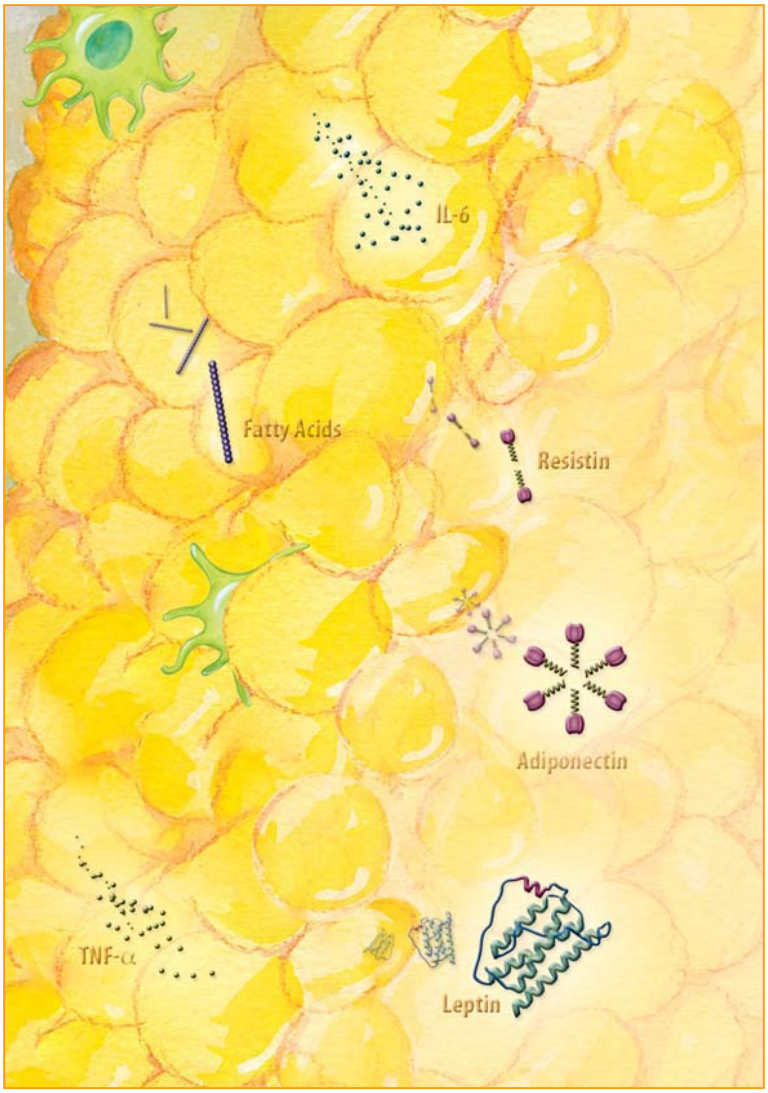
Lipid Metabolism & Obesity

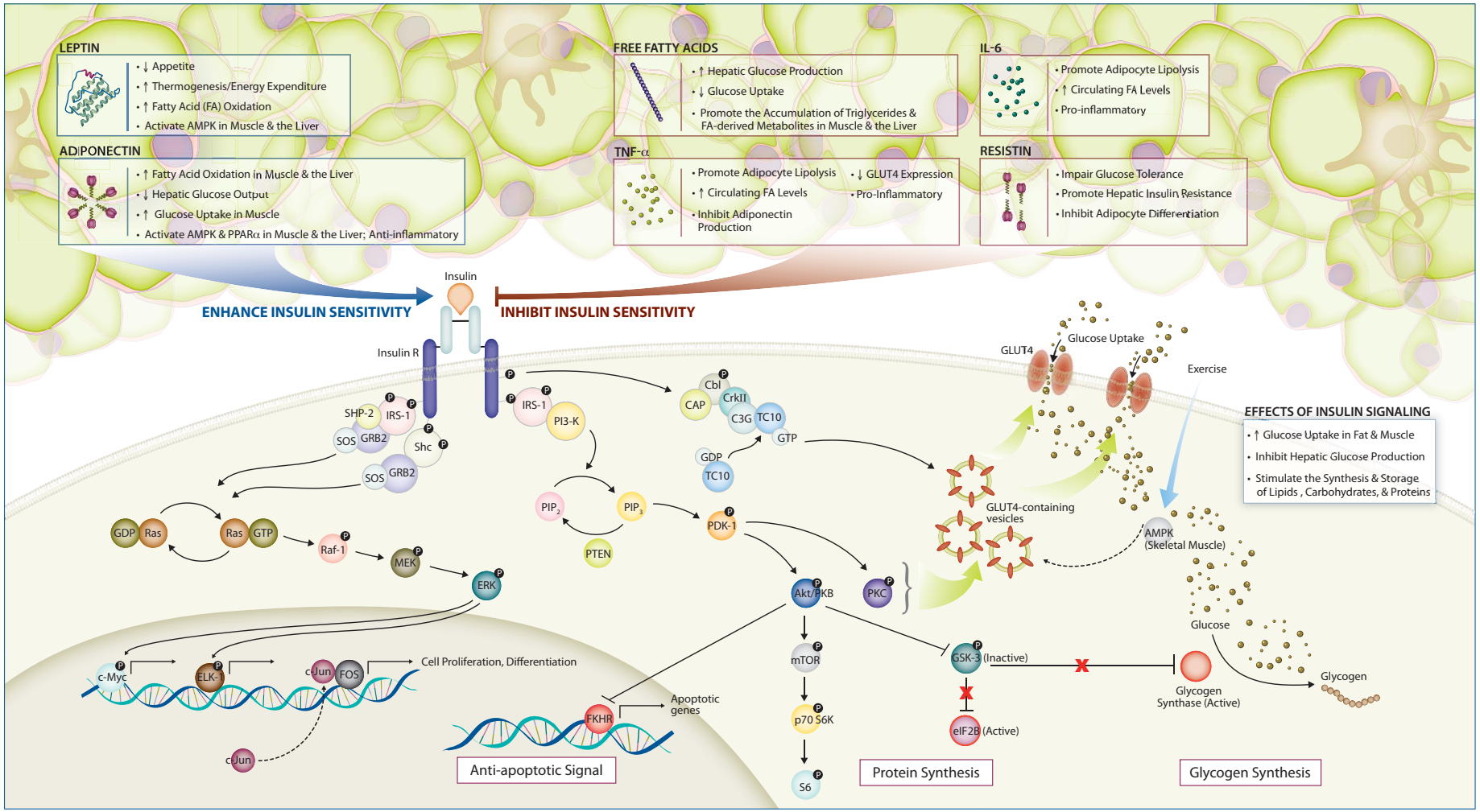


R&D SYSTEMS®

Lipid Metabolism & Obesity

Insulin, secreted by the pancreatic β cells, is the main regulator of blood glucose levels. It stimulates glucose uptake in muscle and fat, inhibits glucose production in the liver, promotes glycogen and lipid synthesis, and inhibits lipolysis. Several factors secreted by the adipose tissue either promote or inhibit insulin sensitivity including Leptin, Adiponectin, TNF-α, IL-6, and Resistin (in mice). The ability of these cytokines to influence insulin signaling suggests that changes in their levels may contribute to the development of insulin-related metabolic disorders such as Type II diabetes. One of the leading risk factors for Type II diabetes is obesity, a condition characterized by an increase in adipocyte size, mild inflammation, and altered adipocytokine secretion. Obesity is associated with reduced Leptin sensitivity and a decrease in the production of Adiponectin, two adipocytokines that normally enhance insulin sensitivity. These changes are coupled with an increase in the production of Resistin and pro-inflammatory cytokines such as TNF-α and IL-6, which promote insulin resistance. Characterizing the mechanisms by which adipocytokines enhance or interfere with insulin signaling pathways is critical to our understanding of how these factors contribute to the pathogenesis of metabolic disorders.

R&D Systems offers a wide range of research reagents useful for the study of metabolic signaling pathways.



