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5th Edition

Obesity & Diabetes Research

Focus: Crucial Investment in the Future of Health

Obesity is a major public health issue that is on the rise worldwide. It is estimated that over 1.0 billion adults are overweight or obese and this number is expected to continue to grow. Obesity is a risk factor for many chronic diseases, including heart disease, stroke, type 2 diabetes and some types of cancer. It is also a major cause of disability and premature death. Obesity research is essential and requires long-term investments to develop effective treatments and prevention strategies for this complex disease.

The blazing success of weight loss drugs like Wegovy and Mounjaro has electrified obesity research and especially the pursuit of new treatments for obesity. Dozens of companies are jumping into the race to market medications that are oral, longer-lasting, avoid side effects or provide additional benefits besides weight loss. Many of these drugs are targeting glucagon-like peptide-1 receptor (GLP-1R), glucose-dependent insulinotropic polypeptide (GIPR) and glucagon receptor (GCGR), as well as other hormones involved in satiety and metabolism; some are using entirely novel mechanisms.

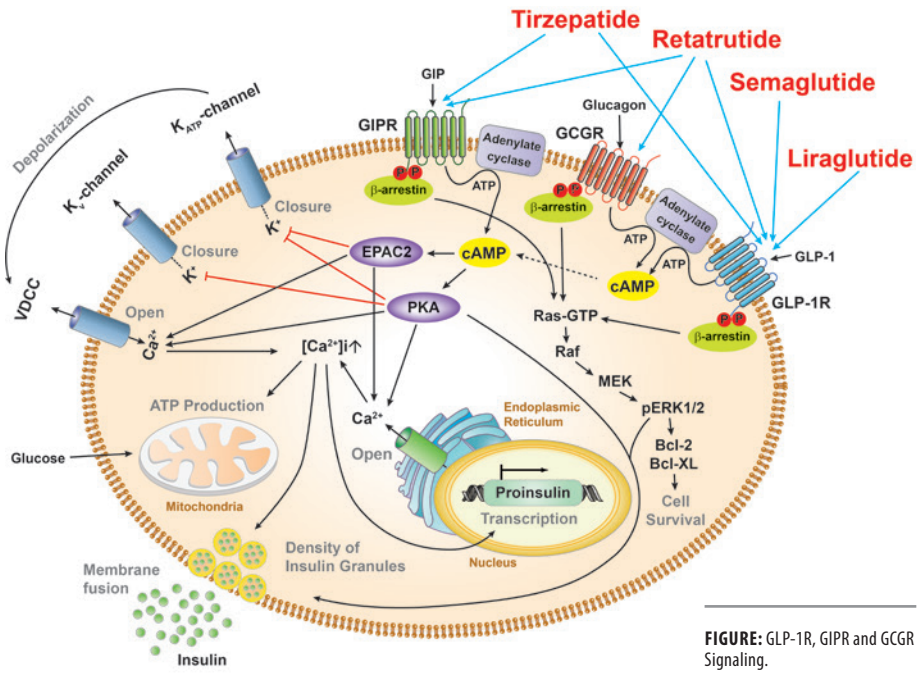

FIGURE: GLP-1R, GIPR and GCGR Signaling.

Panel of GLP-1R Agonists for Obesity Research *see Page 2*
Semaglutide, Liraglutide, Tirzepatide & Retatrutide

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Targeting GLP-1, GIP & GCG in Obesity and Type 2 Diabetes Research

Incretins are gut-derived hormones, members of the glucagon superfamily. There are two main incretin hormones in humans: **GIP** (glucose-dependent insulinotropic peptide; also known as gastric inhibitory peptide) and **GLP-1** (glucagon-like peptide-1). Both hormones are secreted by endocrine cells of the small intestine and are secreted on ingestion of glucose or nutrients to stimulate insulin secretion from pancreatic β cells. GIP and GLP-1 exert their effects by binding to their specific receptors, the GIP receptor (GIPR) and the GLP-1 receptor (GLP-1R), which belong to the G-protein coupled receptor family. Receptor binding mainly activates and increases the level of intracellular cyclic adenosine monophosphate in pancreatic β cells, thereby stimulating insulin secretion glucose-dependently **(see Figure Page 1)**. In addition to their insulinotropic effects, GLP-1 and GIP also have other metabolic effects, such as reducing glucagon secretion from the pancreas, slowing down gastric emptying and promoting satiety. **Glucagon (GCG)**, a hormone secreted from pancreatic α cells, acts in opposition to insulin by promoting gluconeogenesis and glycogenolysis and plays as an essential regulator of glucose and lipid metabolism. GCGR plays a crucial role in managing blood sugar levels and energy balance.

SELECTED REVIEWS: GLP-1 Receptor Agonists: Beyond Their Pancreatic Effects: X. Zhao, et al.; Front. Endocrinol. **12,** 721135 (2021) (Review) • GLP-1 and GIP receptor signaling in beta cells – A review of receptor interactions and co-stimulation: A. Mayendraray, et al.; Peptides **151,** 170749 (2022) (Review) • Tirzepatide, a dual GIP/GLP-1 receptor co-agonist for the treatment of type 2 diabetes with unmatched effectiveness regarding glycaemic control and body weight reduction: M.A. Nauck & D.A. D'Alessio; Cardiovasc. Diabetol. **21,** 169 (2022) (Review)

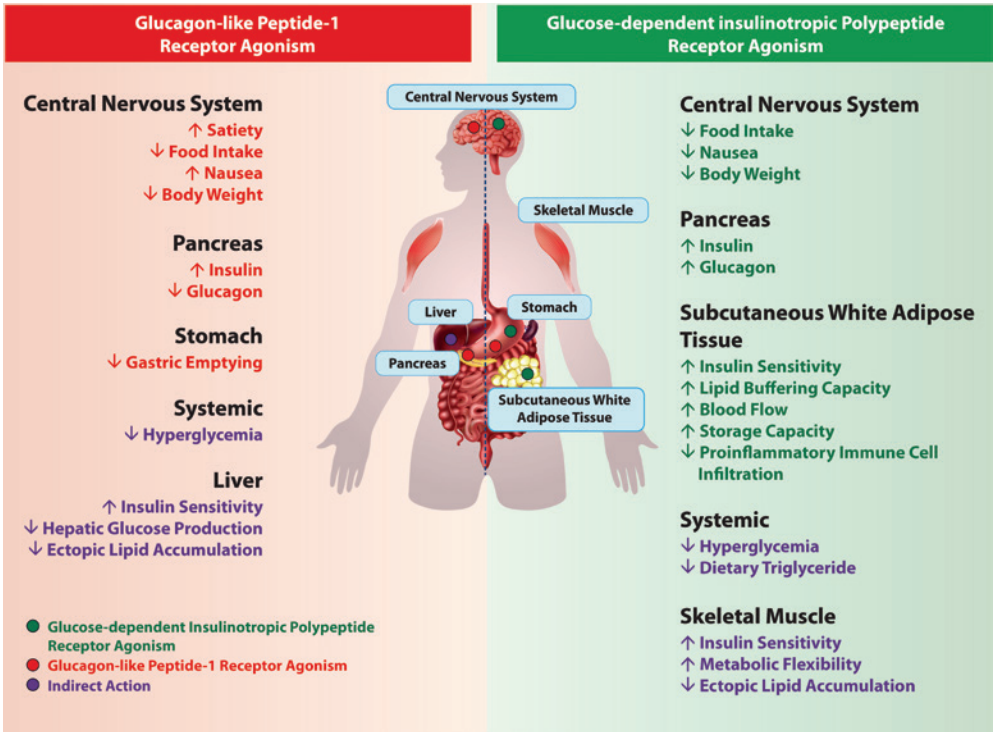

FIGURE: GLP-1R and GIPR Agonists Effects.

GLP-1, GIP & GCG Receptor Agonists

Available from Stock in BULK

PRODUCT NAME	PID	SIZE	PRODUCT DESCRIPTION
Liraglutide	AG-CP3-0034	1 mg | 5 mg | 25 mg	Long-acting acylated GLP-1 receptor agonist.
NEW **Retatrutide . sodium salt**	AG-CP3-0044	1 mg | 5 mg | 25 mg	Novel triple agonist peptide of the GCG receptor, GIP receptor and GLP-1 receptor.
Semaglutide	AG-CP3-0040	1 mg | 5 mg | 25 mg	Longer-acting alternative GLP-1 receptor agonist to Liraglutide.
Semaglutide . acetate	AG-CP3-0032	1 mg | 5 mg | 25 mg	Semaglutide salt form.
NEW **Tirzepatide**	AG-CP3-0043	5 mg | 25 mg	Novel dual GIP and GLP-1 receptor agonist.

Other Small Molecule Modulators of GLP-1 or GIP Signaling

PRODUCT NAME	PID	SIZE	PRODUCT DESCRIPTION
Linagliptin	AG-CR1-3618	10 mg | 50 mg	Highly potent and selective competitive DPP4 inibitor. Prevents the inactivation of endogenous GLP-1 and GIP.
Metformin . HCl	AG-CR1-3689	1 g | 5 g	AMPK activator. Increases plasma concentrations of GLP-1.
Orlistat	AG-CN2-0050	50 mg | 250 mg	Hypolipemic cell permeable and irreversible pancreatic, gastric and carboxylester lipase inhibitor. It promotes gastric emptying and secretion of gut peptides and attenuates the release of GIP.

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APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot
FORMULATION: PF = Preservative free **SPECIES: Dg** = Dog; **Hu** = Human; **Mo** = Monkey; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit

White & Brown Fat Cells as Endocrine Tissues

Two major types of adipose tissue exist in mammals, white (WAT) and brown adipose tissue (BAT) composed mainly of white **(see Figure)** or brown adipocytes (see Page 11), respectively. **White adipose tissue (WAT)** is found throughout the body, primarily under the skin (subcutaneous fat that has low adverse effects and may even be protective against metabolic syndrome) as well as in larger deposits in the abdomen (visceral fat that is associated with insulin resistance and increased risk of metabolic disease). White adipocytes act as storage cells for neutral triacylglycerols, storing excess calories for use in times of scarcity. WAT contributes to whole body insulation and actively communicates with key organs to maintain metabolic homeostasis by secreting adipokines.

