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Obesity Research Tools and Pathways

Key Aspects and Principles of Obesity & Overview of Related Research Reagents

Jan 2025 (V1.1)

Obesity, a condition often associated with metabolic diseases, has its roots in the fundamental biological functions of body fat. Body fat, or adipose tissue, originally evolved to play a critical role in energy storage, protecting delicate organs, and regulating reproduction through complex hormonal signals. In vertebrates, specialized cells known as adipocytes are responsible for storing energy in the form of lipid droplets. However, despite its important role, excess body fat can lead to severe health issues, including cardiovascular diseases (CVD), and an increased risk of certain cancers and type 2 diabetes (T2D). This overview covers the various factors that contribute to obesity as well as the research tools available for studying these pathways.

This handbook is a collaborative effort between Rockland and antibodies-online, two companies united in their commitment to advancing scientific research. Together, we have developed a comprehensive resource, offering a suite of high-quality products specifically designed to facilitate the study of obesity-related mechanisms.

By combining Rockland's expertise in assay development and antibodies-online's extensive catalog of research tools, this guide aims to empower researchers to explore the complexities of obesity and its associated diseases with cutting-edge solutions.

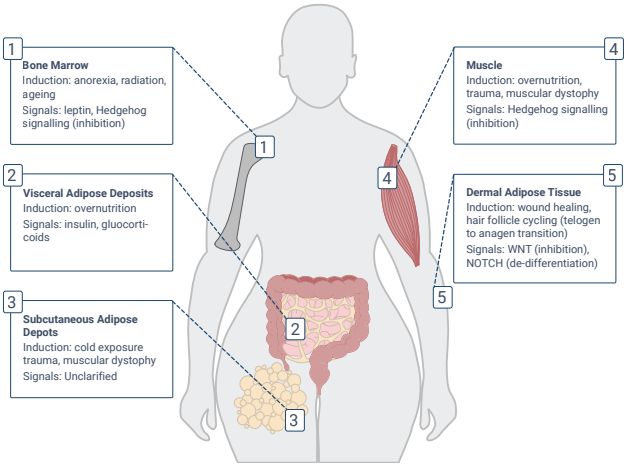

Fig 1. Sites of adipogenesis in adults (Adapted from Ghaben & Scherer, 2019).

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Obesity Research Tools

Other Related Pathways

Obesity Research Tools

Glucagon, GLP-1 and the Obesity Pandemic

Obesity has become a critical global health issue. According to WHO data from 2022, 43% of adults aged 18 and over were overweight, with 16% classified as obese. The prevalence of adult obesity has more than doubled since 1990, and adolescent obesity has quadrupled, affecting countries worldwide regardless of income levels. This alarming trend has led to obesity being recognized as a pandemic, although its progression is slower and its impacts more prolonged compared to rapid viral pandemics like COVID-19.

Obesity and Type 2 Diabetes

Obesity is a significant risk factor for developing T2D due to the complex interplay between excess body fat and metabolic processes (Reviewed in Klein *et al*., 2022). The accumulation of excessive fat, particularly in the abdominal region, leads to insulin resistance, a condition where the body's cells become less responsive to insulin. This resistance is exacerbated by the dysfunctional fat cells in obese individuals, which secrete abnormal amounts of adipokines and free fatty acids, contributing to systemic inflammation and further impairing insulin action. Moreover, obesity-induced insulin resistance involves multiple organs, including the liver, muscles, and pancreatic β-cells. Due to fat accumulation, the liver's increased gluconeogenesis and decreased insulin clearance contribute to higher blood glucose levels. Similarly, muscle cells in obese individuals show impaired glucose uptake and utilization, which is crucial for maintaining normal blood sugar levels.

Pancreatic β-cells initially compensate for insulin resistance by increasing insulin secretion. However, prolonged obesity can lead to β-cell dysfunction and a decrease in insulin production, tipping the balance towards hyperglycemia and the onset of T2D. Adipose tissue in obesity undergoes structural changes, such as fibrosis and increased infiltration of inflammatory immune cells, which release cytokines that further disrupt insulin signaling.

Glucagon in Type 2 Diabetes

Glucagon, a hormone produced by differential processing of proglucagon in the α-cells of the pancreas, plays a crucial role in glucose regulation by stimulating hepatic glucose production (Reviewed in Ahrén, 2015). In T2D, glucagon assumes a significant pathological role. Patients with T2D often exhibit elevated baseline glucagon levels that are inadequately suppressed after meals, contributing to persistent hyperglycemia.

Studies using somatostatin infusion techniques have demonstrated that lowering glucagon levels significantly reduces blood glucose. For instance, in subjects with T2D, reducing glucagon levels during an oral glucose tolerance test diminished the rise in blood glucose, underscoring hyperglucagonemia's substantial contribution to elevated glucose levels in T2D. The mechanism behind this involves impaired regulation of glucagon secretion, possibly due to insulin resistance in alpha cells or defective glucose sensing. This results in increased glucose production by the liver and decreased insulin clearance, both of which are driven by excess glucagon and will ultimately exacerbate hyperglycemia.

Research has shown that therapies targeting glucagon can improve glycemic control in T2D. GLP-1 (glucagon-like peptide-1) receptor agonists and DPP-4 (dipeptidyl peptidase-4) inhibitors lower glucagon levels and have proven effective in managing blood sugar levels. These treatments work by enhancing insulin secretion and reducing glucagon secretion, thereby improving overall glucose regulation. In summary, hyperglucagonemia, driven by the production of glucagon in pancreatic α-cells, is a major factor in the pathology of T2D. Addressing elevated glucagon levels through targeted therapies can significantly enhance glucose control and improve outcomes for individuals with T2D.

GLP-1 in Managing Obesity and T2D

GLP-1 (glucagon-like peptide-1) has emerged as a promising focus for obesity and diabetes research. GLP-1 is a peptide hormone produced in the intestinal epithelial endocrine L-cells by differential processing of proglucagon and helps regulate appetite and food intake. It also plays a crucial role in insulin secretion and blood sugar regulation. Medications like Ozempic (semaglutide), which are GLP-1 receptor agonists, have shown effectiveness in promoting weight loss and improving blood sugar control in people with T2D. Understanding and leveraging GLP-1's functions could be a pivotal step in addressing these interconnected health issues.

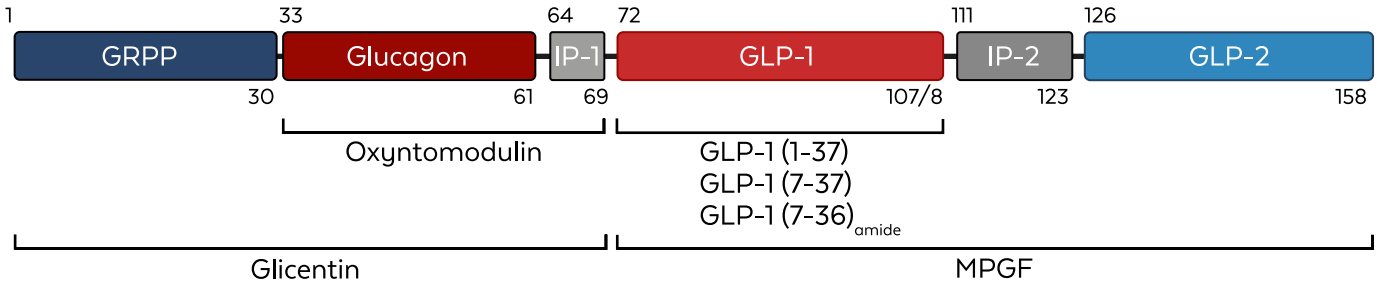


Fig 2. Proglucagon structure and its processed variants. MPGF= major proglucagon fragment. (Adapted from Drucker et al., 2017)

Glucose Metabolism

Glycolysis is a specific pathway within glucose metabolism and describes the energy-producing process where one glucose molecule is broken down into two pyruvate molecules. When oxygen is available, pyruvate typically moves into the mitochondria and is converted to acetyl-CoA as part of the TCA cycle. Without oxygen, pyruvate is transformed into lactate. Glycolysis consists of 10 steps occurring in the cytosol, producing two ATP molecules without needing oxygen. Three main regulatory steps in glycolysis, carried out by hexokinase, phosphofructokinase, and pyruvate kinase, are crucial for ensuring the process flows towards pyruvate and are effectively irreversible. Dysregulation and excessive glucose availability and the subsequent increase in glycolytic flux can lead to enhanced fat storage and insulin resistance, both hallmarks of obesity.

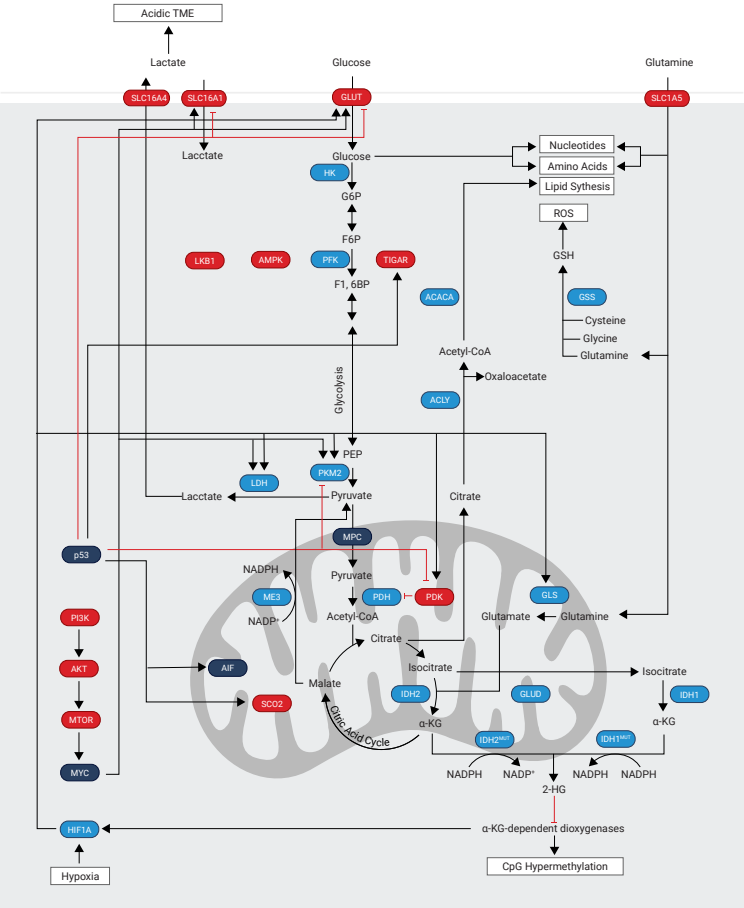


Fig 3. Schematic presentation of the Warburg effect, a metabolic phenomenon observed in many cancer cells, where glycolysis is preferentially used for energy production, even in the presence of sufficient oxygen for oxidative phosphorylation.