Several Adipocytokines Affect Insulin Sensitivity and Metabolism.
Adipose tissue is now recognized not only as a lipid storage site, but also as an active endocrine organ that secretes numerous adipocytokines. These factors affect multiple cellular processes including energy homeostasis, immune system function, and inflammation. Many adipocytokines, such as Leptin, Adiponectin, IL-6, TNF-α, and Resistin, along with free fatty acids, affect insulin sensitivity and metabolism. Insulin regulates blood glucose levels by inhibiting glucose production and activating signaling pathways that promote glucose uptake. Binding of insulin to its receptor induces autophosphorylation of the receptor and subsequent activation of Phosphatidylinositol 3-Kinase (PI 3-K). PI 3-K stimulates the phosphorylation and activation of Akt/PKB and PKC, two kinases that promote the translocation of the GLUT4 glucose transporter to the plasma membrane. Exposure of GLUT4 at the plasma membrane stimulates the uptake of glucose in fat and skeletal muscle. Additionally, active Akt/PKB phosphorylates and inactivates Glycogen Synthase Kinase-3 (GSK-3). Inactivation of GSK-3 keeps Glycogen Synthase active, promoting the storage of glucose as glycogen. Autophosphorylation of the insulin receptor also activates the Cbl-CAP complex, which recruits CrkII, C3G, and TC10. Activated TC10 serves as a second signal for GLUT4 translocation. In addition to stimulating glucose uptake, insulin signaling promotes cell proliferation and differentiation through the activation of Ras/MAPK signaling pathways. Exercise can also stimulate GLUT4 translocation and glucose uptake by activation of AMPK, a master regulator of muscle metabolism and energy homeostasis. AMPK promotes catabolic processes such as fatty acid oxidation and glycolysis to increase cellular energy levels, and inhibits anabolic processes such as glycogen and protein synthesis.

Products for Lipid Metabolism & Obesity Research

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs & Other Kits
Adiponectin/Acrp30	H M	H M R	H M
AgRP	H M	H M	H
Akt Pan Specific		H M R	
Phospho-Akt (S473) Pan Specific		H M R	H M R
Akt1	H	H M R	H M R
Phospho-Akt1 (S473)			H M
AMPKα1		H M R	
Phospho-AMPKα1 (T174)			H
Phospho-AMPKα1/2 (T174/T172)		H	
AMPKα2		H M R	
AMPKβ1		H M R	
AMPKβ2		H M	
Apolipoprotein A-I/ApoA1		H	
Apolipoprotein A-II/ApoA2		H	
Apolipoprotein B/ApoB		H	
Apolipoprotein C-II/ApoC2		H	
Apolipoprotein E/ApoE		H	
Apolipoprotein E3/ApoE3	H		
Apolipoprotein E R2/ApoE R2	H		
CCK-A R		H M R	
CD36/SR-B3	H M	H M	M
Chem R23		H	
Chemerin	H M	H M	H M
CNTF	H R	H R	H R
CNTF Rα	H R	H R	
Complement Component C3a	H	H	
Complement Factor D/Adipsin	H	H	H
Crk		H	
EGR1		H	
ERK1	H	H M R	H
Phospho-ERK1 (T202/Y204)			H M R
ERK1/ERK2		H M R	
Phospho-ERK1/ERK2 (T202/Y204)/(T185/Y187)		H M R	H M R
ERK2	H	H M R	H M R
Phospho-ERK2 (T185/Y187)			H M R
FABP4		H M	
FATP4		H	
Fyn		H M R	
GLP-1R		H	
GLUT4		R	
Glucagon		H M	
gp130	H M R	H M	H
Phospho-gp130			H
GRB2		H M R	
GSK-3α		H	
Phospho-GSK-3α (S21)		H M R	H
GSK-3α/β		H M R	H M R
Phospho-GSK-3α/β (S21/S9)		H M R	H M R
GSK-3β	H	H M R	
Phospho-GSK-3β (S9)			H M R
HMGB1	H	H	
HNF-3β/FoxA2		H	
HNF-4α/NR2A1		H	
HNF-4γ/NR2A2		H	
IκB-α		H M	
Phospho-IκB-α (S32/S36)		H	
IκB-β		H R	
IκB-ε		H M	