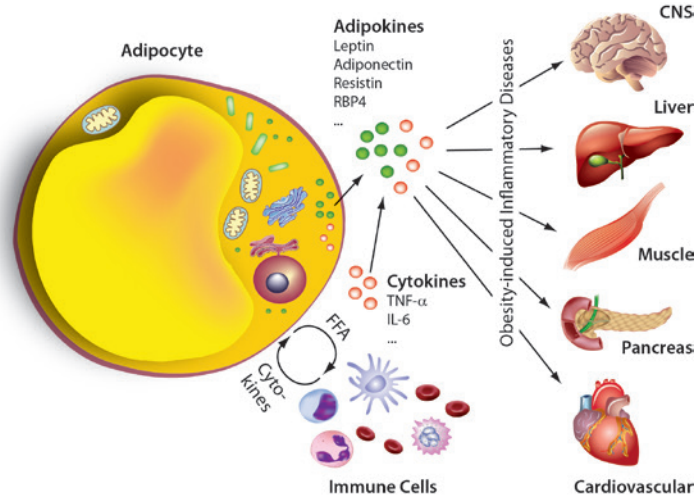

FIGURE: Schematic interaction between adipocytes and immune cells.
Adapted from H. Cao; J. Endocrinol. ***220,*** *T47 (2014)*

Adipokines are defined generally as biologically active substances produced in white adipose tissue (WAT) that act in an autocrine/paracrine or endocrine fashion and communicate with the brain, heart, vasculature, liver, gut and muscle. Some adipokines are produced exclusively or predominantly by adipose tissue, whereas others may be produced in a variety of different tissues. The diversity of the adipokines is considerable, in terms of both, protein structure and function. Adipokines include classical cytokines (e.g. TNF-α, IL-6), chemokines (e.g. MCP-1), proteins of the alternative complement system (e.g. Adipsin), proteins involved in vascular hemostasis (e.g. PAI-1), the regulation of blood pressure (Angiotensinogen), lipid metabolism (e.g. RBP4), glucose homeostasis (e.g. Adiponectin, Leptin, Nampt/Visfatin, Resistin, Vaspin, Omentin, Lipocalin-2, Apelin, DPP-4, CTRPs, selected ANGPTLs), angiogenesis (e.g. VEGF, NGF) and lipid mobilization (Zinc-α-2-glycoprotein). Adipokines have either pro-inflammatory or anti-inflammatory activities and exhibit a wide range of functions including the regulation of food intake and body weight homeostasis, insulin sensitivity, cell proliferation and angiogenesis, immunity, inflammation or vascular homeostasis. During obesity, adipokines are dysregulated and create a state of **chronic low-grade inflammation** responsible for the different obesity-linked pathologies and the onset of insulin resistance **(see Page 7)**. Although **brown adipose tissue (BAT)** also produces adipokines, the endocrine role of BAT in metabolic diseases is not fully investigated **(see Page 11)**. A growing interest in adipokines and myokines as biomarkers of low-grade inflammation and metabolic diseases emerges.

SELECTED REVIEWS: Beige Adipocyte as the Flame of White Adipose Tissue: Regulation of Browning and Impact of Obesity: A.E. Altinova; J. Clin. Endocrinol. Metab. **107,** e1778 (2022) • The Crosstalk between Gut Microbiota and White Adipose Tissue Mitochondria in Obesity: L. Colangeli, et al.; Nutrients **15,** 1726 (2023) • Brown Adipose Tissue - A Translational Perspective: A.C. Carpentier, et al.; Endocr. Rev. **44,** 143 (2023) • Adipokines in obesity and metabolic-related-diseases: J. Pestel, et al.; Biochimie 212, **45** (2023)

Selected Obesity-related Proteins & Antibodies

PROTEINS	PID
CTHRC1 (human) (rec.)	AG-40B-0157
CTHRC1 (mouse) (rec.)	AG-40B-0154
FABP1 (human) (rec.) (His)	AG-40A-0039T
FABP3 (human) (rec.) (untagged)	AG-40B-6002
FABP4 (human) (rec.) (His)	AG-40A-0035
FTO (human) (rec.) (His)	AG-40A-0112
FTO (mouse) (rec.) (His)	AG-40A-0127
IDO (human) (rec.) (His) (highly active)	AG-40B-0161
NAD Kinase (human) (rec.) (His) (highly active)	AG-40T-0091
NMNAT1 (human) (rec.) (His) (highly active)	AG-40T-0092
NMNAT3 (human) (rec.) (His) (highly active)	AG-40T-0093
Omentin (human) (rec.)	AG-40B-0042
PEDF (human) (rec.)	AG-40B-0077
PEDF (mouse) (rec.)	AG-40B-0118

ANTIBODIES	PID
FABP3 (human), pAb	AG-25A-0040
FABP4 (human), pAb	AG-25A-0041
FTO (human), mAb (AG103)	AG-20A-0092
FTO (mouse), mAb (FT62-6)	AG-20A-0083
IDO1 (human), mAb (ID 177)	AG-20A-0035
IDO1 (mouse), pAb	AG-25A-0032
MPC-2, mAb (JCM-1)	AG-20B-0071
NMNAT2 (human), mAb (Nady-1)	AG-20A-0087
Obestatin (human), pAb	AG-25A-0043
PEDF (human), mAb (rec.) (Serpy-1-4)	AG-27B-0014
RELM-β (mouse), mAb (MRB 46L)	AG-20A-0026
Stearoyl-CoA Desaturase-1 (mouse), pAb	AG-25A-0031
TDO (human), pAb	AG-25A-0106
TRB-3 (human), pAb	AG-25A-0059

A Complete Panel of Proteins & Antibodies is available on www.adipogen.com

KEY Adipokines: Novel Biomarkers and Regulators of Diabetes, Obesity, Insulin Resistance and Inflammation

Acyl-CoA-binding Protein [ACBP; Diazepam-binding Inhibitor]

Acyl-coenzyme A (CoA)-binding protein (ACBP) plays a role as an intracellular carrier of acyl-CoA esters and regulates lipid metabolism in the cytoplasm of most cell types. ACBP levels correlate with human body mass index (BMI). Increasing ACBP levels in mice trigger lipogenesis, food intake and weight gain and neutralization of ACBP increases lipolysis, reduces food intake post-starvation and causes weight loss in mice. Obese patients exhibit elevated plasma levels of ACBP. A reduction in the ACBP mRNA and ACBP plasma protein levels is observed in these patients after a substantial weight loss. In humans, ACBP levels increase in the context of aging, obesity, uncontrolled infection or cardiovascular, inflammatory, neurodegenerative and malignant diseases.

ELISA KITS	THE STANDARDS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
NEW Acyl-CoA-binding Protein (human) ELISA Kit		AG-45B-0019	96 wells	30 pg/ml	0.03125 to 2 ng/ml	C, P, S
RECOMBINANT PROTEINS		**PID**	**SIZE**	**SOURCE**	**ENDOTOXIN**	**SPECIES**
Acyl-CoA-binding Protein (human) (rec.) (His)		AG-40B-0197	50 µg | 3 x 50 µg	E. coli	<0.01EU/µg	Hu

Adiponectin

Adiponectin is an important adipocyte-derived anti-inflammatory hormone that regulates metabolism of lipids and glucose. Its receptors (AdipoR1, AdipoR2, T-cadherin) appear to exert actions in peripheral tissues by activating the AMP-activated protein kinase, p38-MAPK, PPARα and NF-κB and exerting a wide range of beneficial physiological actions, including anti-diabetic, anti-inflammatory, anti-atherosclerotic and cardioprotective effects. Adiponectin is the most abundant adipokine in the circulation and its levels are substantially altered in obesity, type 2 diabetes, cardiovascular disease, nonalcoholic fatty liver disease (NAFLD), obesity-related inflammation and various cancers.

ELISA KITS	THE STANDARDS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
Adiponectin (human) ELISA Kit		AG-45A-0001Y	96 wells | 2 x 96 wells	100 pg/ml	0.5 to 32 ng/ml	C, P, S, U
Adiponectin (mouse) ELISA Kit		AG-45A-0004Y	96 wells | 2 x 96 wells	50 pg/ml	0.125 to 8 ng/ml	C, P, S
Adiponectin (rat) ELISA Kit		AG-45B-0026	96 wells	50 pg/ml	0.0625 to 4 ng/ml	C, P, S
RECOMBINANT PROTEINS		**PID**	**SIZE**	**SOURCE**	**ENDOTOXIN**	**SPECIES**
Adiponectin (human) (rec.)		AG-40B-0030	50 µg	HEK 293 cells	<0.01EU/µg	Hu
Adiponectin (mouse) (rec.)		AG-40B-0026	50 µg	HEK 293 cells	<0.01EU/µg	Ms

Nampt [Visfatin; PBEF]

Nicotinamide phosphoribosyltransferase (NAMPT) is a regulator of the intracellular NAD^+ pool. Through its NAD^+-biosynthetic activity, NAMPT influences the activity of NAD^+-dependent enzymes, thereby regulating cellular metabolism. In addition to its enzymatic function, extracellular NAMPT (also called Visfatin or PBEF1) has cytokine-like activity. Altered levels are associated with various metabolic disorders, including obesity, nonalcoholic fatty liver disease (NAFLD) and type 2 diabetes by influencing the oxidative stress response, apoptosis, lipid and glucose metabolism, inflammation and insulin resistance. NAMPT plays a crucial role in cancer cell metabolism and is often overexpressed in tumor tissues, making it an attractive therapeutic cancer drug target.