Key Antibodies & Proteins

Product	Reactivity	Application	Item No.
Aldolase Antibody	Human, Rabbit	WB, ELISA, IP	200-1141-0100
Fructose-6-Phosphate Kinase Antibody	Rabbit	WB, ELISA, IF, Multiplex	200-1156-0100
GAPDH Antibody	Human, Mouse, Rabbit	WB, ELISA, Multiplex	200-301-A33
Glucose-6-Phosphate Dehydrogenase Antibody	*Leuconostoc mesenteroides*	WB	200-1153-0100
Hexokinase Antibody	Hexokinase (Yeast)	WB, ELISA	200-4159-0100
Lactate Dehydrogenase Antibody	Human, Rabbit	WB, ELISA, IF, Other	200-1173-0100
PGK1 antibody (AA 117-145)	Human	WB, IHC (p), IF, FC	ABIN391135
GAPDH antibody	Human	WB, IF, IHC (p), IP, ICC	ABIN2857072
Lactate Dehydrogenase ELISA Kit	Human	ELISA	ABIN6957356

Glucose Transporters

A family of facilitative glucose transporters (GLUTs) play a critical role in regulating glucose uptake within adipose tissue. Growing evidence strongly supports the involvement of various GLUT family members in the development and progression of insulin resistance and type 2 diabetes (T2D). Among these transporters, GLUT4 is the most prevalent isoform in adipocytes and is primarily responsible for insulin-stimulated glucose uptake, with its expression significantly downregulated in T2D. GLUT1 contributes to basal glucose transport and undergoes recycling through internal membrane compartments, while GLUT8 expression increases during fat cell differentiation, suggesting a potential role in embryonic tissue development.

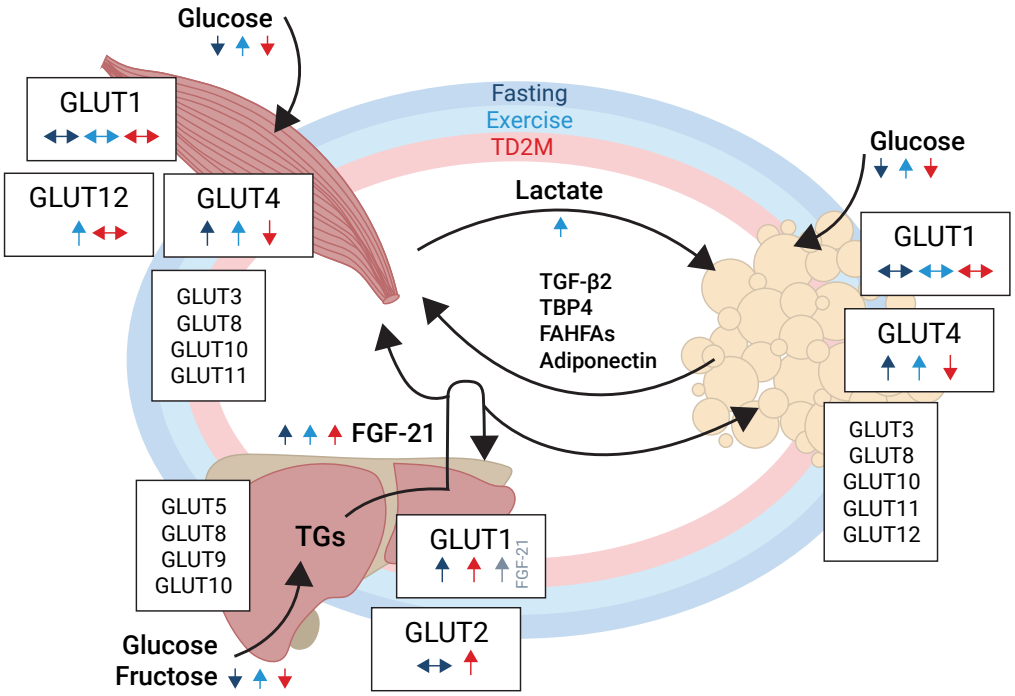


Fig 4. Overview of glucose transporters in adipose tissue, liver, and skeletal muscle.

Key Antibodies & Kits

Product	Reactivity	Application	Item No.
GLUT1 antibody (AA 203-305)	Human	WB, IHC, ELISA, IF, FC, Coat, StM	ABIN6940594
GLUT1 antibody (AA 251-329)	Human	WB, IHC, IP, ICC	ABIN7426217
GLUT2 Antibody	Human, Mouse	WB, ELISA, IHC, IF	600-401-GN3
GLUT4 antibody (AA 224-353)	Human, Mouse	WB, IHC, ELISA, ICC, FC	ABIN1724743
GLUT4 antibody (C-Term)	Human	WB, IHC, IF	ABIN6147963
SLC2A2 antibody	Human	WB, IF	ABIN7270414
SLC2A2 antibody (C-Term)	Human, Mouse, Rat	WB, ELISA, IHC, FLISA	ABIN5596790
SLC2A8 antibody (AA 401-477)	Human, Mouse, Rat	WB, ELISA	ABIN705746
GLUT1 ELISA Kit	Human	ELISA	ABIN6574259
SLC2A2 ELISA Kit	Rat	ELISA	ABIN6959572

Adipokine Antibodies, Proteins, and Kits

In recent years, extensive research has shed light on the pathological changes that occur in adipose tissue, particularly in obesity. Adipose tissue, which primarily functions as the body's energy reservoir by storing neutral triglycerides, also acts as an endocrine organ. It produces and releases active biomolecules, known as adipokines, that are involved in a wide range of physiological processes, including energy homeostasis, glucose metabolism, lipid metabolism, feeding behavior, and immune regulation. A major alteration in obesity is the dysregulation of adipokine production (See figure). To date, over 600 adipokines have been identified.

Disruptions in adipokine secretion are largely responsible for the prevalence of numerous diseases common in Western societies, such as cancer, type 2 diabetes, hypertension, fatty liver disease, and atherosclerosis. Adipokines also play a role in neuropsychiatric disorders, including depression, anxiety, schizophrenia, bipolar disorder, as well as eating disorders.

The detection and analysis of adipokines is critical for understanding their roles in health and disease. Antibodies play a crucial role in adipokine research. Monoclonal and polyclonal antibodies are used for the specific detection of adipokines in various assays, including ELISA and Western blot. These methods enable researchers to identify adipokines as potential diagnostic biomarkers for conditions such as obesity, metabolic syndrome, type 2 diabetes, cardiovascular diseases, autoimmune diseases, and inflammatory diseases.

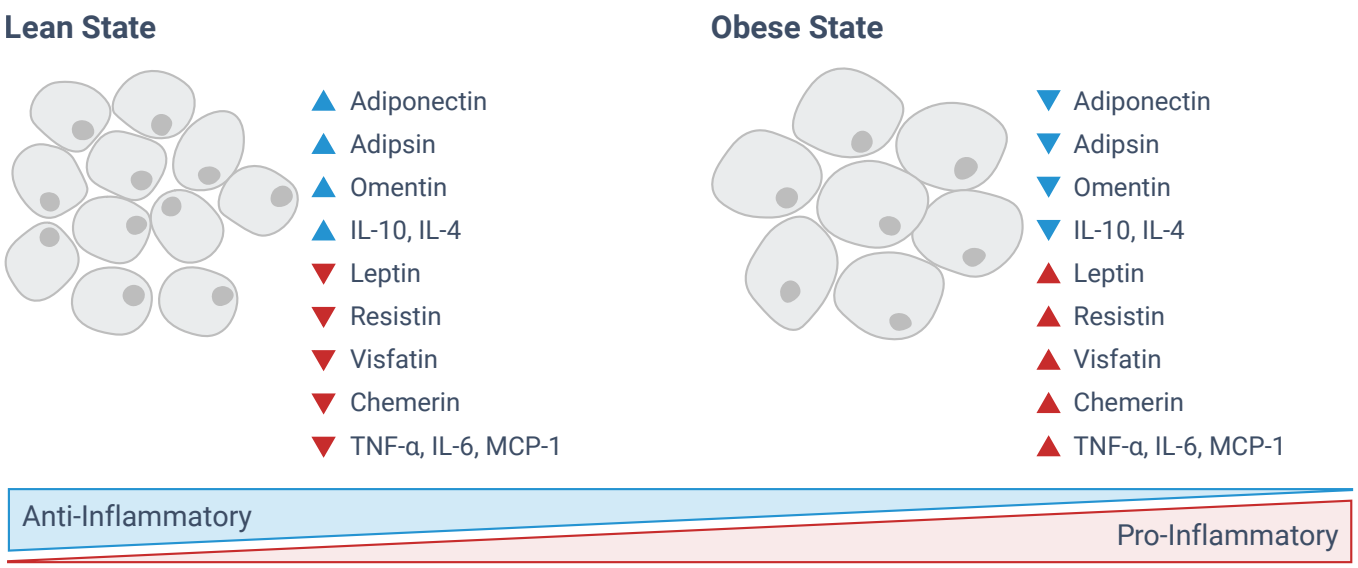


Fig 5. Adipokines in lean and obese states (Adapted from Taylor, 2021)

Key Adipokines

Leptin

Among adipokines, leptin is perhaps the most studied. Discovered in 1994, leptin is the product of the ob gene in mice and the lep gene in humans. Leptin helps to regulate body weight by decreasing appetite and increasing energy expenditure through its interaction with the long form of the leptin receptor (LEPR-B), which activates several signaling pathways, such as the JAK-STAT pathway, PI3K/AKT signaling, MAPK pathway, and AMPK. Apart from its role in energy regulation, leptin exhibits pro-inflammatory properties, enhancing the production of cytokines like IL-6, IL-12, IL-18, and TNF-α. Interestingly, studies have observed a link between lower circulating leptin levels and depression, with some clinical trials suggesting that leptin administration may alleviate depressive symptoms.

Explore Leptin Products

Adiponectin

Adiponectin is the most abundant adipokine found in the bloodstream, but its levels are inversely related to body mass index (BMI), triglyceride levels, and insulin resistance. Adiponectin serves as an endogenous insulin sensitizer, acting on organs like the liver and skeletal muscle, thus enhancing insulin sensitivity. It also possesses anti-inflammatory and pro-inflammatory properties, demonstrating its dual role in immune regulation. Research in animal models has shown that recombinant adiponectin can lower blood glucose levels and reverse insulin resistance in obese mice. Adiponectin plays a role in regulating lipid metabolism, inflammation, and glucose homeostasis.

Explore ADIPOQ Products

Resistin

Resistin, another key adipokine, was initially identified as an adipocyte-derived protein linked to insulin resistance in obese mice. Resistin contributes to the impairment of insulin receptor regulation and signaling in adipocytes by activating SOCS3. It is also implicated in promoting inflammation, driving the production of cytokines like IL-1, IL-6, IL-8, IL-12, TNF-α, and MCP-1, and triggering NF-κB signaling. In addition, resistin is released from epicardial adipose tissue and has been associated with systemic inflammation, insulin resistance, and inflammatory pathways.