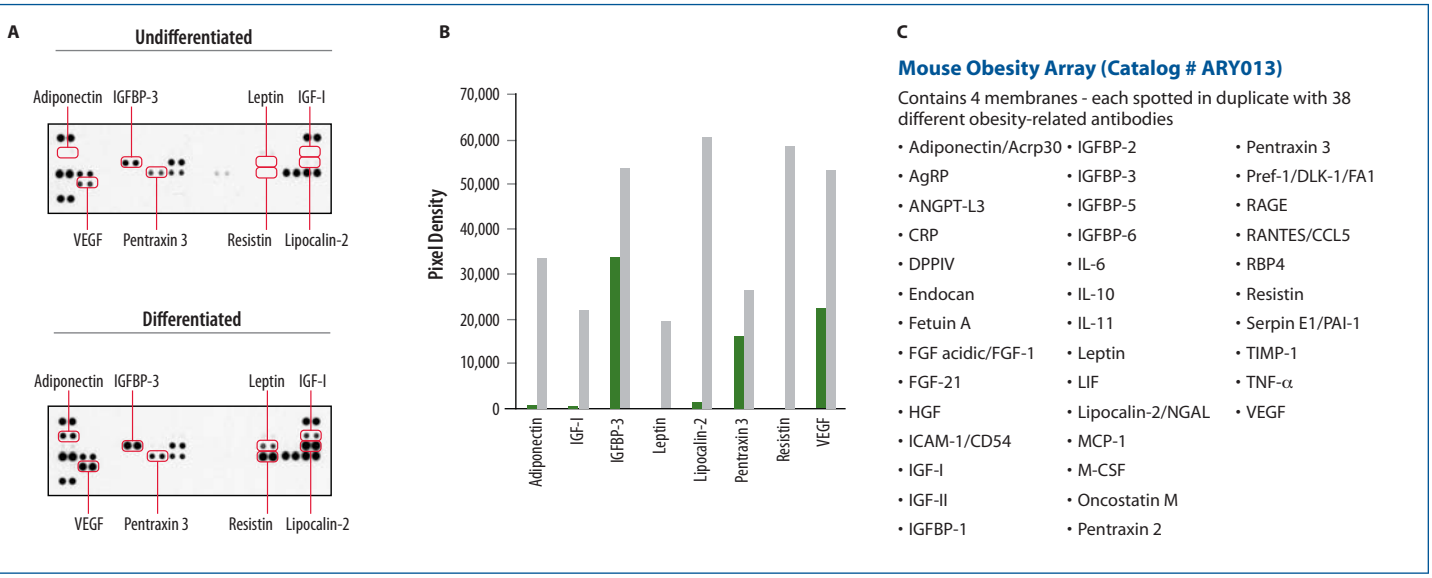
Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs & Other Kits
IKKα		H M R	
IKKβ		H	
IKKε		H M R	
IKKγ		H M R	
IGF-I	H M R	H M	H M
IGF-I R	H	H	H
Phospho-IGF-I R		H	H
IGFBP-1	H M	H M	H
IGFBP-2, -3	H M	H M	H M
IGFBP-4	H	H	
IGFBP-5, -6	H M	H M	H M
IL-6	H M R Ca CR E F P	H M R Ca CR E F P	H M R Ca F P
IL-6 Rα	H M	H M	H M
INSRR		H	
Insulin		H M B	
Insulin R/CD220	H	H	H
Phospho-Insulin R/CD220		H	H
Proinsulin	H	H M	H
Insulysin/IDE	H	H	
IRS-1		H M R	
Jak2		M R	
JNK Pan Specific		H M R	H M R
Phospho-JNK Pan Specific			H M R
Phospho-JNK (T183/Y185)		H M R	
JNK1	M	H M R	H M R
JNK1/JNK2		H M R	
JNK2		H M R	H M R
Phospho-JNK2 (T183/Y185)			H M R
LDL R	H M	H M	
Leptin	H M R	H M	H M
Leptin R	H M	H M	H M
Phospho-Leptin R (Y985)		H	
LIMPII/SR-B2	H M	H M	H
Lipocalin-2/NGAL	H M R	H M R	H M
LRP-1		H	
Melanocortin 3R/MC3R		M	
MEK1		H M R	
Phospho-MEK1 (T292)		H	
Phospho-MEK1 (T386)		H	
MEK1/MEK2		H M R	
Phospho-MEK1/MEK2 (S218/S222)/(S222/S226)		H M R	H
MEK2	H	H M R	
NFκB1		H M	
NFκB2		H	
Orexin A		H M R	
Orexin B		H	
p70 S6 Kinase	H		H M R
Phospho-p70 S6 Kinase (T229)		H	
Phospho-p70 S6 Kinase (T389)		H	H M
Phospho-p70 S6 Kinase (T421/S424)		H M R	H M R
PBEF		H M	
PDK-1	H	H	
Pentraxin 3	H M	H M	H M
PI 3-Kinase p85α		H M R	
PI 3-Kinase p110		H M R	
PI 3-Kinase p110β		H	
PI 3-Kinase p110γ		H	
PI 3-Kinase p110δ		H	

