

### 4<sup>th</sup> Edition

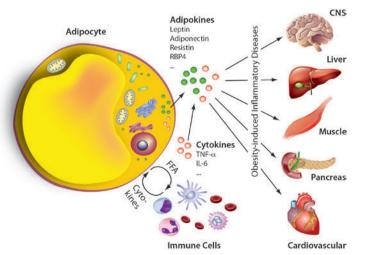
www.adipogen.com

# **Obesity & Diabetes Research**

Focus: 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 below **Figure**) or brown adipocytes (see page 8), respectively. **White adipose tissue (WAT)** is found throughout the body, primarily under the skin (subcutaneous fat that has no 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.

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 and muscle. Some adjpokines 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- $\alpha$ , 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, Progranulin, Nampt/Visfatin/PBEF, Resistin, Vaspin, Omentin, Lipocalin-2, Apelin, DPP-4, CTRPs, selected ANGPTLs), angiogenesis (e.g. VEGF, NGF) and lipid mobilization (Zinc- $\alpha$ -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 (see page 4), 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. Although brown adipose tissue (BAT) also produces adipokines (see page 8), the endocrine role of BAT in metabolic diseases is not fully investigated. A growing interest in adipokines and myokines as biomarkers of low-grade inflammation and metabolic diseases emerges.



#### CONTENTS

KEY Adipokines 2 Adiponectin, Nampt/Visfatin, RBP4, Progranulin, Vaspin, ZAG	2–3
IL-36 – Protective Role in Obesity	4
Obesity & Immunometabolist Related Reagents	m I–5
IL-33 & Adipose Tissue Homeostasis	6
Highly Active IL-33 Proteins IL-33 Blocking Antibody	
BEST ST2 Antibody for FACS	
<b>Obesity &amp; Angiogenesis</b> Potent ANGPT2 Blocking Antiboo VEGF Reagents	<b>7</b> lies
WAT Browning 8	8-9
Important Batokines (Slit2-C, Nrg4, Meteorin-like, FGF-	21)
Browning Inducers (CK2 Inhibitors, UCP1 Inducers, PDE10A Inhibitors)	
Myokines	10
Asprosin –	

A New Fasting-induced Protein IL-6 & Irisin ELISA Kits & Proteins

Small Molecules Modulators 11–12

AMPK Activators PPAR Agonists

#### Immunometabolism Modulators

Metabolic Research Reagents Microbiota-related Reagents Long-acting Antidiabetic Peptides

SELECTED	REVIEW	ARTICLE
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Two Faces of White Adipose Tissue with Heterogeneous Adipogenic Progenitors: I. Hwang & J.B. Kim; Diabetes Metab. J. **43**, 752 (2019)

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

### 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, PPAR $\alpha$  and NF- $\kappa$ B and exerting a wide range of beneficial physiological actions, including antidiabetic, 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) ELIS	SA Kit	AG-45A-0005Y	96 wells   2 x 96 wells	50 pg/ml	0.375 to 24 ng/ml	C, P, S
<b>RECOMBINANT PROTEINS</b>		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<sup>+</sup> pool. Through its NAD<sup>+</sup>-biosynthetic activity, NAMPT influences the activity of NAD<sup>+</sup>-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) ELIS	A Kit	AG-45A-0006Y	96 wells   2 x 96 wells	30 pg/ml	0.125 to 8 ng/ml	S
Nampt (human) (Intr	aCellular) ELISA Kit	AG-45A-0008Y	96 wells   2 x 96 wells	30 pg/ml	0.25 to 16 ng/ml	L
Nampt (mouse/rat) D	ual 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	From The Manufacturer		iror
CHS-828		AG-CR1-0064	5 mg   25 mg			
FK-866		AG-CR1-0011	1 mg   5 mg			

### **Retinol-binding Protein 4 [RBP4]**

The physiological role of RBP4 is 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



SAMPLES: C: Cell Culture Supernatant, P: Plasma, S: Serum; U: Urine; L: Cell Lysate; F: CSF

### Progranulin [PGRN]

Progranulin (PGRN) is a cysteine rich secreted protein, expressed in epithelial cells, immune cells, neurons and adipocytes. PGRN was first identified as a growth factor and recently characterized as an adipokine implicated in obesity, insulin resistance and rheumatic disease. At a central level, PGRN acts as a neurotropic and neuroprotective factor and protects from neural degeneration. PGRN has pleiotropic actions and participates in several processes, such as inflammation or tumorigenesis.