Explore Resistin Products

Chemerin

Chemerin, another adipokine, plays a role in adipogenesis, angiogenesis, and inflammation. Chemerin is a chemokine derived from inflammatory cells, structurally and evolutionarily related to proteins such as cathelicidin precursors (antibacterial peptides), cystatins (inhibitors of cysteine proteases), and kininogens. Elevated chemerin levels have been associated with increased cardiovascular risk and severity of coronary artery disease, possibly due to chemerin's role in endothelial dysfunction and increased arterial stiffness.

Explore Chemerin Products

Visfatin/Nampt

Visfatin, also known as nicotinamide phosphoribosyltransferase (Nampt) or pre-B cell colony-enhancing factor (PBEF), is encoded by the NAMPT gene. High visfatin levels are correlated with obesity and, more specifically, visceral fat accumulation. Like other adipokines, visfatin exerts pro-inflammatory, proliferative, anti-apoptotic, and proangiogenic effects. Elevated plasma visfatin levels have also been linked to various cancers, including colorectal and breast cancer.

Explore Nampt Products

Adipocyte Differentiation & Function

Mammals, including humans, possess three distinct types of adipose tissues: white adipose tissue (WAT), beige (or brite) adipose tissue, and brown adipose tissue (BAT). While all these tissues originate from mesenchymal progenitor cells, the differentiation of adipocytes during adipogenesis is guided by specific proteins and transcriptional factors. Key among these are the transcription factors of the C/EBP family and proliferator-activated receptor gamma (PPARgamma), with PPARgamma being acknowledged as the primary regulator of adipose tissue biology. Additionally, members of the Kruppel-like factor (KLF) family of zinc-finger transcription factors act as both promoters and inhibitors of adipogenesis, while the tumor suppressor p53 appears to specifically inhibit the formation of white adipocytes. The figure below illustrates the differentiation of mesenchymal stem cells into white or beige adipocytes as well as skeletal muscle cells.

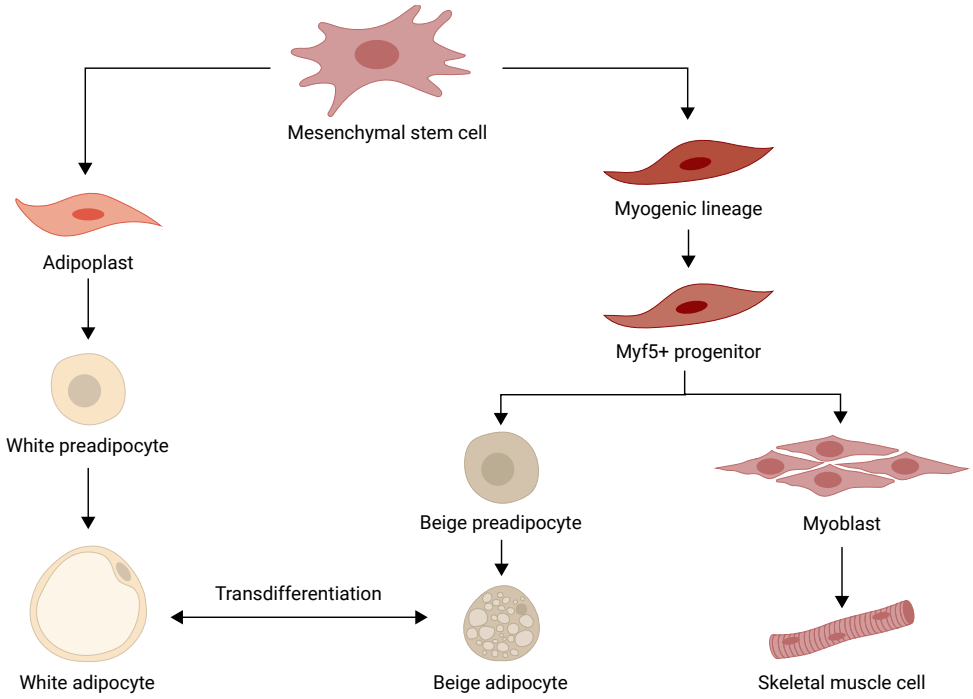


Fig 6. Schematic representation of the differentiation pathways of mesenchymal stem cells into either adipogenic or myogenic lineages.

Key Antibodies & Proteins

Product	Reactivity	Application	Item No.
KLF2 antibody (AA 251-355)	Human, Mouse, Rat	WB, FC, IF (cc), IF (p), IHC (p), IHC (fro)	ABIN680473
KLF3 antibody (N-Term)	Human	WB, IF, ELISA, FC	ABIN184727
KLF4 Antibody	Human, Mouse	WB, ELISA, IF	600-401-GU2
KLF5 antibody (C-Term)	Human	WB, IF, IHC (p), FC	ABIN391515
KLF5 antibody	Human	WB, IP, IF, IHC (p), IHC (fro)	ABIN2855604
KLF7 antibody (AA 1-230)	Human	WB, ELISA	ABIN563712
KLF9 antibody (N-Term)	Broad	WB, IHC	ABIN2777263
p53 Antibody	Human	WB, IF, Multiplex	200-301-174
PPAR gamma 1 + 2 Antibody	Broad	WB, ELISA	600-401-419
KLF4 Protein (AA 1-470) (GST tag)	-	WB, ELISA, AP, AA	ABIN1308754

Extracellular Matrix (ECM) Components

The extracellular matrix (ECM) plays a crucial role in adipose tissue, providing structural support to adipocytes, protecting them from mechanical stress, and acting as a reservoir for growth factors and cytokines. In adipose tissue, the ECM primarily consists of collagens (types I, II, III, and IV), fibronectin, and a small amount of laminin. Remodeling of healthy adipose tissue involves the continuous turnover of ECM proteins through a cycle of matrix deposition and degradation, primarily mediated by enzymes such as metalloproteinases (MMPs). These MMPs are regulated by specific endogenous inhibitors, like tissue inhibitors of metalloproteinases (TIMPs). The balance between activated MMPs and TIMPs determines the overall activity of MMPs, and an imbalance is often observed in obese adipose tissues.

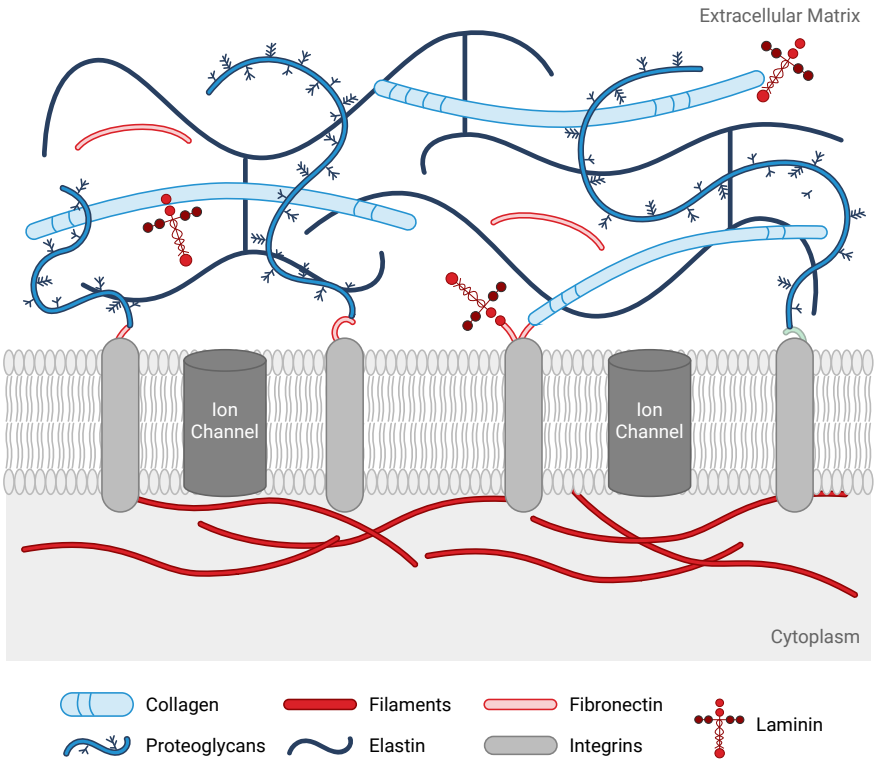


Fig 7. Structure of the Intercellular Matrix

Key Antibodies & Proteins

Product	Reactivity	Application	Item No.
Collagen Type I Antibody	Human, Mouse, Rat, Bovine, Pig	WB, ELISA, IHC, IF, FC, Dot Blot, EM, IP, Multiplex	600-401-103-0.1
Collagen Type I Antibody Biotin Conjugated	Human, Mouse, Rat	WB, ELISA, IHC, IF, FC, Dot Blot, Multiplex	600-406-103
Collagen Type II Antibody	Human, Bovine	WB, IHC, IF, Dot Blot, Multiplex	600-401-104-0.1
Collagen Type III Antibody	Human, Bovine, Pig	WB, ELISA, IHC, IF, FC, Dot Blot, Multiplex	600-401-105-0.1
Collagen Type IV Antibody	Human, Bovine	WB, IHC, IF, Dot Blot, EM, Multiplex	600-401-106-0.1
Collagen Type V Antibody	Human, Bovine	ELISA, IHC, IF, Dot Blot	600-401-107-0.1
Collagen Type VI Antibody	Human, Bovine	WB, IHC, IF, Dot Blot, Multiplex	600-401-108-0.1
Human Collagen Type I Protein	-	WB, SDS-PAGE, Cellular Assay	009-001-103
Human Collagen Type II Protein	-	WB, SDS-PAGE	009-001-104
Human Collagen Type VI Protein	-	ELISA, IF, SDS-PAGE, Cellular Assay	009-001-108

Fibrosis Markers

Fibrosis is one of the hallmarks of obese adipose tissue, marked by excessive deposition of extracellular matrix (ECM) and increased collagen alignment. The platelet-derived growth factor (PDGF) pathway plays a central role in regulating fibroblast activation and promotes the de-differentiation of adipocytes into fibroblasts/myofibroblasts. This process is associated with increased expression of fibrotic markers, including collagen I, collagen VI, alpha-smooth muscle actin (ASMA), and fibroblast-specific protein 1 (FSP1). The involvement of the transforming growth factor-beta (TGF-beta) pathway in tissue fibrosis is also well-established. When TGF-beta binds to its receptors, TGF-beta receptor 1 (TGFBR1) and TGF-beta receptor 2 (TGFBR2), it activates the canonical SMAD2/3 pathway, leading to the expression of various ECM-related genes. PDGFR and fibroblast growth factor receptors (FGFR) belong to the family of receptor tyrosine kinases (RTKs). The following pathway highlights signaling cascades of different RTKs.