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs & Other Kits
PKA C (pan)		H M R	
PKA Cα	H	H M R	
PKA Cβ	H		
PKA R1β		H M R	
PKC α		H M R	
PKC β1		H R	
PKC β2		H M	
PKC γ		H M R	
PKC δ	H		
PKC ε		H M R	
PKC ι/λ		H M R	
PKC θ		H M	
PPARα/NR1C1		H	
PPARγ/NR1C3		H	
PPARδ/NR1C2		H	
Pref-1/DLK-1/FA1		H	H
PTEN	H	H M R	H M R
Phospho-PTEN (S380)		H M R	
PTP1B	H	H M R	H
Raf-1	H		
Phospho-Raf-1 (S301)		H M R X	
Phospho-Raf-1 (S642)		H M R	
RAGE	H M R Ca	H M R Ca	H M
RARα/NR1B1		H	
RARβ/NR1B2		H	
RARγ/NR1B3		H	
Ras		H M R	
RBP4	H M	H M	H
Relaxin-1	H	H	
Relaxin-2	H	H	H
Relaxin-3	H	H	
RELMα		M	
RELMβ		H M	
RELMγ		R	
Resistin	M	H M	H M
Rheb		H M R	
Ribosomal Protein S6		H M R	
Phospho-Ribosomal Protein S6 (S235/S236)		H M R	
SHIP		H M R	
SHP-2	H	H M R	H M R
Phospho-SHP-2 (Y542)		H M	H M R
SR-AI/MSR	H M	H M	
STAT3		H M R	H M
Phospho-STAT3 (Y705)		H	H M
TNF-α	H M R B Ca CR E P Pr	H M R B Ca CR E F P Pr	H M R Ca E F P Pr
TNF RI	H M Ca	H M	H M
TNF RII	H M	H M	H M
TOR		H M R	
Phospho-TOR (S2448)		H	H
TRα/NR1A1		H	
TRβ1/NR1A2		H	
TSH α/β	H		
TSH β		R	
VEGF	H M R Ca Z	H M R Ca Z	H M R Ca
VLDLR	M	M	

KEY:
H: Human **M:** Mouse **R:** Rat **B:** Bovine **Ca:** Canine **Ch:** Chicken **CR:** Cotton Rat **E:** Equine **F:** Feline **P:** Porcine **Pr:** Primate **X:** *Xenopus* **Z:** Zebrafish

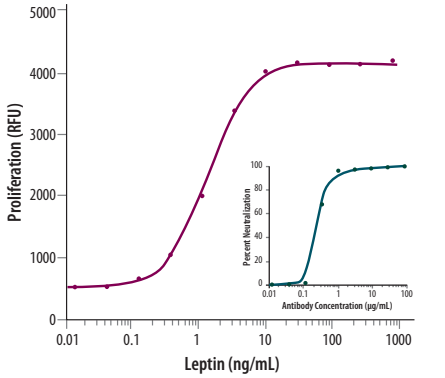
Proteome Profiler™ Mouse Obesity Array Kit

R&D Systems Proteome Profiler Antibody Arrays offer a rapid, sensitive approach to simultaneously detect the relative levels of multiple analytes in a single sample. Each array is designed using carefully selected capture antibodies that are spotted in duplicate onto nitrocellulose membranes. Membranes are incubated with experimental samples containing the proteins of interest and a cocktail of biotinylated detection antibodies. Streptavidin-HRP and chemiluminescent detection reagents are subsequently added to produce a signal that is proportional to the amount of analyte bound. The use of these arrays requires no specialized equipment and eliminates the need to perform multiple immunoprecipitation/ Western blot experiments.