### **Tag-free Progranulins**

- Higher activity compared to tagged Progranulins
- Suitable for in vitro and in vivo studies
- Reflects the native sequence with no additional amino acids
- Affinity purified
- Low endotoxin levels (<0.01 EU/µg)</li>

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
Progranulin (human) ELISA Kit	AG-45A-0018Y	96 wells   2 x 96 wells	32 pg/ml	0.063 to 4 ng/ml	C, P, S, U
Progranulin (mouse) ELISA Kit	AG-45A-0019Y	96 wells   2 x 96 wells	60 pg/ml	0.125 to 8 ng/ml	C, S
Progranulin (rat) ELISA Kit	AG-45A-0043Y	96 wells   2 x 96 wells	40 pg/ml	0.063 to 4 ng/ml	C, S
RECOMBINANT PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Progranulin (human) (rec.) <mark>(untagged)</mark>	AG-40A-0188Y	10 µg   50 µg	HEK 293 cells	<0.01EU/µg	Hu
Progranulin (mouse) (rec.) (untagged)	AG-40A-0189Y	10 µg   50 µg	HEK 293 cells	<0.01EU/µg	Ms
Progranulin (rat) (rec.) (untagged)	AG-40A-0196Y	10 µg   50 µg	HEK 293 cells	<0.01EU/µg	Rt

### 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-0094	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 IgG1ĸ	IHC, WB	Hu
anti-Vaspin (mouse), pAb	AG-25A-0075	100 µg	Rabbit	WB	Ms

### Zinc- $\alpha$ -2-glycoprotein [ZAG]

Zinc- $\alpha$ -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- $\alpha$ -2-glycoprotein (human) (rec.)	AG-40B-0146	10 µg   50 µg   3 x 50 µg	E. coli	<0.1EU/µg	Hu

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



#### IL-36 Cytokines – Protective Role in Obesity & Metabolic Diseases

Interleukin- $36\alpha$ ,  $\beta$  and  $\gamma$  (IL- $36\alpha$ ,  $\beta$  and  $\gamma$ ), members of the interleukin-1 (IL-1) family, are pro-inflammatory cytokines mainly involved in skin inflammatory diseases, but also in the inflammation of lung or gut. Recently, the lab of Prof. Patrick T. Walsh (Trinity College Dublin, Ireland) describes in Nature Communication a new protective role of the IL-36 family of cytokines in obesity and metabolic diseases. They observed that IL- $36\gamma$  is increased in serum of obese patients with diabetes, indicating that elevated IL-36 cytokines may play a protective role in reducing blood sugar levels. IL-36 cytokines enhance mucus secretion from goblet cells in the colon, which promote the outgrowth of the commensal bacterial strain *Akkermansia muciniphila*, known to play an important protective role against obesity and metabolic dysfunction.

LIT: Interleukin-36 cytokines alter the intestinal microbiome and can protect against obesity and metabolic dysfunction: F. Giannoudaki, et al.; Nat. Commun. 10, 4003 (2019)

ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
IL-36 $\alpha$ (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-36 $\beta$ (human) Matched Pair Detection Set	AG-46B-0009	5 x 96 wells	10 pg/ml	15.6 to 1000 pg/ml	С
IL-36Ra (human) Matched Pair Detection Set	AG-46B-0006	5 x 96 wells	0.5 ng/ml	0.78 to 50 ng/ml	С

#### **Also Available:**

**NEW IL-36**α/**IL-36**γ (human) Tandem ELISA Kit AG-45B-4502 Visit our Website for a Complete Range of IL-36-related Reagents!