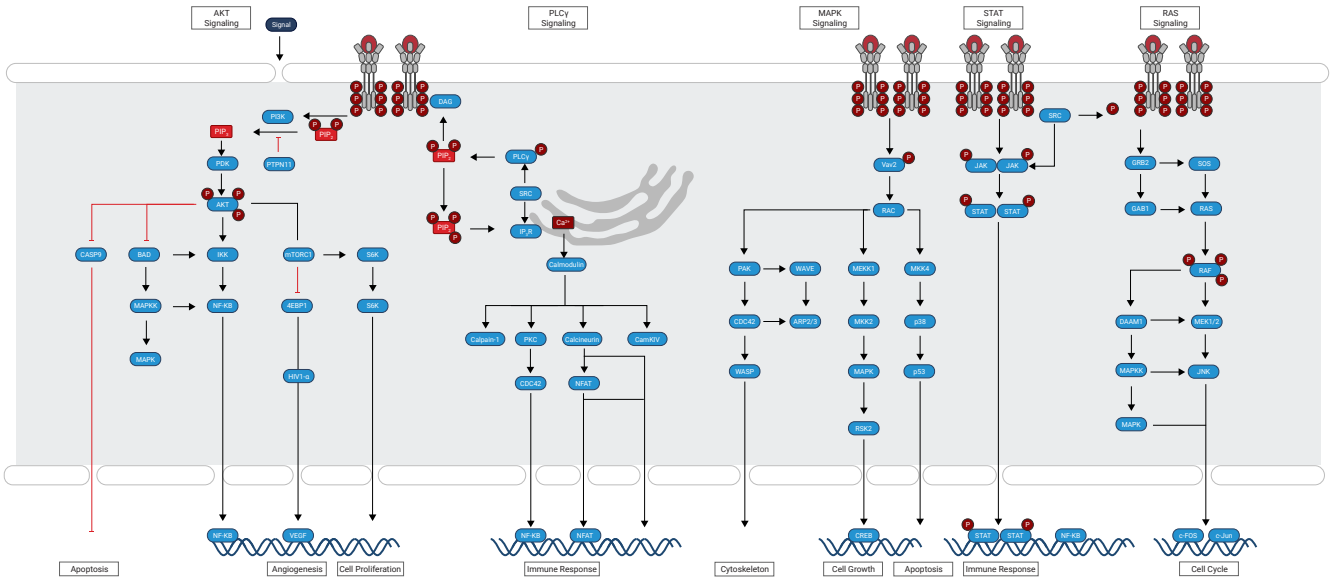


Fig 8. Overview of receptor tyrosine kinase (RTK) signaling pathways.

Key Antibodies & Proteins

Product	Reactivity	Application	Item No.
PDGF-B Antibody	Human, Mouse, Rat	WB, ELISA, IF	600-401-DK7
s100a4 antibody (AA 1-101)	Human	WB, ELISA, IF	ABIN562767
s100a4 antibody (AA 15-101)	Human, Mouse, Rat, Rabbit	WB, ELISA, FC, IHC (p), IF (cc), IF (p), IHC (fro)	ABIN703706
TGF-beta 1 Antibody	Human	WB, ELISA, IHC	600-401-432
TGF-beta antibody	Human, Mouse, Rat, Rabbit, Mammalian	WB, ELISA, IHC (p)	ABIN2476753
TGF-beta antibody (AA 301-350)	Human, Mouse, Rat, Rabbit, Sheep	WB, ELISA, FC, IF (cc), IF (p), IHC (p), IHC (fro)	ABIN707021
rHuman PDGF-AA Protein	-	SDS-PAGE, Cellular Assay	009-001-W08-0010
rMouse PDGF-AA Protein	-	SDS-PAGE, Cellular Assay	010-001-W08-0010
rHuman PDGF-AB Protein	-	SDS-PAGE, Cellular Assay	009-001-W10-0010
PDGF ELISA Kit	Human	ELISA	ABIN6969388

Gut Microbiota-Related Targets

The gut acts as the main habitat for a diverse and abundant collection of microorganisms, including bacteria, archaea, fungi, protists, and algae, collectively known as the gut microbiota. Chronic, low-grade systemic inflammation is widely recognized as a hallmark of metabolic diseases and is largely attributed to elevated levels of lipopolysaccharide (LPS) in the bloodstream. Individuals with obesity often experience gut microbiota imbalances, characterized by an overabundance of LPS-producing gram-negative bacteria. This increase in LPS can directly activate the TLR4/MyD88/IRAK4 signaling pathway in intestinal mucosal epithelial cells, leading to increased intestinal permeability. The disruption of tight junction integrity is believed to be a potential driver of inflammation in obesity.

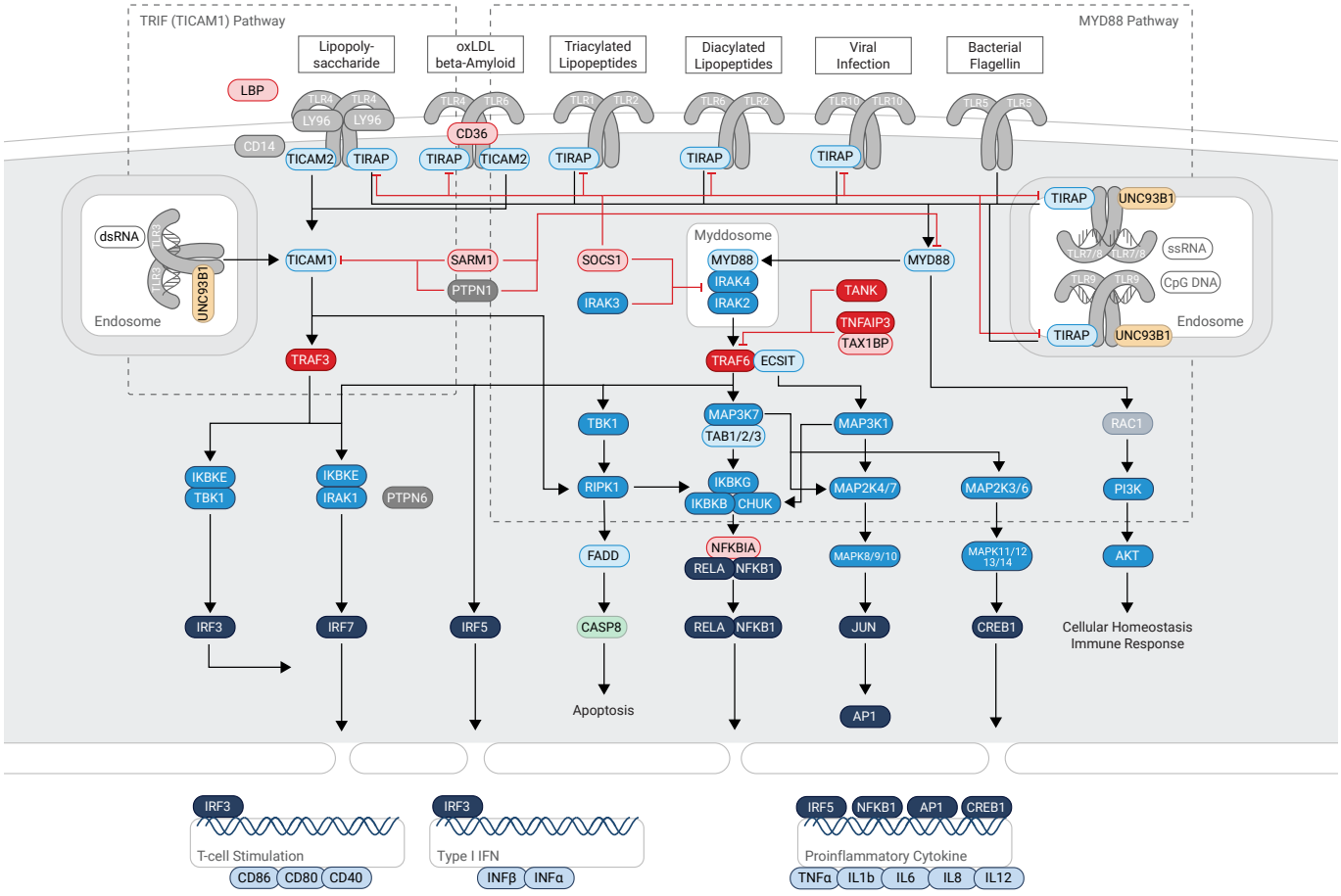


Fig 9. Toll-like receptor (TLR) signaling pathways.

Key Antibodies & Kits

Product	Reactivity	Application	Item No.
Lipopolysaccharides (LPS) antibody	Broad	ELISA, ICC, IHC (fro), CLIA	ABIN7426676
Lipopolysaccharides (LPS) antibody	*Legionella pneumophila*	PrA, DB	ABIN235748
Lipopolysaccharides (LPS) antibody	Broad	ELISA, ICC, IHC (fro), CLIA	ABIN7429382
Lipopolysaccharides (LPS) ELISA Kit	Broad	ELISA	ABIN6574100
Lipopolysaccharides (LPS) ELISA Kit	Broad	ELISA	ABIN6957515

Hormones and Metabolic Regulators

Gut hormones are crucial regulators of metabolism, orchestrating the body's response to food intake by influencing appetite, energy expenditure, and glucose homeostasis. Among these hormones, incretins, particularly glucagon-like peptide-1 (GLP-1), have gained significant attention not only for their role in enhancing insulin secretion in response to food intake but also for their impact on body weight. Originally studied for their anti-diabetic properties, GLP-1 and its analogs were found to induce weight loss through mechanisms that include reducing appetite and slowing gastric emptying. Similarly, amylin, another hormone co-secreted with insulin by pancreatic beta cells, has been observed to contribute to weight regulation by promoting satiety and inhibiting food intake. Ghrelin, known as the "hunger hormone", is the most proximally located hormone that influences appetite. Beyond these hormones, other metabolic regulators also contribute to the pathophysiology of obesity.

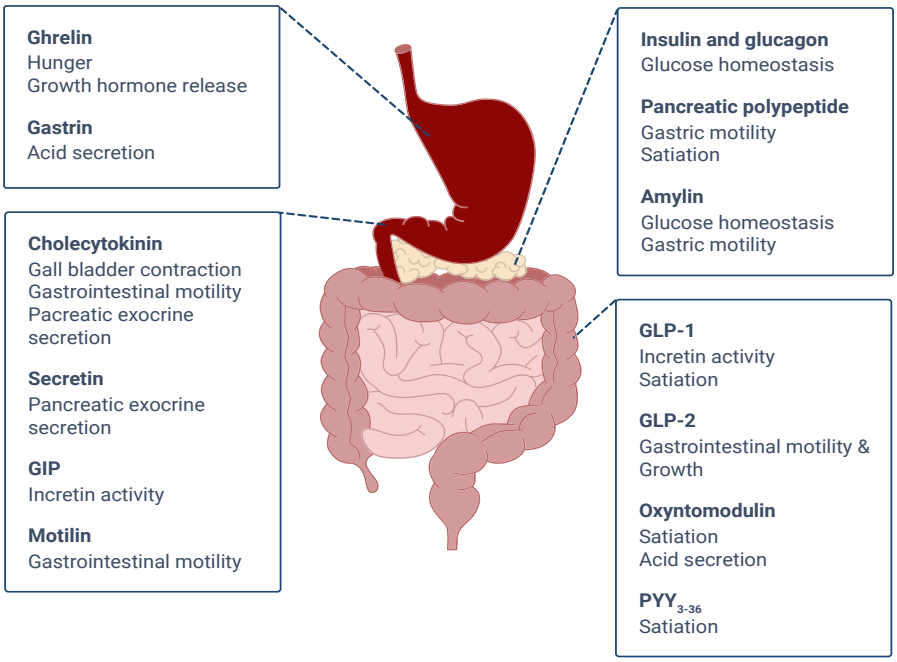


Fig 10. Overview of gut hormones and their functions.