ELISA KITS	THE STANDARDS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
Nampt (human) ELISA Kit		AG-45A-0006Y	96 wells | 2 x 96 wells	30 pg/ml	0.125 to 8 ng/ml	S
Nampt (human) (IntraCellular) ELISA Kit		AG-45A-0008Y	96 wells | 2 x 96 wells	30 pg/ml	0.25 to 16 ng/ml	L
Nampt (mouse/rat) Dual ELISA Kit		AG-45A-0007Y	96 wells | 2 x 96 wells	50 pg/ml	0.5 to 32 ng/ml	S
RECOMBINANT PROTEINS		**PID**	**SIZE**	**SOURCE**	**ENDOTOXIN**	**SPECIES**
Nampt (human) (rec.)		AG-40A-0031Y	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Hu
Nampt (mouse) (rec.) (enzymatically active)		AG-40B-0179	50 µg	HEK 293 cells	<0.01EU/µg	Ms
Nampt (mouse) (rec.)		AG-40A-0056Y	10 µg | 3 x 10 µg	CHO cells	<0.01EU/µg	Ms
POTENT INHIBITORS		**PID**	**SIZE**			
CHS-828		AG-CR1-0064	5 mg | 25 mg			
FK-866		AG-CR1-0011	1 mg | 5 mg			

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SAMPLES: C: Cell Culture Supernatant, **P:** Plasma, **S:** Serum; **U:** Urine; **L:** Cell Lysate; **F:** CSF
APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot
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Retinol-binding Protein 4 [RBP4]

The physiological role of RBP4 is the transport of retinol from the liver to peripheral tissues. RBP4 is produced in hepatocytes and adipocytes. Excessive visceral fat accumulation, followed by the development of inflammation and consequently a hormonal adipose tissue dysfunction is in direct relation with excessive RBP4 expression, orchestrated by GLUT4. Circulating RBP4 inhibits the signal pathways stimulated by insulin in skeletal muscle cells, resulting in the development of insulin resistance. Altered levels are associated with various metabolic disorders, including obesity, cardiovascular disease, nonalcoholic fatty liver disease (NAFLD) and type 2 diabetes.

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
RBP4 (human) ELISA Kit (Quantitative)	AG-45A-0035Y	96 wells | 2 x 96 wells	380 pg/ml	0.39 to 25 ng/ml	C, P, S, U
RBP4 (human) Competitive ELISA Kit	AG-45A-0010Y	96 wells | 2 x 96 wells	1 ng/ml	0.001 to 5 µg/ml	C, P, S, U
RBP4 (mouse/rat) Dual ELISA Kit	AG-45A-0012Y	96 wells | 2 x 96 wells	60 pg/ml	0.188 to 12 ng/ml	C, S, U

Vaspin [Visceral Adipose Tissue-derived Serpin; Serpin A12]

Vaspin, a serine protease inhibitor, is an insulin-sensitizing adipokine that has been isolated from both visceral and subcutaneous white adipose tissue. Vaspin is suggested to regulate immune responses and inflammation and was found to be correlated with various metabolic parameters. Vaspin represents a novel biomarker for obesity and impaired insulin sensitivity and might serve as a new therapeutic target of metabolic syndrome diseases, such as obesity-related insulin resistance and inflammation.

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
Vaspin (human) ELISA Kit	AG-45A-0017Y	96 wells | 2 x 96 wells	12 pg/ml	0.016 to 1 ng/ml	C, P, S
RECOMBINANT PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Vaspin (human) (rec.)	AG-40A-0064Y	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Hu
Vaspin (mouse) (rec.)	AG-40A-0094Y	10 µg | 3 x 10 µg	HEK 293 cells	<0.1EU/µg	Ms
ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Vaspin (human), mAb (VP63)	AG-20A-0045	50 µg | 100 µg	Mouse IgG1κ	IHC, WB	Hu
anti-Vaspin (mouse), pAb	AG-25A-0075	100 µg	Rabbit	WB	Ms

Zinc-α-2-glycoprotein [ZAG]

Zinc-α-2-glycoprotein (ZAG) is expressed in the major white fat depots and in the interscapular brown fat of mice defining it as an adipokine. ZAG has been shown to stimulate lipolysis in *in vitro* and *in vivo* experiments. Data from genetic studies suggest that ZAG may be a candidate gene for body weight regulation. ZAG is up-regulated in urine from diabetic patients and is reported to be associated with several diseases, such as cancers, metabolic syndrome and acute sepsis.

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
Zinc-α-2-glycoprotein (human) TurboELISA™ Kit	AG-48B-1000	96 wells	0.23 ng/ml	0.9375 to 60 ng/ml	C, P, S
Zinc-α-2-glycoprotein (human) Matched Pair Detection Set	AG-46B-0008	5 x 96 wells	100 pg/ml	0.0156 to 1 ng/ml	C, P, S
RECOMBINANT PROTEIN	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Zinc-α-2-glycoprotein (human) (rec.) (untagged)	AG-40B-0146	10 µg | 50 µg | 3 x 50 µg	E. coli	<0.1EU/µg	Hu

A Complete Panel of ACBP, Adiponectin, Nampt/Visfatin, RBP4, Vaspin and ZAG Proteins & Antibodies is available on www.adipogen.com

Insulin – Key Biomarker for Type I and Type II Diabetes

Glucose is the main fuel for the human body and blood glucose values are tightly regulated in healthy individuals. Regulation of glucose uptake in cells is performed by the hormone called insulin which is glucose-responsively secreted from pancreatic β cells. When the glucose concentration in the blood is increased, insulin lowers it by increasing glucose uptake by muscle, liver and fat cells. Insulin mediates its signal through the insulin receptor (IR), but also through its highly homologous insulin-like growth factor 1 receptor (IGF1R). Binding of insulin on IR or IGF1R results in the phosphorylation of insulin receptor substrate 1/2 (IRS1/2) at its tyrosine residues and in the subsequent activation of two main pathways, PI3K/AKT pathway and the MAPK pathway. Once secreted from the pancreatic β cells, insulin circulates in the bloodstream with an approximate half-life of 12 min. Insulin causes the translocation of GLUT-4 from intracellular vesicles to the cell membrane and, thus, increases the rate of glucose entry for a given concentration into the target tissue. Insulin deficiency or resistance are hallmarks of variants of diabetes mellitus, which can be subdivided into the insulin-dependent (type 1) and non-insulin-dependent (type 2) diabetes, both of which can cause severe hyperglycemia. Immune cells express insulin receptors following activation and insulin mediates an anti-inflammatory effect in a range of clinical settings.

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
NEW Insulin (human) ELISA Kit	AG-45B-0031	96 wells	10 pg/ml	7.81 to 500 pg/ml	C, P, S

NEW

Isthmin-1 (ISM1) – A New Insulin-like Adipokine

Recent studies have found that ISM1 can lower blood glucose, inhibit insulin-regulated lipid synthesis, promote protein synthesis and affect the body's glucolipid and protein metabolism. In addition, ISM1 plays an important anti-tumor role promoting apoptosis and anti-angiogenesis and by regulating multiple inflammatory pathways to influence the body's immune response.

SELECTED REVIEWS: A brief overview about the adipokine: Isthmin-1: M. Hu, et al.; Front. Cardiovasc. Med. **9,** 939757 (2022) • Advances in research of biological functions of Isthmin-1: L. Menghuan, et al.; J. Cell Commun. Signal. **17,** 507 (2023)

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
Isthmin-1 (human) ELISA Kit	AG-45B-0032	96 wells	*COMING SOON!*		
RECOMBINANT PROTEINS	**PID**	**SIZE**	**SOURCE**	**ENDOTOXIN**	**SPECIES**
NEW Isthmin-1 (human) (rec.) (His)	AG-40B-0214	50 µg | 3 x 50 µg	HEK 293 cells	<0.01EU/µg	Hu
NEW Isthmin-1 (mouse) (rec.) (His)	AG-40B-0215	50 µg | 3 x 50 µg	HEK 293 cells	<0.01EU/µg	Ms
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE/SOURCE**	**APPLICATION**	**SPECIES**
NEW anti-Isthmin-1, mAb (rec.) (Giusepi-1-4)	AG-27B-0022	100 µg	Mouse IgG2bλ	ELISA, WB	Hu, Ms

Glucose Transporter Family – GLUTs

GLUT1 and GLUT2 belong to the family of glucose transporters (GLUTs). GLUT1 is a pivotal rate-limiting element in the transport of glucose in malignancy cells and is overexpressed in different types of human cancers. GLUT1 is involved in the progression and metastasis of cancer cells. In pancreatic β cells, GLUT2 is required for glucose-stimulated insulin secretion. GLUT2-dependent glucose-sensing controls feeding, thermoregulation and pancreatic islet cell mass and function, as well as sympathetic and parasympathetic activities.

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
NEW anti-GLUT1, pAb (IN116)	AG-25B-0040	50 µg	Rabbit	IHC, IP, WB	Hu, Ms, Rt
NEW anti-GLUT2 (human), pAb (IN117)	AG-25B-0041	50 µg	Rabbit	IHC, IP, WB	Hu, Ms, Rt
NEW anti-GLUT2 (mouse), pAb (IN118)	AG-25B-0042	50 µg	Rabbit	IHC, IP, WB	Hu, Ms, Rt
NEW anti-GLUT2 (rat), pAb (IN119)	AG-25B-0043	50 µg	Rabbit	IHC, IP, WB	Hu, Ms, Rt

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Obesity & Immunometabolism

During **obesity,** excess fat accumulates in adipose tissue leading to low-grade chronic inflammation. Obesity is a major risk factor for many metabolic diseases, especially diabetes and cardiovascular diseases, increasing the risk of hypertension, hyperglycemia and dyslipidemia, recognized as the **metabolic syndrome**. Obesity is also linked to a broad spectrum of pathological disorders including neurodegenerative diseases, airway disorders and cancer.

Dysregulation in **adipokines secretion**, adipocyte mitochondrial dysfunction, alteration in the gut microbiota composition are among factors involved in the development of obesity and its associated metabolic disorders. During obesity, a modulation of immune cells is observed (see below section immunometabolism and **Figure**). In **lean healthy adipose tissue**, Th2 cells and eosinophils secrete Th2 cytokines IL-4, IL-10 and IL-13 leading to an anti-inflammatory macrophage M2 phenotype, ensuring tissue remodeling. In **obese adipose tissue**, overnutrition leads to bigger adipocytes, which coupled with various cellular stress consequently leads to the recruitment of different immune cells and the development of a pro-inflammatory environment.

Immunometabolism describes the ability of the immune system to communicate and coordinate systemic metabolic homeostasis. Immunometabolism can be studied at macroscopic level, the whole-body metabolism and at microscopic level, the cellular bio-energetics of immune cells. Adipose tissue illustrates best the interdependency of both arms of immunometabolism (whole-body metabolism and the microscopic metabolism) and provides examples of changes in both the lean and obese states (see **Figure**). Lean adipose tissue is characterized by an enrichment of immune cells whose phenotype and cytokine profiles maintain a state of type 2 immunity necessary for the health of the tissue. Obesity is characterized by an accumulation of inflammatory immune cells and loss of protective lymphocytes due to change in the composition of fatty acids, glucose and oxygen availability that may provide different metabolic substrates to immune cells and adipocytes.