### **Other Obesity-related Proteins & Antibodies**

PROTEINS	PID	ANTIBODIES	PID
Calreticulin (human) (rec.) (His)	AG-40A-0132	Calreticulin (human), mAb (CR213-2AG)	AG-20A-0079
Clusterin (secretory form) (human) (rec.)	AG-40A-0050Y	Calreticulin (human), pAb	AG-25A-0094
Clusterin (nuclear form) (human) (rec.) (His)	AG-40A-0047	Clusterin (human), pAb	AG-25A-0099
Clusterin (nuclear form) (mouse) (rec.) (His)	AG-40A-0057	Clusterin (mouse), pAb	AG-25A-0054
CREB-binding Protein (mouse) (rec.) (His)	AG-40T-0016	FABP3 (human), pAb	AG-25A-0040
CTHRC1 (human) (rec.)	AG-40B-0157	FABP4 (human), pAb	AG-25A-0041
CTHRC1 (mouse) (rec.)	AG-40B-0154	FTO (human), mAb (AG103)	AG-20A-0092
FABP1 (human) (rec.) (His)	AG-40A-0039T	FTO (mouse), mAb (FT62-6)	AG-20A-0083
FABP3 (human) (rec.) (untagged)	AG-40B-6002	IDO (human), mAb (ID 177)	AG-20A-0035
FABP4 (human) (rec.) (His)	AG-40A-0035	IDO (mouse), pAb	AG-25A-0032
FTO (human) (rec.) (His)	AG-40A-0112	MPC-2, mAb (JCM-1)	AG-20B-0071
FTO (mouse) (rec.) (His)	AG-40A-0127	NMNAT2 (human), mAb (Nady-1)	AG-20A-0087
IDO (human) (rec.) (His) (highly active)	AG-40B-0161	Obestatin (human), pAb	AG-25A-0043
Lipocalin-2 (human) (rec.)	AG-40B-6001	PEDF (human), mAb (rec.) (Serpy-1-4)	AG-27B-0014
NAD Kinase (human) (rec.) (His) (highly active)	AG-40T-0091	RELM- $\beta$ (mouse), mAb (MRB 46L)	AG-20A-0026
NMNAT1 (human) (rec.) (His) (highly active)	AG-40T-0092	Resistin (human), mAb (HRES106)	AG-20B-0076
NMNAT3 (human) (rec.) (His) (highly active)	AG-40T-0093	Resistin (human), pAb	AG-25A-0013
Omentin (human) (rec.)	AG-40B-0042	Resistin (mouse), mAb (MRES06)	AG-20A-0004
PEDF (human) (rec.)	AG-40B-0077	Resistin (mouse), mAb (MRES18)	AG-20B-0077
PEDF (mouse) (rec.)	AG-40B-0118	Resistin (rat), mAb (RRES07)	AG-20A-0015
Resistin (human) (rec.)	AG-40A-0010Y	Stearoyl-CoA Desaturase-1 (mouse), pAb	AG-25A-0031
Resistin (mouse) (rec.)	AG-40A-0011	TDO (human), pAb	AG-25A-0106
		TRB-3 (human), pAb	AG-25A-0059

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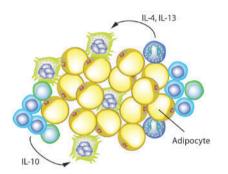
### **Obesity & Immunometabolism**

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 bioenergetics of immune cells. Adipose tissue illustrates best the interdependency of both arms of immunometabolism (whole-body 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)



Lean Adipose Tissue – Anti-Inflammatory Milieu Immune cells promoting: Remodeling Tissue, Immune Surveillance

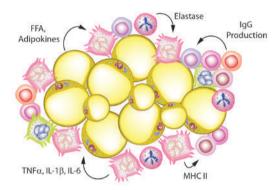


FIGURE: Modulation of immunometabolism during obesity. Adapted from H.L. Kammoun, et al.; Rev. Endocr. Metab. Disord. 15, 31 (2014)

Obese Adipose Tissue – Pro-Inflammatory Milieu Immune cells promoting: Insulin Resistance, Chemotaxis, Lipolysis



### 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	<b>inhibitor) BULK</b>
AG-CN2-0100	250 μg   1 mg
Heptelidic acid (GAPDH inhibitor	) ( <u>UNIQUE</u> )
AG-CN2-0118	250 μg   1 mg
<b>Itaconate (PFKII and SDH inhibite</b>	<b>Dr) BULK</b>
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-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- $\gamma$ , 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.



### **NEW** Highly Active Human 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)

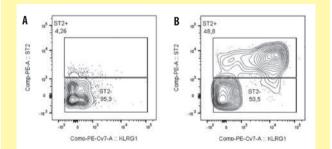


FIGURE: Activation in vivo of Innate Lymphoid Cells 2 (ILC2) by IL-33 (oxidation resistant) (human) (rec.) (untagged) (AG-40B-0160). Method: C57BL/6 mice were injected daily for 3 days with PBS (Figure A) or IL-33 (oxidation resistant) (human) (rec.) (untagged) (AG-40B-0160) (at 0.4µg per mouse) (Figure B). At day 4, cells from bone marrows were stained and analyzed by flow cytometry. Levels of ST2 and KLRG1 on Innate Lymphoid Cells (gated as lineage negative, CD127 positive cells) are shown. *Picture courtesy of Dr G.Verdeil / Dr S. Trabanelli (Camilla Jandus Group, Department of Fundamental Oncology, University of Lausanne)*.