Key Antibodies & Kits

Product	Reactivity	Application	Item No.
Amylin/DAP antibody	Human	WB, IHC, IP, ICC	ABIN7426055
Cholecystokinin antibody (AA 1-115)	Human	WB, IHC, IP, ICC	ABIN7432655
GIP antibody (AA 22-153)	Human	WB, IHC, IP, ICC	ABIN7429760
GDF15 Antibody	Human, Mouse	WB, ELISA, IHC	600-401-B07
Glucagon Antibody	Human	WB, ELISA, IHC, IF	600-401-MV9
Insulin Antibody	Human	ELISA, Dot Blot	200-301-389
Peptide YY antibody (C-Term)	Human	WB, IF, FC, IHC (p)	ABIN651296
UCP1 antibody (AA 101-200)	Human, Mouse, Rat, Goat	WB, ELISA, IHC (p), FC, IF (cc), IF (p), IHC (fro)	ABIN675413
Cholecystokinin ELISA Kit	Human	ELISA	ABIN6954720
Insulin ELISA Kit	Rat	ELISA	ABIN6574081

Inflammatory Markers

Obesity is a multifaceted condition linked to elevated levels of various inflammatory markers, resulting in persistent low-grade inflammation. Overweight and obese individuals exhibit modified serum concentrations of inflammatory cytokines, including tumor necrosis factor-alpha (TNF-alpha), C-reactive protein (CRP), and interleukins (IL-6, IL-18). These pro-inflammatory agents are crucial in the development of insulin resistance and the heightened risk of cardiovascular diseases seen in obesity. It is proposed that visceral fat contributes to systemic inflammation by directly releasing free fatty acids and inflammatory cytokines into the portal circulation.

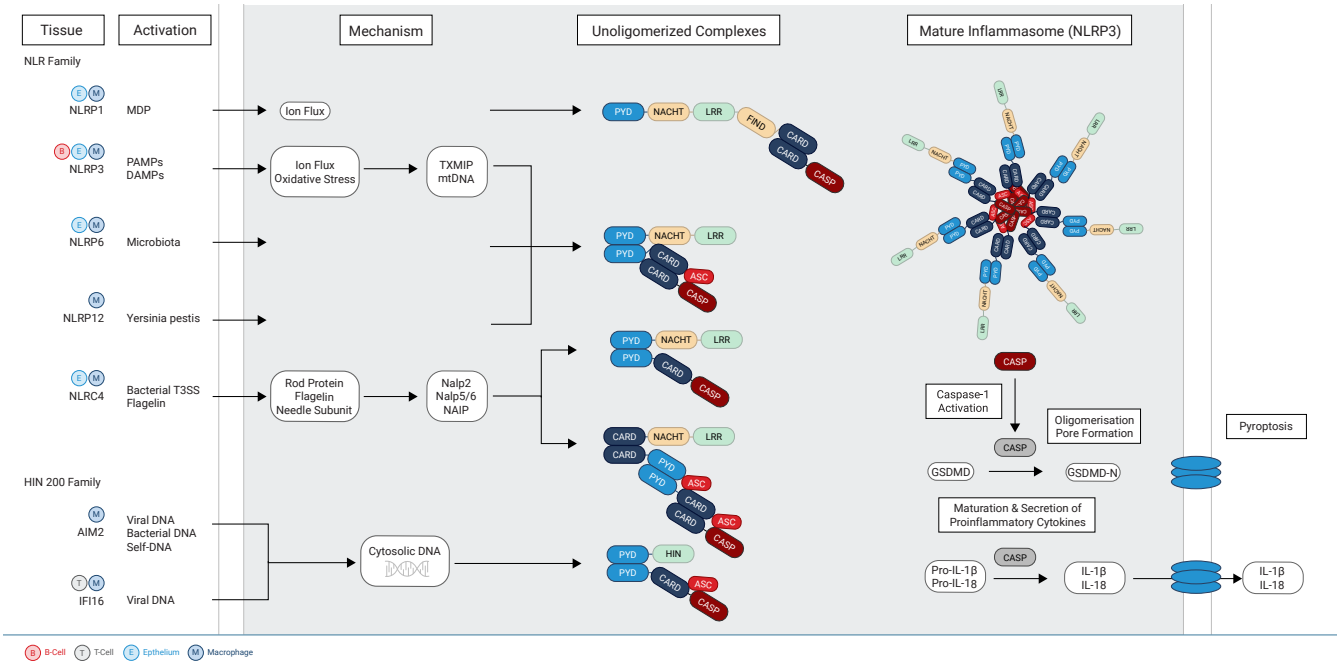


Fig 11. Inflammasome activation and signaling pathway.

Key Antibodies & Kits

Product	Reactivity	Application	Item No.
CRP Antibody	Human	WB, Dot Blot	209-1132-0100
IL-6 Antibody	Human	WB, ELISA, FC, Multiplex	209-301-310
IL-18 Antibody	Mouse	WB, IHC, IF	210-401-323
Recombinant Anti-TNF alpha Fab Antibody	Human	WB, ELISA	400-001-MT3
TNF alpha Antibody	Human	WB, IHC, IF	209-401-306-0100
TNF alpha antibody (AA 181-235)	Human, Mouse, Rat, Rabbit, Horse	WB, ELISA, IHC (p), IF (p), IHC (fro)	ABIN677318
IL-6 ELISA Kit	Human	ELISA	ABIN365163
IL-6 ELISA Kit	Rat	ELISA	ABIN6957174
IL-18 ELISA Kit	Human	ELISA	ABIN365215
TNF alpha ELISA Kit	Human	ELISA	ABIN411361

Lipid Metabolism Enzymes

Lipid metabolism is a fundamental process in energy homeostasis, involving the breakdown and storage of fatty acids. ATGL is the initial enzyme responsible for the hydrolysis of triglycerides (TG) within adipocytes. LIPE, also known as hormone-sensitive lipase (HSL), is responsible for the second step of lipolysis resulting and hydrolyzes diacylglycerols (DAG) into monoacylglycerols (MAG) and free fatty acids. LPL is another critical enzyme in lipid metabolism, primarily responsible for the hydrolysis of triglycerides in circulating lipoproteins. LPL is anchored to the endothelial surface of capillaries in tissues, where it acts at the interface between the bloodstream and tissue cells.

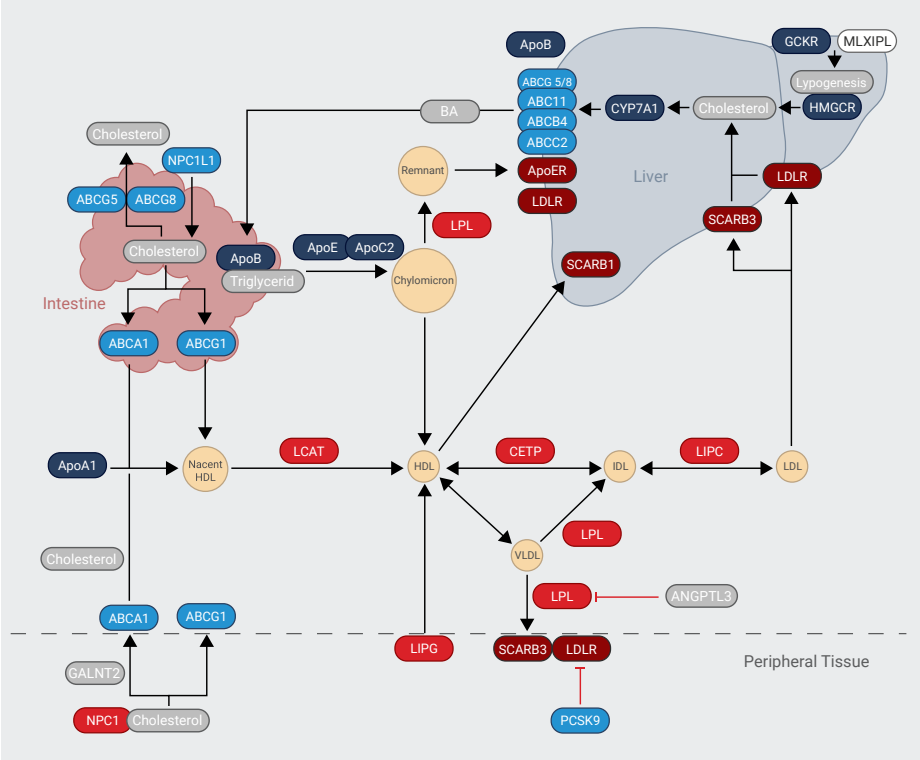


Fig 12. Overview of the lipid metabolism pathway. This diagram illustrates the key processes and molecular players involved in lipid absorption, transport, and metabolism.

Key Antibodies & Kits

Product	Reactivity	Application	Item No.
LIPE antibody (C-Term)	Human	WB, IHC (p), FC	ABIN653323
LIPE antibody (pSer552)	Human, Mouse, Rat	WB, ELISA, IHC, IF, ICC	ABIN6255406
Lipoprotein Lipase antibody (AA 28-474)	Rat	WB, IHC, IP, ICC	ABIN7429373
Lipoprotein Lipase antibody (AA 55-316)	Human	WB, IHC, IP, ICC	ABIN7429370
Lipoprotein Lipase antibody (AA 300-327)	Human	WB, IHC, ELISA, FC	ABIN3031635
PNPLA2 antibody (AA 1-504)	Human	WB, ELISA, IHC, IF	ABIN7162692
PNPLA2 antibody (AA 347-446)	Human	WB, ELISA	ABIN566087
PNPLA2 Protein (AA 1-504) (GST tag)	-	WB, ELISA, AP, AA	ABIN1315583
Lipoprotein Lipase ELISA Kit	Human	ELISA	ABIN6957519
PNPLA2 ELISA Kit	Human	ELISA	ABIN6975754

Oxidative Stress Markers

Oxidative stress plays a crucial role in the pathophysiology of obesity, driving the development of various metabolic complications. In conditions such as obesity, insulin resistance, hyperglycemia, chronic inflammation, and dyslipidemia, overproduction of reactive oxygen species (ROS) can occur. The excessive ROS generated in these pathological states can cause significant cellular damage, including DNA damage and lipid peroxidation. NADPH Oxidase 4 (NOX4) is a major source of ROS production, and its expression is frequently upregulated in adipose tissue, further amplifying oxidative stress and tissue damage. Counteracting this, the superoxide dismutase (SOD) family, comprising SOD1, SOD2, and SOD3, plays a vital role in mitigating oxidative stress by catalyzing the conversion of superoxide radicals into less harmful molecules like hydrogen peroxide.