SELECTED REVIEWS: Extrinsic and Intrinsic Immunometabolism Converge: Perspectives on Future Research and Therapeutic Development for Obesity: H.L. Caslin & A.H. Hasty; Curr. Obes. Rep. **3,** 210 (2019) • Obesity: a neuroimmunometabolic perspective: C.M. Larabee, et al.; Nat. Rev. Endocrinol. **16,** 30 (2020) • Adipose tissue macrophages: Regulators of adipose tissue immunometabolism during obesity: S.A. Nance, et al.; Mol. Metab. **66,** 101642 (2022)

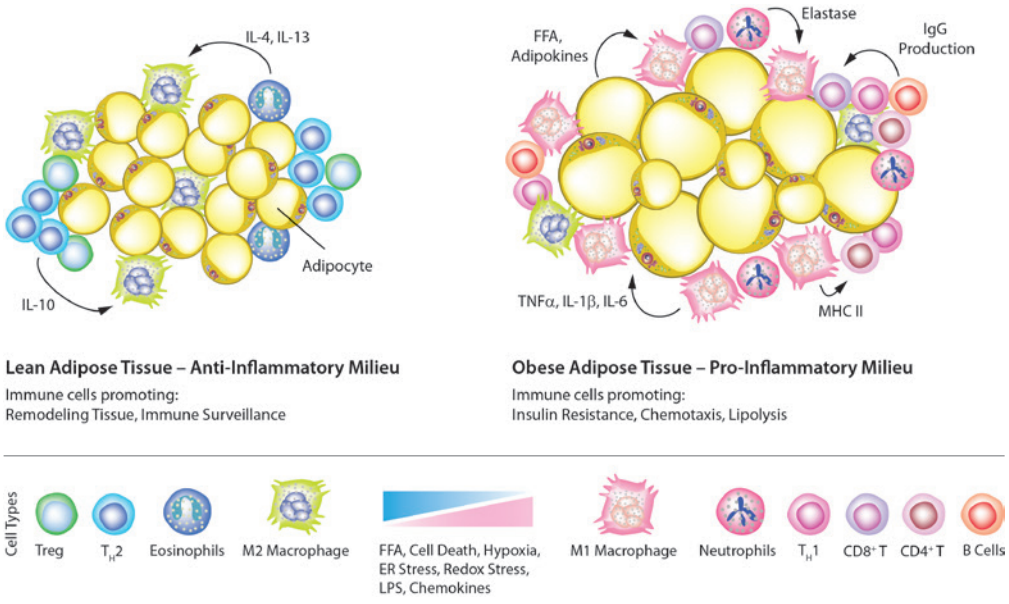


FIGURE: Modulation of immunometabolism during obesity.

*Adapted from H.L. Kammoun, et al.; Rev. Endocr. Metab. Disord. **15,** 31 (2014)*

Immunometabolism Modulators

AdipoGen Life Sciences offers a broad range of small molecule modulators of glycolysis, TCA cycle, fatty acid oxidation, fatty acid synthesis and amino acid pathways, as well as IDO1 and Nampt inhibitors.

Atpenin A5 (synthetic) (OXPHOS inhibitor) BULK
AG-CN2-0100 — 250 µg | 1 mg

Heptelidic acid (GAPDH inhibitor) UNIQUE
AG-CN2-0118 — 250 µg | 1 mg

Itaconate (PFKII and SDH inhibitor) BULK
AG-CN2-0426 — 1 g | 5 g

STF-31 (Nampt inhibitor) NEW
AG-CR1-3693 — 1 mg | 5 mg | 25mg

Download from our Website or ask for the Immunometabolism Brochure!

IL-36 – IL-37 – IL-38 in Obesity, Diabetes & Metabolic Diseases

The interleukin 1 (IL-1) family and their receptors are a group of cytokines crucially involved in modulating innate immunity and inflammation, regulating immune responses to infectious challenges and sterile insults and emerging as critical factors in insulin resistance, obesity and diabetes. This protein family consists of IL-1α and IL-1β, IL-18, IL-33, several IL-36 isoforms, IL-37, IL-38 and the two IL-1R antagonist (IL-1Ra) and IL-36Ra. To gain biological activity IL-1β and IL-18 require processing by the protease caspase-1 which is associated with the multi-protein complex inflammasome (see below). IL-33 has been implicated in adipose tissue homeostasis **(see Page 9)**. IL-36, IL-37 and IL-38 are new members of the IL-1 family, play an indispensable role in the regulation of immune system homeostasis and are involved in the pathogenesis of inflammatory and autoimmune diseases, and abnormal expression of IL-36, IL-37 and IL-38 has been reported in diabetes and obesity. The pro-inflammatory cytokine IL-36 has been implicated in obesity-associated inflammation and a protective role of the IL-36 family of cytokines in obesity and metabolic diseases, in reducing blood sugar levels suggested. The anti-inflammatory cytokines IL-37 and IL-38 have been attributed a modulatory role in obesity-induced inflammation and insulin resistance.

LIT: IL-1 family members in the pathogenesis and treatment of metabolic disease: Focus on adipose tissue inflammation and insulin resistance: D.B. Ballak, et al.; Cytokine **75,** 280 (2015) • The Emerging Roles of IL-36, IL-37, and IL-38 in Diabetes Mellitus and its Complications: G. Huang, et al.; Endocr. Metab. Immune Disord. Drug Targets **22,** 997 (2022)

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
IL-1β (human) ELISA Kit	AG-45B-0021	96 wells	0.7 pg/ml	1.5625 to 100 pg/ml	C, P, S
IL-36α (human) ELISA Kit	AG-45B-0013	96 wells	4 pg/ml	7.8 to 500 pg/ml	C, P, S
IL-36γ (human) ELISA Kit	AG-45B-0008	96 wells	3 pg/ml	3.9 to 250 pg/ml	C, S
IL-36β (human) Matched Pair Detection Set	AG-46B-0009	5 x 96 wells	10 pg/ml	15.6 to 1000 pg/ml	C
IL-36Ra (human) Matched Pair Detection Set	AG-46B-0006	5 x 96 wells	0.5 ng/ml	0.78 to 50 ng/ml	C
IL-37 (human) ELISA Kit	AG-45A-0041	96 wells | 2 x 96 wells	10 pg/ml	0.016 to 1 ng/ml	P, S
IL-38 (human) Matched Pair Detection Set	AG-46B-0007	5 x 96 wells	20 pg/ml	0.031 to 2 ng/ml	C, P, S
RECOMBINANT PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
IL-37 (human) (monomeric):Fc-KIH	AG-40B-0221	10 µg | 100 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms
IL-38 (aa 1-152) (human) (monomeric):Fc-KIH	AG-40B-0241	10 µg | 100 µg	HEK 293 cells	<0.01EU/µg	Hu
IL-38 (aa 20-152) (human) (monomeric):Fc-KIH	AG-40B-0226	10 µg | 100 µg	HEK 293 cells	<0.01EU/µg	Hu
IL-38 (aa 3-152) (mouse) (monomeric):Fc-KIH	AG-40B-0227	10 µg | 100 µg	HEK 293 cells	<0.01EU/µg	Hu

Visit our Website for a Complete Range of IL-1 Family Related Reagents!

Obesity, Diabetes & Inflammasomes

Aberrant inflammasome activation is implicated in chronic inflammation that leads to the development of many diseases as they play a crucial role in regulating the immune response and the production of proinflammatory cytokines. Targeting inflammasomes has become a promising strategy for the treatment of a variety of diseases, including metabolic diseases (such as type II diabetes, obesity or cardiovascular diseases).

SAMPLES: C: Cell Culture Supernatant, **P:** Plasma, **S:** Serum; **U:** Urine; **L:** Cell Lysate; **F:** CSF
APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot
FORMULATION: PF = Preservative free **SPECIES: Dg** = Dog; **Hu** = Human; **Mo** = Monkey; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit

IL-33 – Guardian of Adipose Tissue Homeostasis

Lean adipose tissue contains adipocytes, regulatory immune cells and adipose stroma that contribute to fat tissue homeostasis. Adipocytes of lean tissue secrete adipokines (e.g. adiponectin, an anti-inflammatory protein), which play important roles in immunometabolism and on immune cell behavior. Various immune cells are implicated in lean adipose tissue remodeling, such as iNKT cells, eosinophils, ILC2s and Tregs. These immune cells maintain homeostasis, preserving insulin sensitivity and glucose tolerance and keeping adipose tissue macrophages in an anti-inflammatory, M2-like state [1] (see **Figure**).

During high-fat diet and obesity, fat cells increase (hypertrophy) producing less adiponectin and more pro-inflammatory molecules such as leptin, IL-6 and MCP-1. Inflammatory immune cells such as neutrophils or NK cells detect adipose stress and secrete IFN-γ, driving pro-inflammatory M1 macrophage differentiation leading to a chronic inflammatory state.

IL-33, a cytokine abundantly expressed by adipose tissue stroma, is of particular importance for adipose homeostasis. Although upon infection and allergy, IL-33 is classified as a pro-inflammatory mediator, under non-inflammatory conditions, IL-33 sustains Tregs, eosinophils, as well as ILC2 to keep an anti-inflammatory state in adipose tissue (see **Figure**). IL-33 is also involved in the formation of brown adipocytes from adipocyte precursors by a mechanism involving IL-13 and the endogenous opioid Met-Enkephalin secreted by activating ILC2s [2]. A direct negative role of IL-33 on adipocyte differentiation has been reported recently [3]. IL-33 works toward the resolution of inflammation and metabolic alterations associated with obesity, and IL-33 is key to the homeostasis of fat tissues not only in healthy conditions, but also in pathological settings such as obesity.

