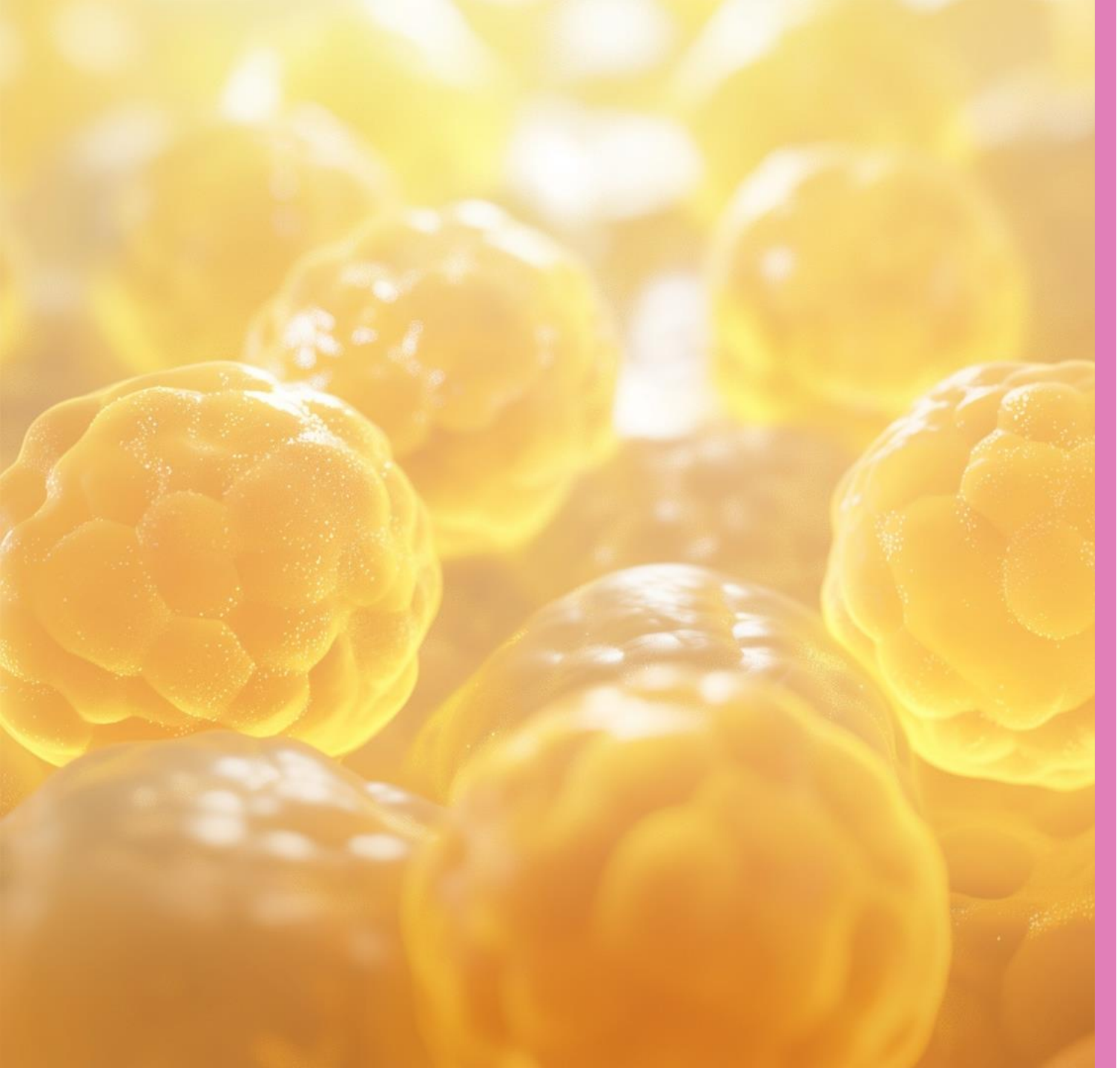
MOLECULAR ENDOCRINOLOGY AND PHARMACOLOGY LAB

Harry Perkins Institute of Medical Research and Centre for Medical Research, The University of Western Australia



Acronym of the project: `POLIBIOSAN`

Title of the Project: `Research, development and marketing of a pool of molecules derived from olive pomace`



GET IN TOUCH!

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