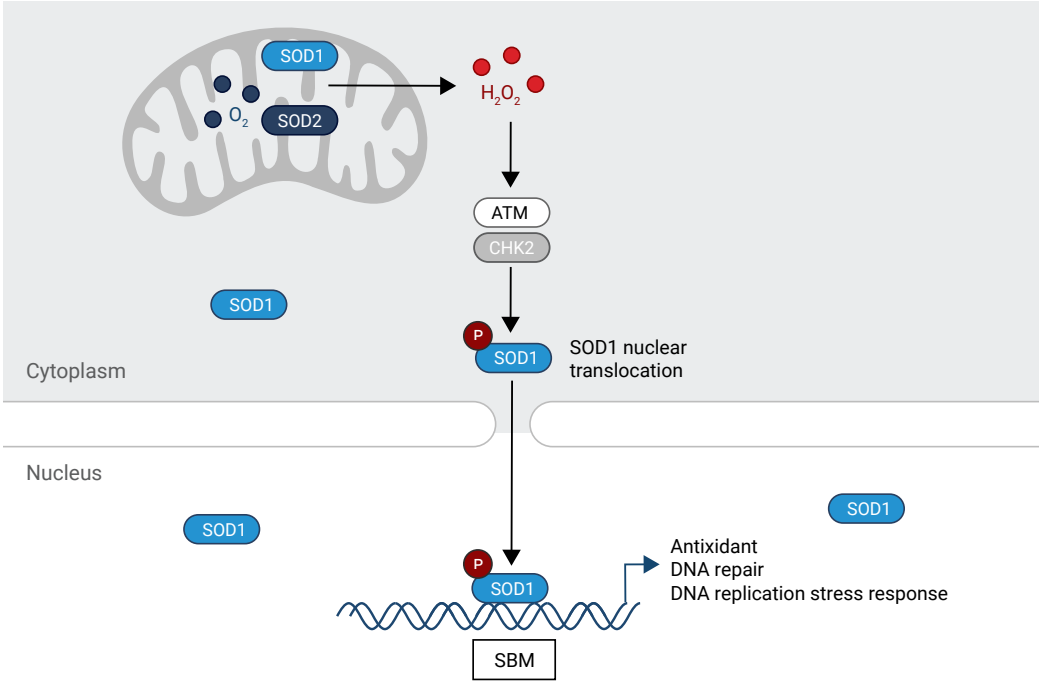


Fig 13. This figure illustrates the role of superoxide dismutases (SOD1 and SOD2) in cellular oxidative stress responses.

Key Antibodies & Kits

Product	Reactivity	Application	Item No.
Recombinant FTO antibody	Human	WB, ELISA, IHC, IF	ABIN7127502
NADPH Oxidase 4 antibody (AA 210-310)	Human	WB, ELISA, IHC, FC, ICC	ABIN5542344
SOD1 antibody	Human	WB, ELISA, IHC (p)	ABIN2854793
SOD2 antibody (AA 25-222)	Human	WB, IHC, IF	ABIN3021904
SOD3 antibody	Human	WB, IHC, ELISA, ICC, IF	ABIN361742
SOD1 ELISA Kit	Rat	ELISA	ABIN6963720
SOD2 ELISA Kit	Human	ELISA	ABIN6959751
SOD2 ELISA Kit	Rat	ELISA	ABIN6959752
SOD3 ELISA Kit	Human	ELISA	ABIN6976128
NADPH Oxidase 4 ELISA Kit	Human	ELISA	ABIN6958026

Other Related Pathways

Signaling Pathways Overview

The “bone-fat switch” is a key concept where pathways, such as Wnt and hedgehog promote osteogenesis while inhibiting adipogenesis in precursor cells. Wnt signaling suppresses adipogenesis by activating β-catenin, favoring bone formation over fat development. The hedgehog pathway similarly inhibits fat cell formation while encouraging bone growth. TGF-β/BMP signaling plays a dual role, where TGF-β inhibits and BMP4 promotes adipogenesis, influencing the balance between fat and bone cell differentiation. Notch signaling, known for its complex effects, can both promote early adipocyte differentiation and inhibit it through repression of PPARgamma. The MAPK pathway, through ERK1 and p38, regulates adipocyte proliferation and differentiation phases, impacting fat tissue expansion. The Fibroblast Growth Factor (FGF) pathway, particularly through FGFs like FGF1 and FGF10, promotes adipogenesis and plays a role in energy metabolism, linking it to obesity.

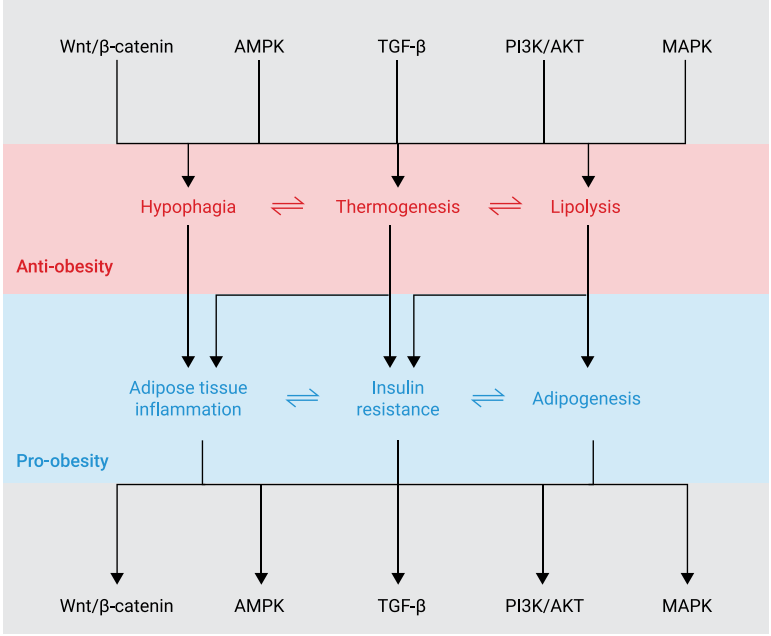


Fig 14. Key molecular pathways and their dual roles in anti-obesity and pro-obesity mechanisms.

Key Pathway Antibodies

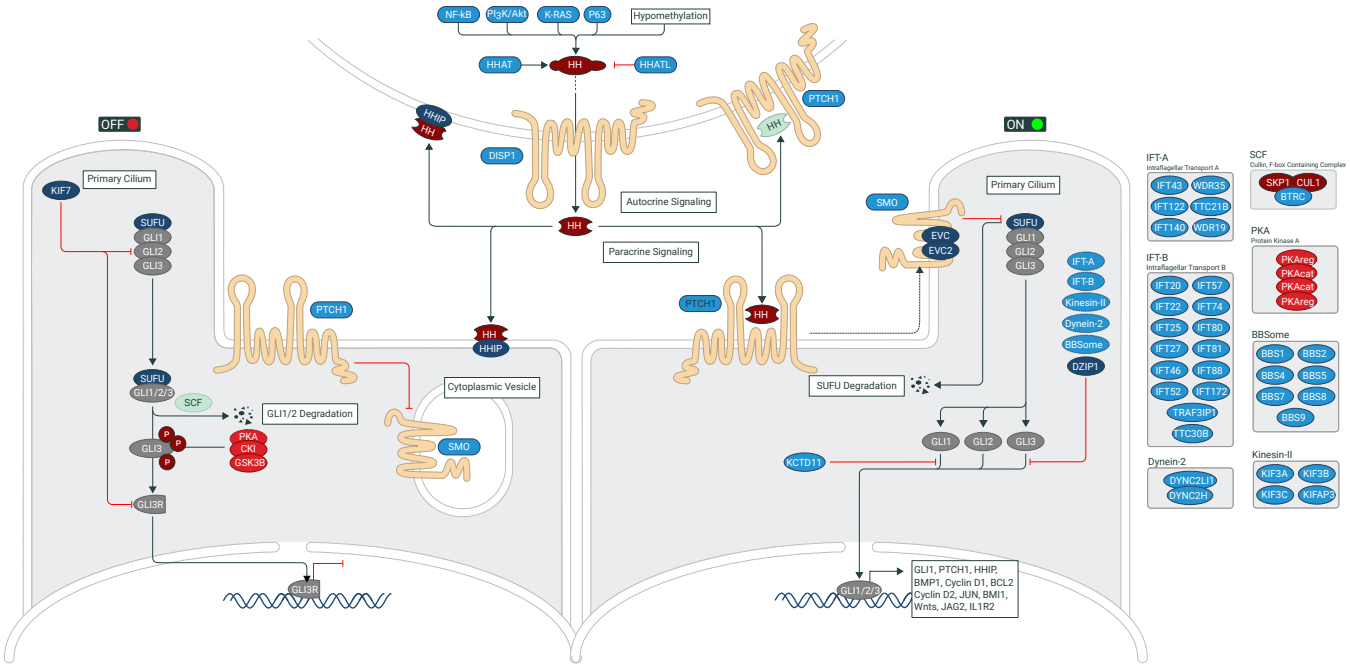
Product	Reactivity	Application	Item No.
AKT Antibody	Human, Mouse, Rat, Chicken	WB, IHC, IF	100-401-401
AKT phospho S473 Antibody	Human, Mouse, Rat, Monkey	WB, ELISA, IHC, IF, FC, Multiplex	200-301-268
beta Catenin Antibody	Human, Zebrafish	WB, ELISA, IHC, IF	600-401-C68
Gli1 Antibody	Human, Mouse	WB, ELISA, IHC, IF, ChIP, IP	100-401-223
GLI2 Antibody	Human, Rat	WB, ELISA, IHC	600-401-845
GLI3 Antibody	Human	WB, ELISA, IHC, IF, Multiplex	600-401-694
mTOR Antibody	Human	WB, ELISA, IF	600-401-897
NOTCH 1 Antibody	Human, Mouse	WB, ELISA, IHC, IF, Dot Blot, IP, Multiplex	100-401-407
NOTCH 2 Antibody	Human	WB, ELISA, IHC	100-401-408
Wnt1 Antibody	Human, Mouse	WB, ELISA	600-401-A37

Hedgehog Signaling

First described in Drosophila and named after the “spiked” phenotype of the mutant fruit fly larva, the hedgehog (Hh) signaling pathway is highly conserved from flies to humans and regulates normal cell growth and differentiation in embryonic development. In adult organisms, the signaling pathway is largely inactive and limited to stem cell subpopulations to maintain tissue homeostasis. If imbalanced, the signaling pathway can lead to tumorigenesis and promote the spread of existing tumors (Reviewed in Doheny *et al.*, 2020). A consistently activated Hh signaling pathway is found in a group of human cancers that together account for about 25% of all cancer deaths. This has also led to the recognition of this signaling pathway as an important therapeutic target in the fight against malignant tumors.

Three homologs of the Hh protein are expressed in mammals. These include Sonic hedgehog (SHH), named after the video game character that helped SEGA gain success in the 1990s, indian hedgehog (IHH), and desert hedgehog (DHH). These proteins are generated from precursors through a multitude of processing steps including autocatalytic cleavage, ligation of cholesterol, and subsequent palmitoylation catalyzed by Hh acyl transferase (HHAT). Mature Hh is then secreted through cell surface protein dispatched-1 (DISP1) and binds to patched receptor (PTCH1) in target cells, lifting its inhibitory function on smoothened receptor (SMO). SMO subsequently activates the glioma-associated oncogene transcription factors (GLIs) that translocate to the nucleus and turn on the transcription of target genes.