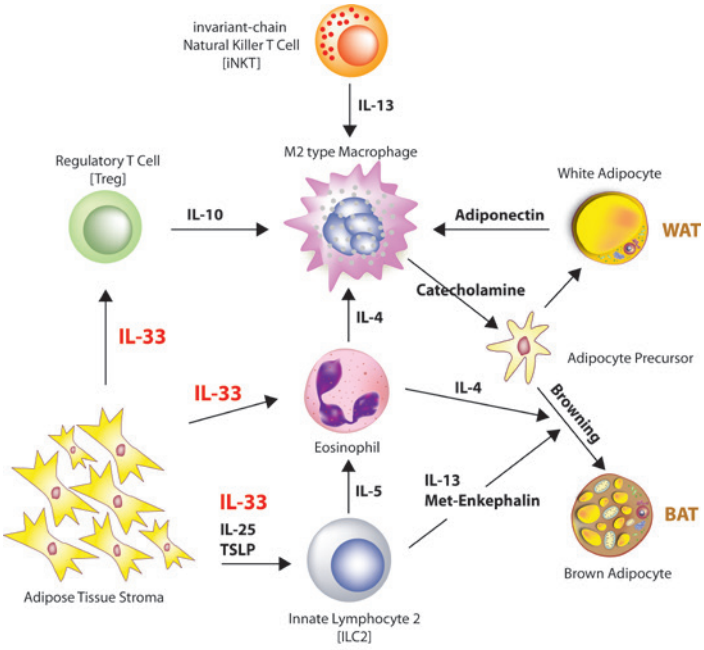


FIGURE: Role of IL-33 in the control of adipose tissue homeostasis.

LIT: [1] ILC2s chew the fat: R.R. Ricardo-Gonzalez & R.M. Locksley; J. Exp. Med. **216,** 1972 (2019) • **[2]** IL-33 in obesity: where do we go from here? M.F.A. de Oliveira, et al.; Inflamm. Res. **68,** 185 (2019) • **[3]** Regulation of de novo adipocyte differentiation through crosstalk between adipocytes and pre-adipocytes: T.D. Challa, et al.; Diabetes **64,** 4075 (2015)

UNIQUE

Highly Active IL-33 Proteins

IL-33 (oxidation resistant) (human) (rec.)

AG 40B-0160	Untagged	10 µg | 100 µg
AG-40B-0167	His-Tag	10 µg | 100 µg

LIT: Oxidation of the alarmin IL-33 regulates ST2-dependent inflammation: E.S. Cohen, et al.; Nat. Commun. **6,** ID8327 (2015)

Monomeric & Prolonged Half-life

NEW IL-33 (oxidation resistant) (human) (monomeric): Fc-KIH (human) (rec.)

AG-40B-0233	Fc-KIH	50 µg

IL-33 & Prolonged Half-life

NEW HpARI (CCP1/2) (rec.) (His)

AG-40B-0201	His-Tag	50 µg | 3 x 50 µg

HpARI (Alarmin Release Inhibitor) (rec.) (His)

AG-40B-0178	His-Tag	50 µg | 3 x 50 µg

UNIQUE

Antibody Inhibiting the Binding of Mouse IL-33 to ST2/IL-1RAcP

IL-33 (mouse), mAb (rec.) (blocking) (Bondy-1-1)

AG-27B-0013		100 µg
AG-27B-0013PF	Preservative Free	100 µg | 500 µg | 1mg

LIT: Regulation of de novo adipocyte differentiation through crosstalk between adipocytes and pre-adipocytes: T.D. Challa, et al.; Diabetes **64,** 4075 (2015)

BEST ST2 Antibody for FACS

anti-ST2 (human), pAb

AG-25A-0058		100 µg
AG-25A-0058YTD	ATTO 488	100 tests
AG-25A-0058YTS	ATTO 647N	100 tests

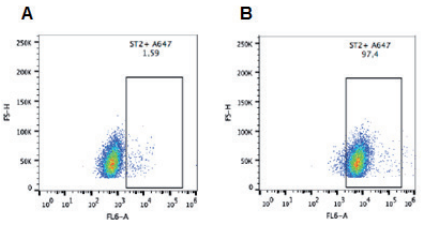


FIGURE: Detection of endogenous human ST2 with anti-ST2 (human), pAb (AG-25A-0058).

METHOD: THP1 cells were stained with anti-ST2 (human), pAb (1:100 in PBS + 2% FCS) (Figure B) or with the secondary antibody alone (Figure A) for 1h at 4°C.

Obesity & Angiogenesis

Adipose tissue is the most dynamic and plastic organ in adults. Upon exposure to different metabolic challenges, adipose tissue has the capacity to either expand or shrink according to the nutrient status. Elasticity of adipose tissue is tightly related with angiogenesis, the growth of new blood vessels, and angiogenesis plays an essential role in the modulation of adipogenesis and obesity. In growing adipose tissue, the new blood vessels contribute to adipogenesis by performing multiple functions, such as providing nutrients and oxygen to nourish adipocytes, removing waste products from the adipose tissue, carrying monocytes and neutrophils that can affect adipocyte function and also providing adipose precursors and stem cells [1].

There exist several pro-angiogenic factors secreted by adipocytes, such as leptin, adiponectin, vascular endothelial growth factor-A (VEGF-A), VEGF-B and angiopoietins (mainly ANG-1 and ANG-2) that function by stimulating proliferation and migration of endothelial cells. An, et al. (2017) demonstrated that angiopoietin-2 (ANG-2) overexpression induces a pro-angiogenic program in white adipose tissue (WAT), protecting against high fat diet (HFD)-induced metabolic challenges. Decreasing the angiopoietin-2 levels using **a neutralization antibody (anti-Angiopoietin-2, mAb (rec.) (blocking) (Angy-2-1) (AG-27B-0016PF))** confirms the beneficial effects of endogenous ANG-2. Mechanistically, increasing vascular function and decreasing adipose tissue inflammation contribute to the beneficial effects of ANG-2. Due to the essential role of angiogenesis in the modulation of adipogenesis and obesity, anti-angiogenesis therapy has emerged as a potential treatment for obesity.

LIT: [1] Angiogenesis in adipose tissue and obesity: S. Corvera, et al.; Angiogenesis **25,** 439 (2022) • **[2]** Angiopoietin-2 in white adipose tissue improves metabolic homeostasis through enhanced angiogenesis: Y.A. An, et al.; Elife **29,** 6 (2017)

NEW

Potent ANG-2 Blocking Antibodies

anti-Angiopoietin-2, mAb (rec.) (blocking) (Angy-2-1) (preservative free)
AG-27B-0016PF — 100 µg | 500 µg | 1mg

anti-Angiopoietin-2 (human), mAb (rec.) (blocking) (Angy-1-4) (preservative free)
AG-27B-0015PF — 100 µg | 500 µg | 1mg

Also Available:

Angiopoietin-2 (human) (rec.) AG-40B-0114

Angiopoietin-2 (mouse) (rec.) AG-40B-0131

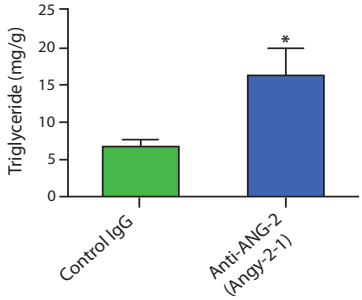


FIGURE: Antagonizing Angiopoietin-2 *in vivo* with anti-ANG-2, mAb (rec.) (blocking) (Angy-2-1) (AG-27B-0016PF) increases triglyceride levels.

METHOD: After High Fat Diet (HFD) challenges for five weeks in wild-type C57BL/6 mice, control IgG (left panel) or anti-ANG-2 (Clone Angy-2-1) blocking antibody (right panel) (4 µg/g body weight; twice/week) were administrated and afterwards the mice underwent metabolic analyses of the triglycerides levels from both groups.

Vascular Endothelial Growth Factor [VEGF]-related Reagents

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
VEGF 164 (mouse) (rec.)	AG-40T-0044	5 µg | 20 µg	Sf9 cells	n.d.	Ms
VEGF 165 (human) (rec.)	AG-40T-0043	5 µg | 20 µg	E. coli	n.d.	Hu
VEGF 165 (human) (rec.)	AG-40T-0045	5 µg | 20 µg	Sf9 cells	n.d.	Hu
VEGFR-1, Soluble (human) (rec.)	AG-40T-0049	5 µg | 20 µg	Sf9 cells	n.d.	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
VEGF-A (human), mAb (3(6D3))	AG-20T-0105	200 µg	Mouse IgG1	ELISA, WB, FUNC	Hu
VEGFR-1 (human), mAb (EWC)	AG-20T-0106	100 µg	Mouse IgG1	ELISA, WB	Hu
VEGFR-1 (human), mAb (EWF)	AG-20T-0107	100 µg	Mouse IgG1	ELISA, IP, WB	Hu

A Complete Panel of Angiogenesis-related Reagents is available on www.adipogen.com

AdipoGen® LIFE SCIENCES

APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot
FORMULATION: PF = Preservative free **SPECIES: Dg** = Dog; **Hu** = Human; **Mo** = Monkey; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit

Factors that Regulate WAT Browning and Thermogenesis

Brown adipose tissue (BAT) found in hibernating animals, also exists in human where it represents 1% to 2% of fat and is found in the cervical, axillary and paraspinal regions. Beige/brite adipose tissue is a type of white fat tissue interspersed within WAT that are capable of transforming into brown-like adipocytes through transdifferentiation following cold exposure, adrenergic or other stimulations. In contrast to white adipocytes, with large unilocular lipid droplets, brown and beige adipocytes have multilocular droplets and high mitochondrial density. Brown adipose tissue (BAT) is the main site of adaptive thermogenesis, using a specific brown fat protein, uncoupling protein 1 (UCP1) that dissipates the mitochondrial membrane potential energy as heat instead of producing ATP. The ability of BAT to protect against obesity and metabolic diseases has traditionally been attributed to its capacity to utilize glucose and lipids for thermogenesis. However, BAT might also have a secretory role, which could contribute to the systemic consequences of BAT activity. Several BAT-derived molecules (called Batokines) acting in a paracrine, autocrine or endocrine manner have been identified. These Batokines control expansion and activity of BAT and the extent of browning of white adipose tissue (see **Figure**). They also promote hypertrophy and hyperplasia of BAT, vascularization, innervation and blood flow, processes that are all associated with BAT recruitment when thermogenic activity is enhanced. Some **Batokines** also target peripheral tissues such as liver, pancreas, white adipose tissue, bone and heart, and affect systemic metabolism by interacting with the central nervous system (CNS).