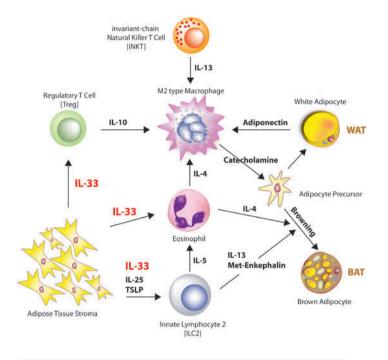


FIGURE: Role of IL-33 in the control of adipose tissue homeostasis.

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)



### 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**

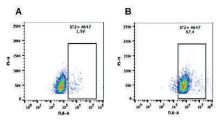
#### anti-ST2 (human), pAb

AG-25A-0058 AG-25A-0058YTD AG-25A-0058YTS

**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  $4^{\circ}$ C.



100 μg 100 tests 100 tests



6

### **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. A recent study [2] demonstrates 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] Role of VEGFs in metabolic disorders. M. di Somma, et al.; Angiogenesis (Epub ahead of print) (2019) • [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 A	ntibodies	25 ]
anti-Angiopoietin-2, mAb (rec.) (blo (Angy-2-1) (preservative free)	cking)	(6) 20 - * 15 - 10
AG-27B-0016PF	100 μg   500 μg   1mg	
anti-Angiopoietin-2 (human), mAb ( (Angy-1-4) (preservative free)	rec.) (blocking)	Controlles Pritrates
AG-27B-0015PF	100 μg 500 μg 1mg	Co. Preven
Also Available:		<b>FIGURE:</b> Antagonizing Angiopoietin-2 <i>in vivo</i> with anti-ANG-2, mAb (rec.) (blocking) (Angy-2-1) (AG-27B-0016PF) increases triglyceride levels.
Angiopoietin-2 (human) (rec.)	AG-40B-0114	<b>METHOD:</b> After High Fat Diet (HFD) challenges for five weeks in wild-type C57BL/6 mice, control lgG (left panel) or anti-ANG-2 (Clone Angy-2-1)
Angiopoietin-2 (mouse) (rec.)	AG-40B-0131	blocking antibody (right panel) (4 µg/g body weight; twice/week) were administrated and afterwards the mice underwent metabolic analyses of

the trialycerides 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



### **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 brown fat that is composed of cells interspersed within WAT that are capable of transforming into brown-like adipocytes 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: New Advances in Adaptive Thermogenesis: UCP1 and Beyond: E.T. Chouchani, et al.; Cell Metabolism 29, 27 (2019) • Importance of adipocyte browning in the evolution of endothermy: M. Jastroch & F. Seebacher; Philos. Trans. R Soc. Lond. B Biol. Sci. 375, 20190134 (2020)

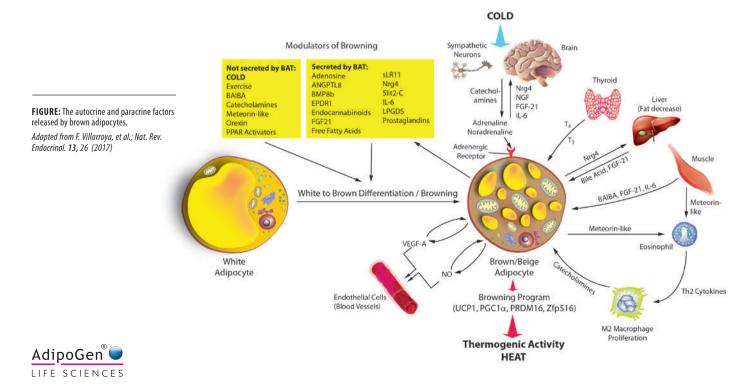
#### **Overview of Important Batokines:**

- 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

8

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.