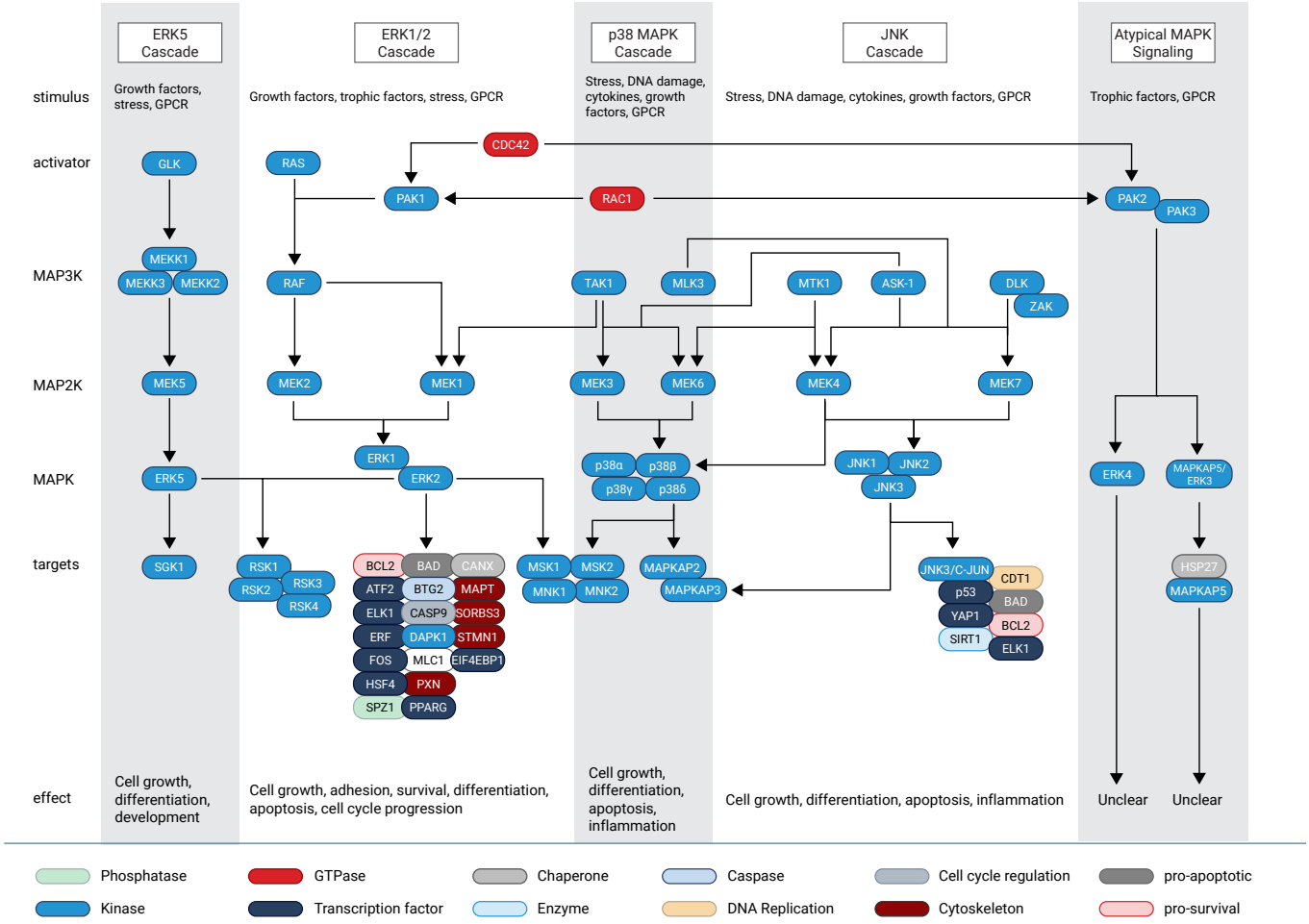
In the off-state, inactive PTCH1 prevents the translocation of SMO to the cell surface. GLI proteins are then sequestered by suppressor of fused (SUFU) and phosphorylated by several kinases such as PKA, CK1, and GSK3β. Partial degradation of GLI proteins generates the repressor GLI3R which suppresses transcription of Hh target genes in the nucleus. Rockland and antibodies-online provides several antibodies to help study the hedgehog signaling pathway including highly specific polyclonals against GLI1, GLI2, GLI3, and SMO.



MAPK Signaling

Phosphorylation is the reversible process of attaching a phosphate group to a specific amino-acid residue on a protein. Functionally, phosphorylation acts as a simple molecular switch that can activate, deactivate, or modulate the function of a protein. Addition and removal of phosphate groups provide spatial and temporal control over protein activity. Phosphorylation is tightly controlled by a competing interdependent network of kinases - which donate phosphate groups to a substrate protein, and phosphorylases - which remove them from a substrate.

Mitogen-activated protein kinases (MAPKs) are a highly conserved and ubiquitously expressed family of enzymatic kinases that phosphorylate many different target substrates. MAP-kinases are part of a larger, tiered phosphorylation cascade that includes MAP2Ks and MAP3Ks. This tiered organization affords flexibility, allowing a broad range of higher-order kinases to respond to stimuli and control cellular function through activation of a smaller subset of MAP-kinases that interact directly with other functional proteins. MAP-kinases play a major role in nearly every cellular process. MAPK dependent phosphorylation is implicated in signaling cascades that regulate cell-cycle progression, differentiation, development, and apoptosis.

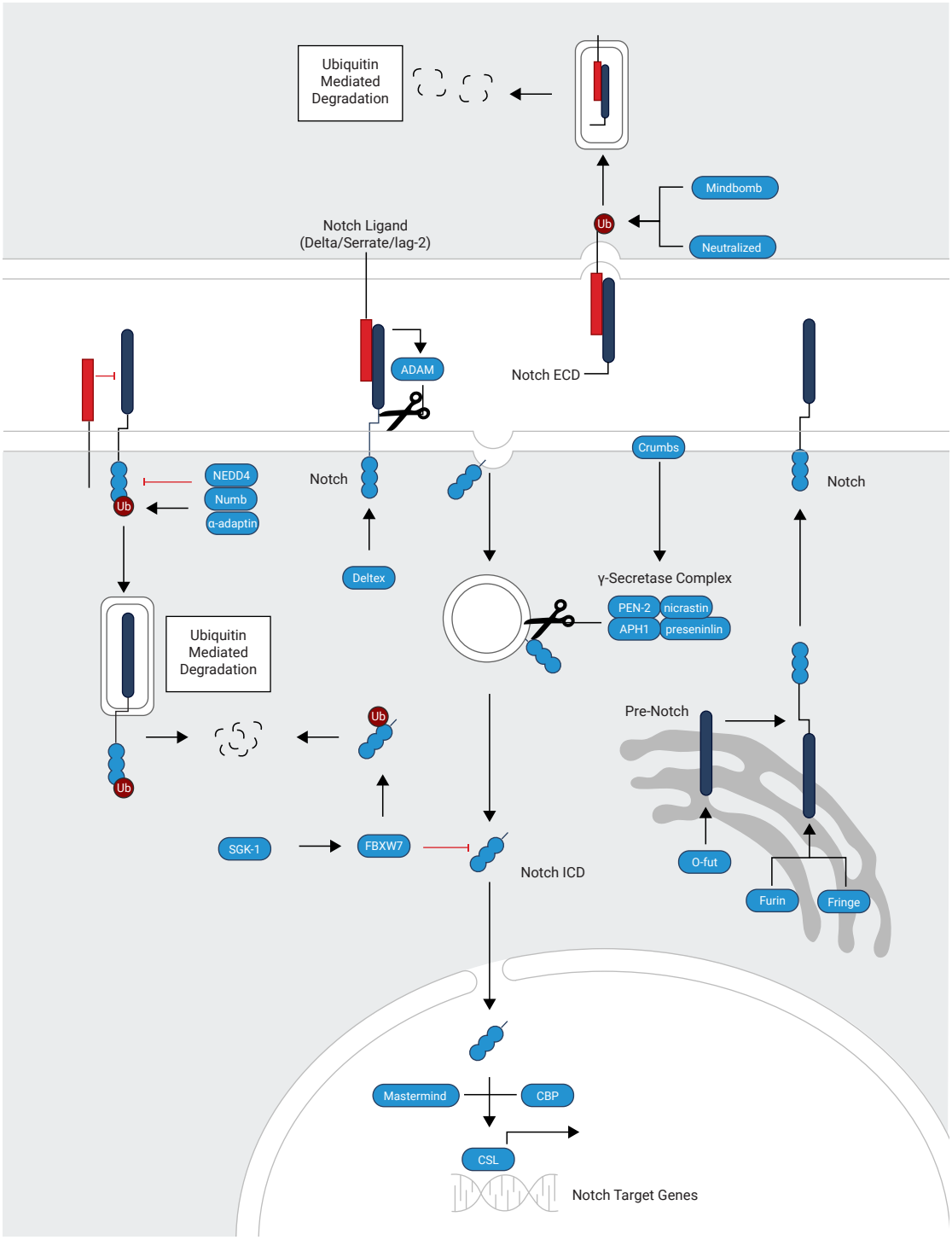


NOTCH Signaling

The highly-conserved Notch signaling pathway is unique, as both the Notch receptor and most of its respective ligands (canonically the DSL or Delta/Serrate/lag-2 family members) are transmembrane proteins attached to the cell surface. Therefore, Notch signaling is limited to interaction between adjacent cells.

Communication between adjacent cells is paramount, particularly during early development, when cell fate and function are yet to be determined. Notch signaling provides a method for cells to specify their own identity, and to simultaneously influence the role and identity of neighboring cells through lateral inhibition.

The core of the Notch signaling pathway involves two adjacent cells, one expressing a DSL family ligand, and the other expressing the Notch (the receptor). When receptor and ligand interact, two separate protease enzymes cleave Notch into extracellular and cytosolic components. ADAM proteases cleave the extracellular portion of Notch, which remains bound to its respective ligand and is endocytosed by the signaling cell. γ-secretase cleaves the cytosolic portion of notch. This cytosolic region migrates to the nucleus where it binds to the transcription factor CSL, transforming it from a transcriptional repressor to an activator, and upregulating expression of Notch target genes.