REVIEWS: Beige Adipocyte as the Flame of White Adipose Tissue: Regulation of Browning and Impact of Obesity: A.E. Altinova, et al.; J. Clin. Endocrinol. Metab. **107,** e1778 (2022) • Browning of the white adipose tissue regulation: new insights into nutritional and metabolic relevance in health and diseases: S. Azevedo Machado, et al.; Nutr. Metab. **19,** 61 (2022) • Browning of Adipocytes: A Potential Therapeutic Approach to Obesity: V. Schirinzi, et al.; Nutrients **15,** 2229 (2023)

Overview of Important Batokines:

- **Fibroblast Growth Factor 21 (FGF-21)** is induced in BAT by cold exposure and induces the thermogenic program in brown adipocytes. FGF-21 is also expressed in organs such as liver or skeletal muscle. Metabolic benefits of FGF-21 include weight loss, glucose and lipid metabolism and insulin sensitivity. FGF-21 also acts directly in the brain.
- **Interleukin-6 (IL-6),** released by skeletal muscle and by BAT in response to exercise, promotes insulin sensitivity, is required for the induction of browning of WAT and acts on the pancreas and the brain (see page 10).
- **Nrg4 (Neuregulin-4)** is a cold-induced adipokine, highly expressed in adipose tissue, enriched in brown fat. It promotes neurite outgrowth and protects against diet-induced insulin resistance and hepatic steatosis through attenuating hepatic lipogenic signaling.
- **CTHRC1 (Collagen Triple Helix Repeat Containing 1)** is expressed in BAT but its role is still unclear.
- **Soluble form of the LDL Receptor (sLR11)** suppresses thermogenesis in brown adipocytes, by binding to BMP receptors, despite being increased by cold-induced activation in BAT.
- **Angiopoietin-like 8 (ANGPTL8 or Betatrophin)** is induced in BAT in response to cold. ANGPTL8 can repress the activity of lipoprotein lipase.
- **BMPs (Bone Morphogenetic Protein)** promote brown fat formation and act on the central nervous system to regulate thermogenesis.
- **VEGF-A and VEGF-B (Vascular Endothelial Growth Factor A and B)** regulate angiogenesis, thermogenesis and macrophage function (see page 7).
- **Slit2-C** activates a thermogenic PKA pathway in adipocytes.
- **Lipocalin Prostaglandin D Synthase (LPGDS)** synthesizes D-series prostaglandins. It is highly regulated in BAT and plays a role in lipid and carbohydrate utilization.
- **Adenosine** is released from BAT during stimulation of sympathetic nerves and activates a thermogenic program. Adenosine protects mice from diet-induced obesity.
- **Endocannabinoid system** and metabolites, such as **FFA (Free Fatty Acid), Retinaldehyde, Retinoic Acid** and **Lactate** are released from BAT and play a role in thermogenic activation.
- **Ependymin-related Protein 1 (EPDR1)** is a new batokine that is vital for development into a functional thermogenic adipocyte.

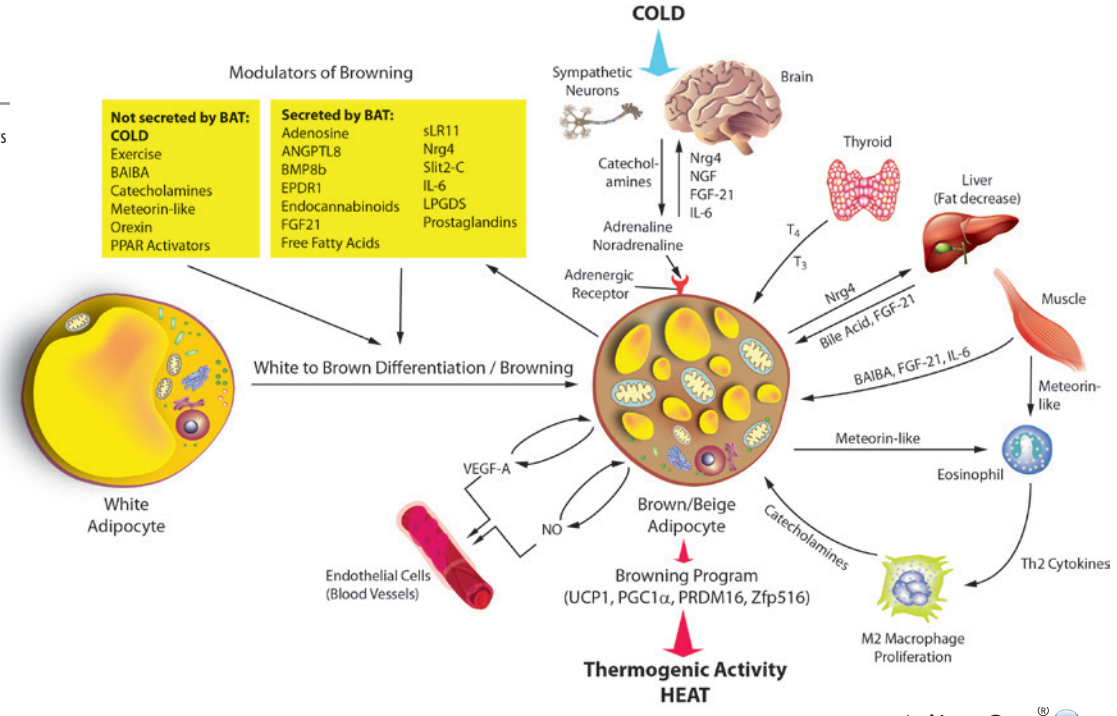


FIGURE: The autocrine and paracrine factors released by brown adipocytes.

Adapted from F. Villarroya, et al.; Nat. Rev. Endocrinol. ***13,*** *26 (2017)*

Browning Inducers not expressed by BAT:

- **Cold exposure** is a strong inducer of brown cells. Thermogenic activity is regulated by a canonical β-adrenergic receptor pathway via the sympathetic nervous system. The **TRPM8 channel** is a cold-sensing cation channel present in sensing neurons that has a role in detecting environmental temperature.
- **Catecholamines** activate β-adrenergic receptors at the surface of brown adipocytes and increase the intracellular cAMP level to activate the thermogenic program.
- **PPARs** are master regulators of adipogenesis. Recently, PPAR-γ activators thiazolidinediones were shown to promote WAT browning as well (see page 11).
- Cold-induced conversion of cholesterol to **Bile acid** shapes the gut microbiome and promotes adaptive thermogenesis.
- The neuropeptide **Orexin and its Receptors** are also involved in the induction of browning and affect brown fat thermogenesis.
- **Meteorin-like Protein** is a novel adipokine expressed by adipose tissue being downregulated upon caloric restriction. Meteorin-like is secreted by muscles during exercise and converts white adipose cells into brown fat tissue. This activation of fat browning is the consequence of a direct effect of meteorin-like on eosinophils in WAT that secretes IL-4 and IL-13, which promotes the activation of adipose tissue macrophages as well as the thermogenic program.
- **T3** (Triiodothyronine) and T4 exert effects locally to promote thermogenesis.
- **3-Aminoisobutyric acid (BAIBA)** is a browning molecule secreted from contracting muscles.

Protein Modulators & Inducers of Brown Adipose Tissue (BAT)

RECOMBINANT PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Betatrophin [ANGPTL8] (human):Fc (human) (rec.)	AG-40B-0145	10 µg | 3 x 10 µg	HEK 293 cells	<0.1EU/µg	Hu
Betatrophin [ANGPTL8] (mouse) (rec.)	AG-40B-0144	10 µg | 3 x 10 µg	CHO cells	<0.1EU/µg	Ms
Betatrophin [ANGPTL8] (mouse):Fc (human) (rec.)	AG-40B-0142	10 µg | 3 x 10 µg	HEK 293 cells	<0.1EU/µg	Ms
FGF-21 (human) (rec.)	AG-40A-0091Y	10 µg | 50 µg	HEK 293 cells	<0.1EU/µg	Hu
FGF-21 (human):Fc (human) (rec.)	AG-40A-0095	10 µg | 50 µg	HEK 293 cells	<0.1EU/µg	Hu
FGF-21 (mouse) (rec.)	AG-40B-0143	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Ms
FGF-21 (mouse) (rec.)	CHI-MF-102FGF21	50 µg	HEK 293 cells	<0.06EU/µg	Ms
FGF-21 (mouse):Fc (human) (rec.)	AG-40A-0097	10 µg | 50 µg	HEK 293 cells	<0.1EU/µg	Ms
Meteorin-like (mouse) (rec.)	AG-40B-0149	10 µg | 3 x 10 µg	HEK 293 cells	<0.1EU/µg	Ms
Neuregulin-4 (human) (rec.)	AG-40B-0155	10 µg | 3 x 10 µg	E. coli	<0.01EU/µg	Hu
Neuregulin-4 (mouse) (rec.)	AG-40B-0159	10 µg | 3 x 10 µg	E. coli	<0.01EU/µg	Hu, Ms
Slit2 (C fragment) (human) (rec.)	AG-40B-0168	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Hu

Various WAT/BAT Browning Inducers

YM-254890 (Potent and selective Gαq family inhibitor)
AG-CN2-0509 — 500 µg | 1 mg

3-Aminoisobutyric acid (Contraction-induced myokine)
AG-CR1-3596 — 250 mg | 1 g

Harmine (UCP1-dependent thermogenesis inducer)
AG-CN2-0510 — 10 mg | 50 mg | 250 mg

Inosine (Brown adipose tissue activator) NEW
AG-CR1-3554 — 100 mg | 500 mg | 1 g

Miglitol (α-Glucosidase inhibitor)
AG-CR1-3635 — 10 mg | 50 mg

PF-2545920 (PDE10A inhibitor)
AG-CR1-3636 — 1 mg | 5 mg | 25 mg

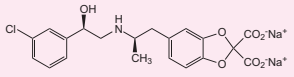
Rutin . trihydrate (Brown fat activator)
AG-CN2-0408 — 5 g

Succinate [Succinic acid] (Metabokine/BAT activator)
AG-CN2-0521 — 1 g | 5 g

NEW

CL 316,243
AG-CR1-3699 — 1 mg | 5 mg

Formula: $C_{20}H_{18}ClNO_7$. 2Na
MW: 419.8 . 46.0
CAS: 138908-40-4



Potent and selective β3-adrenoceptor agonist (EC_{50}=3nM). Increases brown adipose tissue thermogenesis. Induces functionally active mitochondrial UCP in white fat.