#### Browning Inducers not expressed by BAT:

- **Cold exposure** is a strong inducer of brown cells. Thermogenic activity is regulated by a canonical  $\beta$ -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  $\beta$ -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- $\gamma$  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	10 µg   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
NEW 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 G	iα <mark>q family inhibitor)</mark>
AG-CN2-0509	500 μg   1 mg
3-Aminoisobutyric acid (Contracti	ion-induced myokine)
AG-CR1-3596	250 mg   1 g
Harmine (UCP1-dependent thermogen	nesis inducer)
AG-CN2-0510	10 mg   50 mg   250 mg
<b>Miglitol</b> ( $\alpha$ -Glucosidase inhibitor )	
AG-CR1-3635	10 mg   50 mg
Papaverine . HCI (PDE10A inhibitor)	
AG-CN2-0414	1 g   5 g
PF-2545920 (PDE10A inhibitor)	
AG-CR1-3636	1 mg   5 mg   25 mg
Rutin . trihydrate (Brown fat activate	or)
AG-CN2-0408	5 g
Succinate [Succinic acid] (Metabo	kine/BAT activator)
AG-CN2-0521	1 g   5 g

#### NEW CL 316,243 AG-CR1-3699 1 mg | 5 mg Formula: C<sub>20</sub>H<sub>18</sub>CINO<sub>7</sub>. 2Na MW: 419.8.46.0 CAS: 138908-40-4 Potent and selective $\beta$ 3-adrenoceptor agonist (EC<sub>50</sub>=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

 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.



### 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 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.

ELISA KITS		PID	SIZE	SENSITIVITY	RANGE	SAMPLES
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.) (Hi	s)	AG-40B-0174T	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), mA	b (Birdy-2)	AG-20B-0074	100 µg	Mouse IgG2a	WB	Hu

### Selected Myokines: Interleukin-6 and Irisin

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). The role of irisin is still under debate. Initially, described as a browning inducer, recent studies suggest an involvement of irisin in cortical bone mass,  $\beta$  cell proliferation, insulin secretion, in synaptic plasticity and memory in Alzheimer's Disease models.

LIT: Physical activity and muscle-brain crosstalk: B.K. Pedersen; Nat. Rev. Endocrinol. 15, 383 (2019) • Myokines: The endocrine coupling of skeletal muscle and bone: M. Gomarasca, et al.; Adv. Clin. Chem. 94, 155 (2020)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
IL-6 (human) (rec.) (His)	CHI-HF-20106	10 µg   50 µg	HEK 293 cells	<0.01EU/µg	Hu
IL-6 (human):Fc (human) (rec.)	CHI-HF-21006	50 µg   3 x 50 µg	CHO cells	<0.06EU/µg	Hu
IL-6 (mouse):Fc (human) (rec.)	AG-40B-0108	10 µg   3 x 10 µg	HEK 293 cells	<0.01EU/µg	Ms
lrisin (rec.) (CHO)	AG-40B-0136	10 µg   3 x 10 µg	CHO cells	<0.01EU/µg	Hu, Ms
lrisin (rec.) (E. coli) (untagged)	AG-40B-0103	10 µg   5 x 10 µg	E. coli	<0.1EU/µg	Hu, Ms
ELISA KITS	PID	SIZE	SENSITIVITY	RANGE	SAMPLES
Irisin Competitive ELISA Kit	AG-45A-0046Y	96 wells   2 x 96 wells	1 ng/ml	0.001 to 5 μg/ml	C, P, S





### **IBMX**

#### **Enhances Differentiation of 3T3-L1 Cells**

#### IBMX [3-Isobutyl 1-methylxanthine]

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

## Streptozotocin

**STANDARD Diabetes Inducer** 

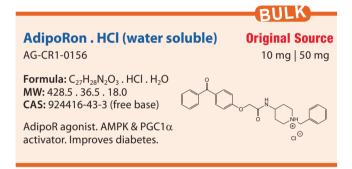
#### Streptozotocin

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  $\beta$  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)



AICAR (Potent AMPK activator)	BULK
AG-CR1-0061	10 mg   50 mg   100 mg
Compound 112254 . HCl (water s	<b>oluble) (AMPK activator)</b>
AG-CR1-0157	10 mg   50 mg
Metformin . HCI (AMPK activator)	<b>NEW</b>
AG-CR1-3689	1 g   5 g
MOTS-c (human) (AMPK inducer)	<mark>NEW</mark>
AG-CP3-0026	1 mg   5 mg