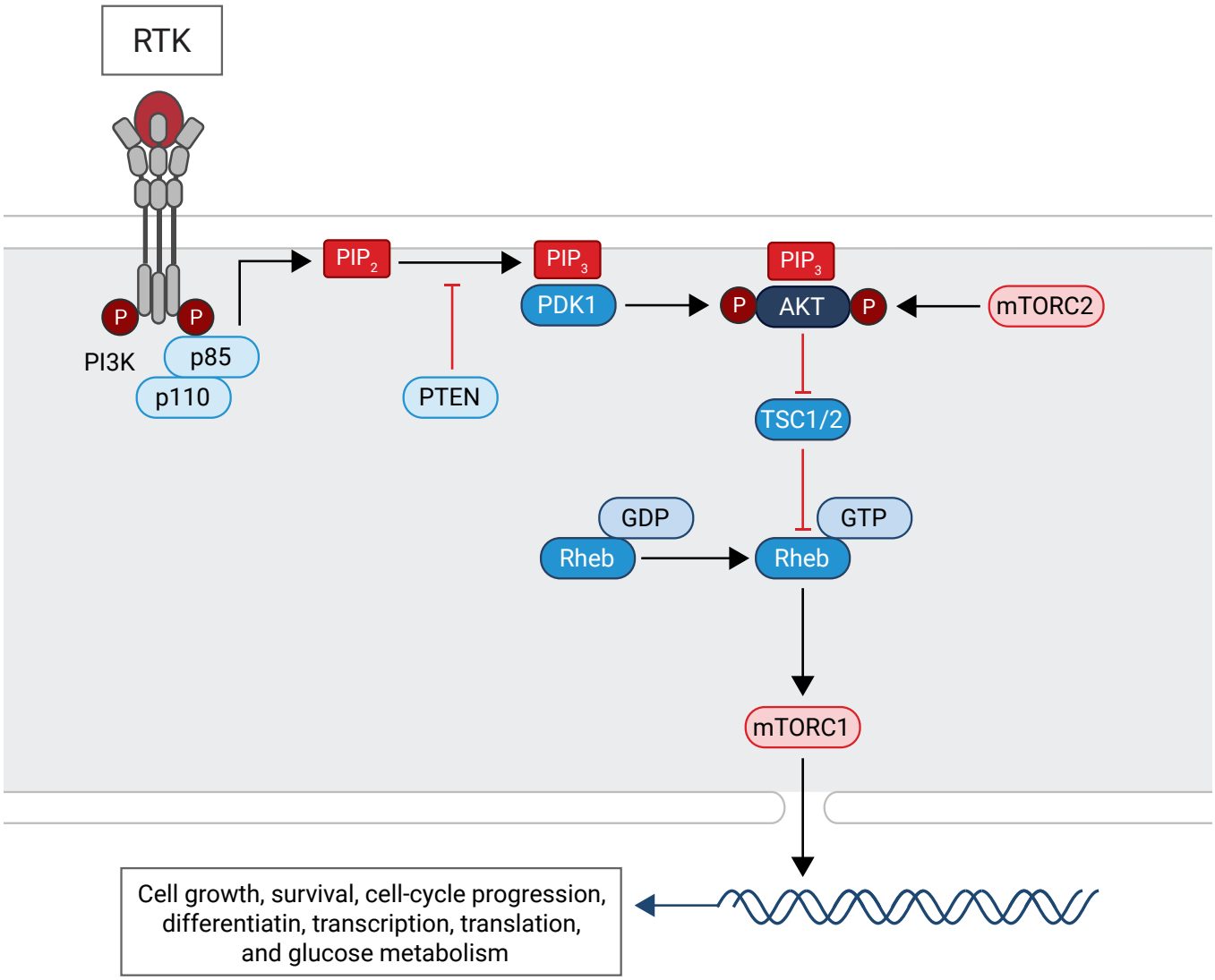


AKT/PI3K Signaling

AKT/PI3K is one of the most actively studied kinase pathways in basic research and drug development, as it plays an integral role in mediating signals for cell growth, survival, cell-cycle progression, differentiation, transcription, translation, and glucose metabolism (See figure below). Recent advances in AKT signaling have focused on understanding cellular processes and identifying cellular substrates that are physiologically relevant *in vivo*. These efforts have uncovered important roles for AKT pathway regulation in cancer research, neuroscience, and disease prevention.

Also known as PKB, AKT is a serine/threonine kinase composed of an N-terminal regulatory domain, a hinge region that connects the regulatory domain to a kinase domain, and a C-terminal region required for the induction and maintenance of the kinase activity. Initially, AKT was discovered as a proto-oncogene. There are three highly homologous isoforms known as AKT1 or simple AKT, AKT2, and AKT3 with alternatively named PKB α, PKB β, and PKB γ, respectively. AKT1 plays an important role in cellular survival by inhibiting apoptotic processes and is implicated as a major factor in many types of cancer. AKT2 required to induce glucose transport is an important signaling molecule in the insulin signaling pathway. The role of AKT3 is less clear, though it appears to be predominantly expressed in the brain. Deregulations in the AKT-related pathway were observed in many human diseases, including cancer, cardiopathies, neurological disorders, and type-2 diabetes.

Thanks to the funding support from the National Cancer Institute (NCI Awards HHSN26100900070C and HHSN261201100087C), Rockland has developed over 100 AKT-related products. Recombinant AKT calibrator proteins have been produced as both AKT active (phosphorylated) and non-active (phosphatase-treated and phosphorylation site double mutant recombinant proteins). These reagents can be used for detecting status of proteins involved in AKT/PI3K pathway including AKT1, AKT2, and AKT3 isoforms and their phosphorylated stages.



WNT Signaling

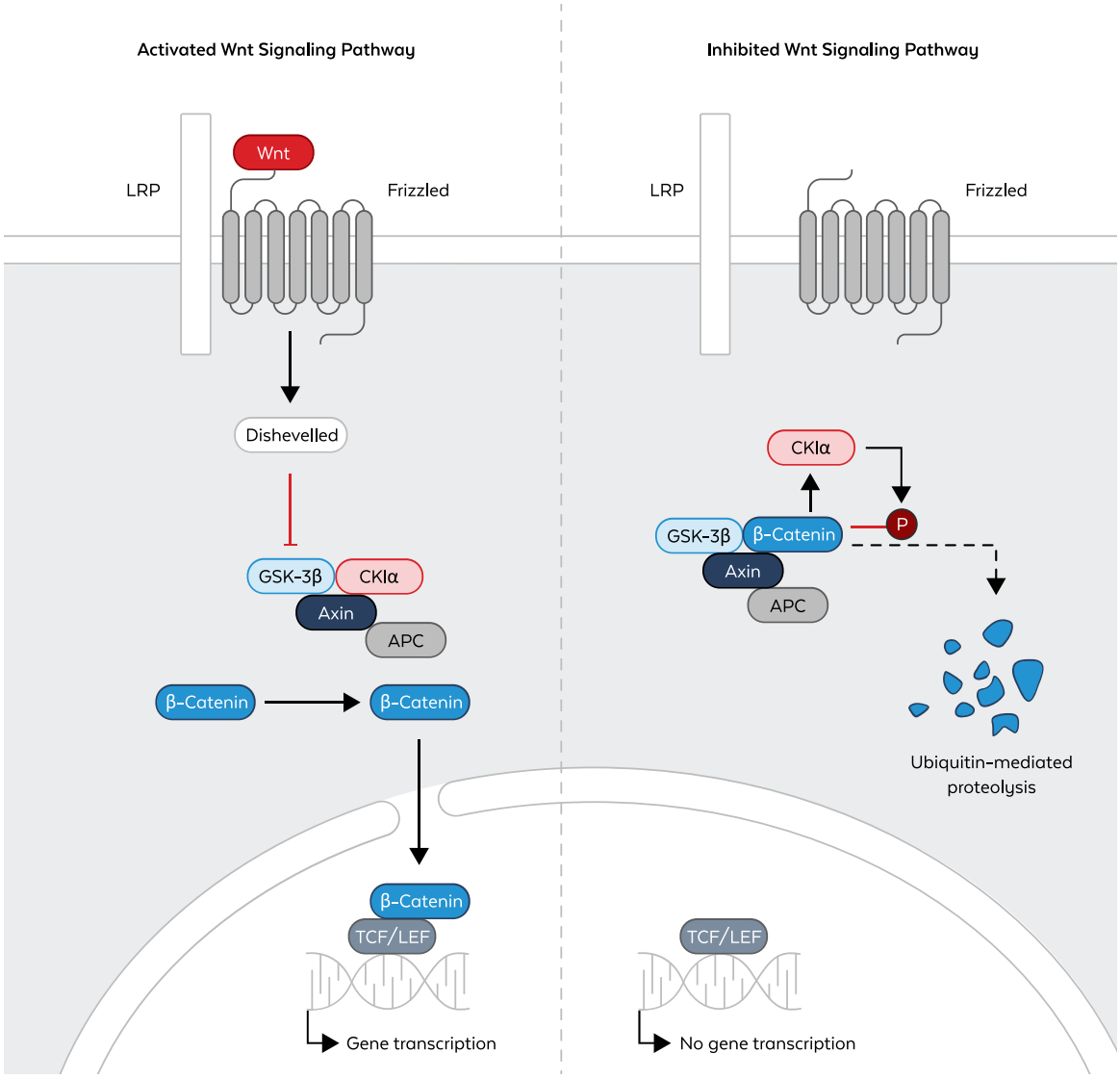
Wnt is a hybrid name derived from the combination of the mouse proto-oncogene int-1 and the segment-polarity gene wingless (wg) from *Drosophila*, which form the Wnt gene family since a revision of the nomenclature in the early 1990s. The evolutionary-conserved Wnt proteins have been implicated in the regulation of cell proliferation and development through several different signal-transduction pathways. Through its numerous interactions, perturbations in these pathways lead to numerous defects such as cancer and degenerative diseases.

The canonical Wnt or Wnt/β-catenin signaling pathway (see figure) begins with the binding of Wnt to a receptor complex consisting of frizzled (Fz) and LRP (lipoprotein receptor-related protein). After activation of the complex, Fz interacts with disheveled (Dsh) in the cytosol, which causes the aggregation of a complex consisting of Axin, GSK-3β, CK1α, and APC at the receptor. In this complex, glycogen synthase kinase 3β (GSK-3ß) is inactivated and prevents the transcriptional cofactor β-catenin from being phosphorylated. Increased levels of cytosolic β-catenin allow translocation to the nucleus, removing the suppression of gene transcription by the TCF/LEF complex.

In its inactive configuration, Axin-bound β-catenin is inactivated due to its phosphorylation by serine-threonine kinases CK1α and GSK-3ß and is subsequently destroyed by ubiquitin-mediated proteolysis. This prevents β-catenin from entering the nucleus and inactivating the repressor complex consisting of TCF (T-cell specific factor) and LEF (lymphoid enhancer-binding factor), which prevents gene transcription of the target genes.

The non-canonical or β-catenin independent Wnt signaling pathway uses other effectors to regulate transcription. One of them is the Wnt/Ca2+ signaling pathway, whose regulation relies on the transcription factors NFAT (nuclear factor of activated T cells) and TAK1-induced Nemo-like kinase (NLK) and is involved in cancer, inflammation, and neurodegenerative diseases. Additionally, the PCP signaling pathway activates a number of Rho family of GTPases as well as Jun-N-terminal kinase (JNK) and regulates cell polarity during morphogenesis.

The most important question in the exploitation of the Wnt pathway to combat disease is how to control aberrations without interfering with the normal functions of this complex pathway.



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