UCP1-dependent Thermogenesis Inducers through CK2

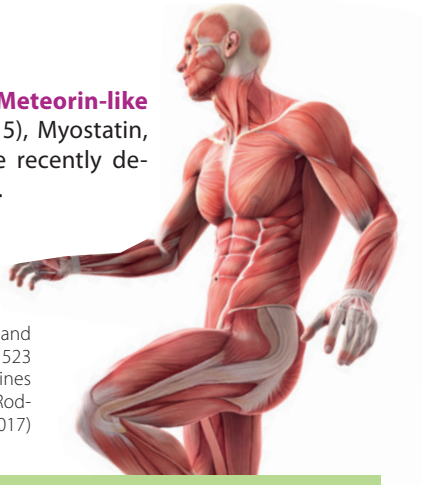
CK2 Inhibitor 10
AG-CR1-3626 — 1 mg | 5 mg

CX-4945 . HCl
AG-CR1-3629 — 1 mg | 5 mg | 25 mg

SAMPLES: C: Cell Culture Supernatant, **P:** Plasma, **S:** Serum; **U:** Urine; **L:** Cell Lysate; **F:** CSF
APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot
FORMULATION: PF = Preservative free
SPECIES: Dg = Dog; **Hu** = Human; **Mo** = Monkey; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit

Myokines: Muscle, Exercise & Obesity

Exercise training enhances muscular endurance and strength, expends calories, exerts beneficial effects on systemic metabolism and combats the development of common diseases such as obesity and type 2 diabetes, by adaptive structural and metabolic changes in skeletal muscle, including a change in the type of muscle fiber, mitochondrial biogenesis and angiogenesis. Additionally, skeletal muscles secrete cytokines and growth factors, called **myokines** that can potentially act in an autocrine, a paracrine and/or an endocrine manner to modulate metabolic, inflammatory and other processes. Several contraction-regulated myokines have been described including **ANGPTL4,** Apelin, BDNF, **FGF-21,** FSTL1, **IL-6, IL-7, IL-8, IL-15, Irisin, LIF,** MCP-1, **Meteorin-like protein**, Myonectin (CTRP15), Myostatin, PAI-1, **PEDF, VEGF** and the recently described **Asprosin** or **Slit2-C**.



SELECTED REVIEWS:
Myokines in metabolic homeostasis and diabetes: J. Eckel; Diabetologia **62,** 1523 (2019) • Crosstalk between adipokines and myokines in fat browning: A. Rodríguez, et al.; Acta Physiol. **219,** 362 (2017)

Myokine: Protein or metabolite that is produced and secreted by muscle fibers and exerts either paracrine or endocrine effects.

NEW

Asprosin

Asprosin is a new fasting-induced protein hormone that targets the liver to increase plasma glucose levels. Asprosin is the C-terminal cleavage product of the protein Fibrillin-1. Asprosin is secreted from white adipose tissue and muscles and increases hepatic glucose production by using cAMP as a second messenger, leading to activation of protein kinase A in the liver. Reduction of asprosin levels protect against metabolic syndrome-associated hyperinsulinism.

SELECTED REVIEWS: Asprosin in health and disease, a new glucose sensor with central and peripheral metabolic effects: M. Farrag, et al.; Front. Endocrinol. **13,** 1101091 (2022) • Fibrillin-1 and asprosin, novel players in metabolic syndrome: K.M. Summers, et al.; Mol. Gen. Metab. **138,** 106979 (2023)

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
NEW Asprosin (human) ELISA Kit	AG-45B-0010	96 wells	230 pg/ml	0.3125 to 20ng/ml	C, P, S
Asprosin (human) Matched Pair Detection Set	AG-46B-0011	5 x 96 wells	100 pg/ml	0.156 to 10 ng/ml	C, S
RECOMBINANT PROTEIN **BULK AVAILABLE**	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Asprosin (human) (rec.) (His)	AG-40B-0174T	10 µg | 3 x 10 µg | 100 µg	E. coli	<0.1EU/µg	Hu
ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Asprosin, mAb (Birdy-1)	AG-20B-0073	100 µg	Mouse IgG1	WB	Hu, Ms
anti-Asprosin (human), mAb (Birdy-2)	AG-20B-0074	100 µg	Mouse IgG2a	WB	Hu
anti-Asprosin, Rabbit Monoclonal (RM463)	REV-31-1355-00	100 µl	Rabbit IgG	IHC, WB	Hu

The Best Characterized Myokine

Several cytokines including IL-6, IL-7, IL-8, IL-15, LIF and MCP-1 have been shown to be secreted from muscle after endurance. IL-6 is the best characterized myokine implicated as a co-inducer of the development of obesity-associated insulin resistance, which precedes the development of type 2 diabetes (T2D).

IL-6 (human):Fc (human) (rec.) (non-lytic)
CHI-HF-22006 — 50 µg | 3 x 50 µg

IL-6 (mouse):Fc (human) (rec.)
AG-40B-0108 — 10 µg | 3 x 10 µg

IL-6 (mouse):Fc (mouse) (rec.) (non-lytic)
CHI-MF-12006 — 50 µg | 3 x 50 µg

LATEST INSIGHT

New Exerkine

Lac-Phe is a new exercise-inducible metabolite, also called exerkine, that suppresses feeding and obesity. It acts to reduce food intake and decrease overall body weight and fat mass. In diet-induced obese mice, pharmacological administration of Lac-Phe led to decreased food intake, adiposity and body weight, as well as improved glucose homeostasis, while movement and energy expenditure were not affected.

NEW **Lac-Phe . acetate**
AG-CR1-3545 — 10 mg | 50 mg
LIT: V.L. Li, et al.; Nature **606,** 785 (2022)

FNDC5/Irisin & FNDC4 – Metabolic Regulators

The FNDC (Fibronectin type III Domain-containing) family of proteins is characterized by at least one fibronectin type III domain (FN3). Eleven members (FNDC1 to FNDC11) of the fibronectin type III domain-containing (FNDC) protein family in humans have been identified. Their various functions include tissue development and cell adhesion, migration, proliferation and metabolism. Several studies showed that FNDCs are regulated by microRNAs. FNDCs reveal a variety of functions in healthy and diseased conditions in multiple organs, with FNDC4 and FNDC5/Irisin being the most extensively studied FNDCs. Soluble FNDC4 (sFNDC4) has been reported to exert anti-inflammatory effects on macrophages, osteoclasts and adipocytes, promoting survival in response to severe chronic inflammation. FNDC4 is also a hepatokine secreted from liver that acts in white adipose tissue via the new orphan adhesion G protein-coupled receptor 116 (GPR116) to control the systemic glucose homeostasis. FNDC4-GPR116 axis is impaired in diabetic patients and therapeutic injections of recombinant Fc-FNDC4 into pre-diabetic mice ameliorate pre-diabetic hyperglycemia. FNDC4 is a factor with direct therapeutic potential in inflammatory diseases and in pre-diabetic patients to control glucose tolerance.

The FNDC5 protein is induced by PGC1α and is involved in metabolic homeostasis. Upon exercise, FNDC5 expressed by skeletal muscles is proteolytically processed and secreted as the myokine Irisin, which has several functions. FNDC5/Irisin not only plays a vital role in energy metabolism but also has crucial roles in a variety of processes such as inflammation, proliferation, metastasis, aging, bone homeostasis and neural differentiation. AdipoGen's monomeric Irisin has been used in many experiments to study muscle, bone or brain functions of Irisin.

SELECTED REVIEW ARTICLES: FNDC4, a novel adipokine that reduces lipogenesis and promotes fat browning in human visceral adipocytes: G. Fruhbeck, et al.; Metabolism **108,** 154261 (2020) • New insights into the cellular activities of Fndc5/Irisin and its signaling pathways: F. Rabiee, et al.; Cell Biosci. **10,** 51 (2020) • Orphan GPR116 mediates the insulin sensitizing effects of the hepatokine FNDC4 in adipose tissue: A. Georgiadi, et al.; Nature Commun. **12,** 2999 (2021)

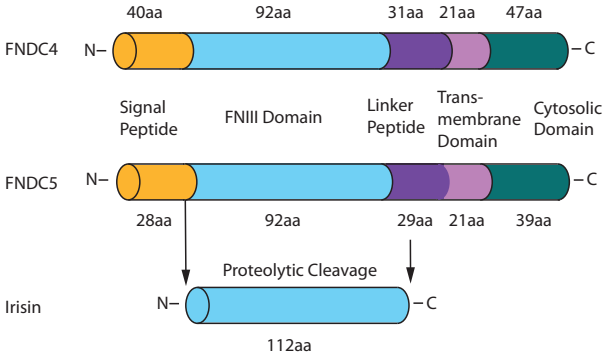


FIGURE: Comparison of FNDC4 and FNDC5 and Irisin sequences.

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
FNDC4 (human) ELISA Kit	AG-45B-0028	96 wells	40 pg/ml	78 to 5 ng/ml	C, P, S
Irisin Competitive ELISA Kit	AG-45A-0046Y	96 wells | 2 x 96 wells	1 ng/ml	01 to 5 µg/ml	C, P, S
RECOMBINANT PROTEINS	**PID**	**SIZE**	**SOURCE**	**ENDOTOXIN**	**SPECIES**
Fc (human):FNDC4 (rec.)	AG-40B-0213	50 µg | 3 x 50 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms, Rt, Dg, Mo
FNDC4 (rec.) (untagged)	AG-40B-0124	10 µg | 50 µg	E. coli	<0.01EU/µg	Hu, Ms, Rt, Dg, Mo
FNDC5:Fc (human) (rec.)	AG-40B-0153	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms, Rt
FNDC5 (rec.) (untagged)	AG-40B-0128	10 µg	E. coli	<0.01EU/µg	Hu, Ms, Rt
Irisin (rec.) (CHO)	AG-40B-0136	10 µg | 3 x 10 µg	CHO cells	<0.01EU/µg	Hu, Ms
Irisin (rec.) (HEK293)	AG-40B-0102	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms
Irisin (rec.) (untagged) (E. coli)	AG-40B-0103	10 µg | 3 x 10 µg	E. coli	<0.01EU/µg	Hu, Ms

GDF15 – Boosts Energy Expenditure for Weight Loss

Growth differentiation factor 15 (GDF15) is a distant TGF-β family member that induces anorexia and weight loss through binding to glial cell-derived neurotrophic factor family receptor α-like (GFRAL) and the recruitment of the receptor tyrosine kinase RET in the hindbrain. Therapeutic targeting of the GDF15-GFRAL pathway may be useful for maintaining energy expenditure in skeletal muscle during caloric restriction. GDF15 levels correlate with lower BMI and cachexia in patients with cancer, heart failure or chronic kidney disease.