### **PPAR (Peroxisome Proliferator-activated Receptor) Agonists**

	NEW
Amorfrutin B AG-CN2-0464	500 μg   1 mg
<b>Formula:</b> C <sub>26</sub> H <sub>32</sub> O <sub>4</sub> <b>MW:</b> 408.5 <b>CAS:</b> 1174387-94-0 <b>Source:</b> <i>Amorpha fruticosa</i>	$H_{3C}$ $H_{3}$ $H_{$
Natural PPARγ agonist with μ	potent glucose-lowering properties.
Also available: <b>Amorfrut</b>	<b>in A</b> (AG-CN2-0462)
Astaxanthin (PPARα ago	nist & PPARy antagonist)
AG-CN2-0055	5 mg   25 mg
<b>Ciglitazone</b> (Selective PPA AG-CR1-0033	ARγ agonist)

<b>GW1929 (Selective PPAR</b> γ agonist)	BULK
AG-CR1-0116	1 mg   5 mg   25 mg
<b>GW501516</b> (Potent and selective PPAR $\delta$ AG-CR1-3641	agonist) NEW 1 mg   5 mg   25 mg
<b>lonomycin (free acid)</b> (PPAR <sub>Y</sub> ligand with AG-CN2-0416	<b>a unique binding mode)</b> 1 mg   5 mg
<b>Pioglitazone (Selective PPAR</b> γ agonist)	BULK
AG-CR1-0067	1 mg   5 mg   25 mg
Rosiglitazone . maleate (Potent PPAR	γ <b>agonist) BULK</b>
AG-CR1-3571	25 mg   100 mg   1 g
<b>Pseudolaric acid B (PPAR</b> α agonist) AG-CN2-0083	100 μg   1 mg
Troglitazone (Potent and selective PPAR)	y <b>agonist)</b>
AG-CR1-3565	5 mg   25 mg
<b>WY-14643 [Pirinixic acid] (Potent PPA</b>	<b>R</b> α <b>activator)</b>
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<sub>8</sub>H<sub>22</sub>N<sub>4</sub>O<sub>4</sub>S MW: 270.0 CAS: 150417-90-6 SO₄2 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 IKKs inhibitor) AG-CR1-3579 10 mg | 50 mg AP-III-a4. HCI (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 11<sup>β</sup>-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 BULK **Glyburide (USP)** (Antidiabetic) AG-CR1-3613 1 g | 5 g | 10 g

#### LATEST INSIGHT

L-Glutamine (Linking Obesity to Infla AG-CR1-3534 LIT: P. Petrus, et al.; Cell Metab. <b>31</b> , 375 (2020)	nmmation) 1 g   5 g
GW311616A (Potent HNE inhibitor)	NEW
AG-CR1-3632	1 mg   5 mg   25 mg
Isoliquiritigenin (Antidiabetic/Antihype	rglycemic)
AG-CN2-0459	10 mg   50 mg
Kaempferitrin (Insulinomimetic/Hypogly	ycemic)
AG-CN2-0039	1 mg   5 mg
Linagliptin (DPP4 inhibitor)	
AG-CR1-3618	10 mg   50 mg
Narciclasine (Anti-obesity agent)	
AG-CN2-0524	500 μg   1 mg
Neuromedin U-25 (human) (NMUR1/	NMUR2 agonist)

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			
<b>Orlistat</b> (DAGL $\alpha$ inhibitor/Antiobesity)	BULK			
AG-CN2-0050	50 mg   250 mg			
Pellitorine (α-Glucosidase inhibitor) BULK				
AG-CN2-0009	1 mg   5 mg   25 mg			
Suramin . 6Na (SIRT1 & SIRT5 inhibitor)				
AG-CR1-3575	50 mg			
(±)-Verapamil . HCI (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!

### **Long-acting Antidiabetic Peptides**

Liraglutide (GLP-1 receptor agonist) AG-CP3-0034 1 mg | 5 mg | 25 mg

Semaglutide . AcOH (GLP-1 receptor agonist) AG-CP3-0032 1 mg | 5 mg | 25 mg

#### LATEST INSIGHT

### **Microbiota-related Reagents**

Indole-3-carbinol	NEW
AG-CR1-3637	500 mg   5 g
trans-Indole-3-acrylic acid	NEW
AG-CR1-3677	250 mg   1 g



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