LIT: GDF15 promotes weight loss by enhancing energy expenditure in muscle: D. Wang, et al.; Nature **619,** 143 (2023) • GDF15 increases insulin action in the liver and adipose tissue via a β-adrenergic receptor-mediated mechanism: K.A. Sjoberg, et al.; Cell Metab. **35,** 1327 (2023)

RECOMBINANT PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Fc-KIH (human) (non-lytic):GDF15 (mouse) (rec.)	AG-40B-0245	50 µg	***COMING SOON!***		
GDF15 (human):Fc (human) (rec.)	CHI-HF-210GDF15	100 µg	HEK 293 cells	<0.06EU/µg	Hu
GDF15 (human):Fc (mouse) (rec.)	CHI-HF-211GDF15	100 µg	HEK 293 cells	<0.06EU/µg	Hu
GDF15 (mouse):Fc (mouse) (rec.)	CHI-MF-110GDF15	100 µg	HEK 293 cells	<0.06EU/µg	Ms
GDF15 (mouse):Fc (human) (rec.)	CHI-MF-111GDF15	100 µg	HEK 293 cells	<0.06EU/µg	Ms
GFRAL (human):Fc (human) (rec.)	CHI-HF-210GFRAL	100 µg	HEK 293 cells	<1EU/mg	Hu
GFRAL (mouse):Fc (mouse) (rec.)	CHI-MF-110GFRAL	100 µg	HEK 293 cells	<0.06EU/µg	Ms

AdipoGen® LIFE SCIENCES

SAMPLES: C: Cell Culture Supernatant, **P:** Plasma, **S:** Serum; **U:** Urine; **L:** Cell Lysate; **F:** CSF
APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot
FORMULATION: PF = Preservative free
SPECIES: Dg = Dog; **Hu** = Human; **Mo** = Monkey; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit

BULK

IBMX

Enhances Differentiation of 3T3-L1 Cells

IBMX [3-Isobutyl 1-methylxanthine]

AG-CR1-3512-M500	500 mg
AG-CR1-3512-G001	1 g

BULK

Streptozotocin

STANDARD Diabetes Inducer

Streptozotocin

AG-CN2-0046-M050	50 mg
AG-CN2-0046-M250	250 mg
AG-CN2-0046-G001	1 g

AMPK Modulators

AMPK (AMP-activated protein kinase) plays a role in cellular energy homeostasis, regulating several intracellular systems including hepatic fatty acid oxidation and ketogenesis, inhibition of cholesterol synthesis, lipogenesis and triglyceride synthesis, stimulation of skeletal muscle fatty acid oxidation and muscle glucose uptake as well as modulation of insulin secretion by pancreatic β cells.

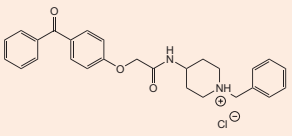
SELECTED REVIEW ARTICLE: Past strategies and future directions for identifying AMP-activated protein kinase (AMPK) modulators: S.E. Sinnett & J.E. Brenman; Pharmacol. Ther. **143,** 111 (2014)

BULK

AdipoRon . HCl (water soluble) **Original Source**

AG-CR1-0156 — 10 mg | 50 mg

Formula: $C_{27}H_{28}N_2O_3$. HCl . H_2O
MW: 428.5 . 36.5 . 18.0
CAS: 924416-43-3 (free base)



AdipoR agonist. AMPK & PGC1α activator. Improves diabetes.

AICAR (Potent AMPK activator) BULK
AG-CR1-0061 — 10 mg | 50 mg | 100 mg

Compound 112254 . HCl (water soluble) (AMPK activator)
AG-CR1-0157 — 10 mg | 50 mg

Metformin . HCl (AMPK activator)
AG-CR1-3689 — 1 g | 5 g

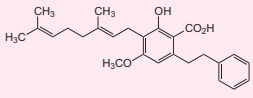
MOTS-c (human) (AMPK inducer)
AG-CP3-0026 — 1 mg | 5 mg

PPAR (Peroxisome Proliferator-activated Receptor) Agonists

Amorfrutin B

AG-CN2-0464 — 500 µg | 1 mg

Formula: $C_{26}H_{32}O_4$
MW: 408.5
CAS: 1174387-94-0
Source: *Amorpha fruticosa*



Natural PPARγ agonist with potent glucose-lowering properties.

Also available: **Amorfrutin A** (AG-CN2-0462)

Astaxanthin (PPARα agonist & PPARγ antagonist)
AG-CN2-0055 — 5 mg | 25 mg

Ciglitazone (Selective PPARγ agonist) BULK
AG-CR1-0033 — 1 mg | 5 mg | 25 mg

GW1929 (Selective PPARγ agonist) BULK
AG-CR1-0116 — 1 mg | 5 mg | 25 mg

GW501516 (Potent and selective PPARδ agonist)
AG-CR1-3641 — 1 mg | 5 mg | 25 mg

Ionomycin (free acid) (PPARγ ligand with a unique binding mode)
AG-CN2-0416 — 1 mg | 5 mg

Pioglitazone (Selective PPARγ agonist) BULK
AG-CR1-0067 — 1 mg | 5 mg | 25 mg

Rosiglitazone . maleate (Potent PPARγ agonist) BULK
AG-CR1-3571 — 25 mg | 100 mg | 1 g

Pseudolaric acid B (PPARα agonist)
AG-CN2-0083 — 100 µg | 1 mg

Troglitazone (Potent and selective PPARγ agonist)
AG-CR1-3565 — 5 mg | 25 mg

WY-14643 [Pirinixic acid] (Potent PPARα activator)
AG-CR1-3566 — 10 mg | 50 mg | 250 mg

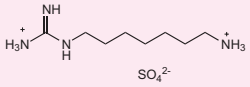
Selection of a Broad Range of Metabolic Research Reagents

NEW

N1-Guanyl-1,7-diaminoheptane [GC7]

AG-CR1-3702 10 mg | 50 mg

Formula: $C_8H_{22}N_4O_4S$
MW: 270.0
CAS: 150417-90-6



Cell permeable competitive deoxyhypusine synthase (DHPS) inhibitor. Blocks OXPHOS in macrophages and is a useful tool for immunometabolism research.

AK-7 (Brain-permeable SIRT2 inhibitor)
AG-CR1-3511 5 mg | 25 mg

Amlexanox (Selective TBK1 and IKKε inhibitor)
AG-CR1-3579 10 mg | 50 mg

AP-III-a4 . HCl (HNE inhibitor) NEW
AG-CR1-3696 1 mg | 5 mg

AZD 7545 (Potent PDK2 inhibitor) NEW
AG-CR1-3692 1 mg | 5 mg | 10 mg

BMS-309403 (Potent and selective FABP4 inhibitor)
AG-CR1-3640 1 mg | 5 mg | 25 mg

3,4-Dimethoxychalcone (Caloric restriction mimetic)
AG-CN2-0531 10 mg | 50 mg | 250 mg

EM574 (Orexigenic; Motilin receptor agonist)
AG-CN2-0102 250 µg | 1 mg

Emodin (Potent selective 11β-HSD1 inhibitor)
AG-CN2-0457 50 mg | 250 mg

Empagliflozin (SGLT-2 inhibitor)
AG-CR1-3619 10 mg | 50 mg

(+)-Etomoxir . Na (CPT-1a inhibitor) NEW
AG-CR1-3688 5 mg | 25 mg

Glyburide (USP) (Antidiabetic) BULK
AG-CR1-3613 1 g | 5 g | 10 g

L-Glutamine (Linking Obesity to Inflammation)
AG-CR1-3534 1 g | 5 g

GW311616A (Potent HNE inhibitor) BULK
AG-CR1-3632 1 mg | 5 mg | 25 mg

Ipragliflozin (SGLT-2 inhibitor) NEW
AG-CR1-3546 10 mg | 50 mg

Isoliquiritigenin (Antidiabetic/Antihyperglycemic)
AG-CN2-0459 10 mg | 50 mg

Kaempferitrin (Insulinomimetic/Hypoglycemic)
AG-CN2-0039 1 mg | 5 mg

Lipofermata (FATP1/FATP2 inhibitor) NEW
AG-CR1-3542 10 mg | 50 mg

Narciclasine (Anti-obesity agent)
AG-CN2-0524 500 µg | 1 mg

Neuromedin U-25 (human) (NMUR1/NMUR2 agonist)
AG-CP3-0031 1 mg | 5 mg

Niclosamide (Neuropetide Y4 receptor ligand)
AG-CR1-3643 100 mg | 1 g
AG-CR1-3644 [Ethanolamine] 25 mg | 100 mg

Pellitorine (α-Glucosidase inhibitor) BULK
AG-CN2-0009 1 mg | 5 mg | 25 mg

Suramin . 6Na (SIRT1 & SIRT5 inhibitor) BULK
AG-CR1-3575 50 mg | 250 mg
AG-CR1-3575V 50 mg | 250 mg | 1 g

Talabostat . mesylate (DPP inhibitor) NEW
AG-CR1-3541 10 mg | 50 mg

(±)-Verapamil . HCl (USP) (Antidiabetic)
AG-CR1-3627 100 mg | 1 g | 5 g

Withaferin A (Leptin sensitizer) BULK
AG-CN2-0490 1 mg | 5 mg | 10 mg

Visit our Website for a Complete Overview!

NEW

Microbiota: Inflammation & Obesity

The gut microbiota and immune system play an important role in the development of adiposity. Dysbiosis of the microbiota leads to increased permeability of the gut barrier and bacterial products in the bloodstream, which triggers metabolic inflammation of adipose tissue, muscle, and liver. Inflammation in these highly metabolic organs exacerbates adiposity and contributes to the development of comorbidities associated with obesity.

Indole-3-carbinol NEW
AG-CR1-3637 500 mg | 5 g

***trans*-Indole-3-acrylic acid** NEW
AG-CR1-3677 250 mg | 1 g

SELECTED REVIEW: What's gut got to do with it? The role of the microbiota and inflammation in the development of adiposity and obesity: T. Jennings, et al.; Immunometabolism **5**, e00029 (2023)

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