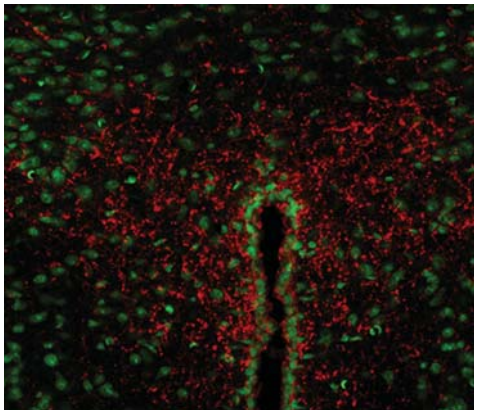
Multiple Proteins in Cell Culture Supernatants from Undifferentiated and Differentiated 3T3-L1 Cells were Assessed using the Mouse Obesity Array. A. The Proteome Profiler Mouse Obesity Array (Catalog # ARY013) was used to simultaneously assess the relative levels of multiple obesity-related proteins in cell culture supernatants from both undifferentiated 3T3-L1 mouse preadipocytes (top) and differentiated 3T3-L1 adipocytes (bottom). **B.** Histogram profiles for select proteins were generated by quantifying the mean spot pixel densities from the arrays using image software analysis. Green bars represent protein levels in supernatants from undifferentiated 3T3-L1 cells and gray bars represent the levels detected in supernatants from differentiated cells. **C.** Proteins detected by the Mouse Obesity Array.

Proteins



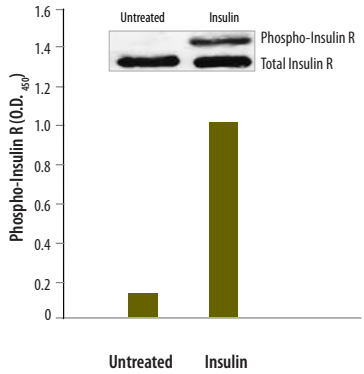
Leptin Stimulates the Proliferation of Leptin Receptor-transfected BaF3 Cells. BaF3 mouse pro B cells transfected with human Leptin Receptor were incubated with increasing concentrations of recombinant human Leptin (Catalog # 398-LP). Cellular proliferation was assessed by a fluorometric assay using the redox-sensitive dye, Resazurin (Catalog # AR002). Leptin activity in this assay was neutralized by incubating the recombinant protein with increasing concentrations of anti-human Leptin polyclonal antibody (Catalog # AF398) prior to its addition to Leptin R-transfected BaF3 cells (inset).

Antibodies



AgRP Expression in Mouse Thalamus. Agouti-Related Protein (AgRP) was detected in a frozen section of mouse thalamus using anti-mouse AgRP monoclonal antibody (Catalog # MAB634). Tissues were stained using NorthernLights™ 557-conjugated anti-rat secondary antibody (Catalog # NL013; red) and counterstained with FluoroNissl™ Green.

ELISAs



Detection of Insulin Receptor Phosphorylation in Insulin-induced HepG2 Cells using the DuoSet® IC ELISA. Lysates from HepG2 human hepatocellular liver carcinoma cells, untreated or treated with recombinant human Insulin, were assessed for Insulin Receptor phosphorylation using the human Phospho-Insulin R DuoSet IC ELISA Development System (Catalog # DYC2718; bar graph). The same lysates were also analyzed by IP-Western blot (inset) using anti-human Insulin R monoclonal antibody and anti-mouse agarose for immunoprecipitation. Biotinylated pan anti-Phospho-Tyrosine monoclonal (Catalog # BAM1676) and anti-Insulin R polyclonal antibodies were used for immunoblotting.

PRODUCT SELECTION EXPANDING WEEKLY.

Please visit our website at www.RnDSystems.com/go/Metabolism for an up-to-date product listing.

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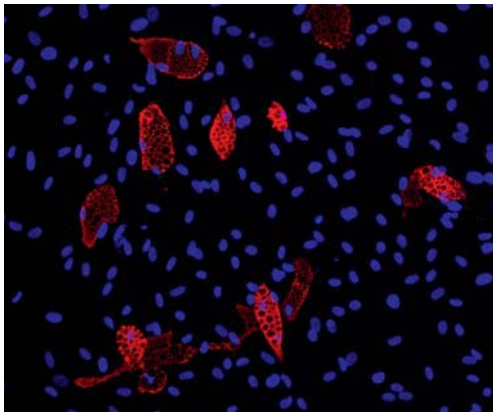
Adipogenic Differentiation

R&D Systems offers base media and supplements specially formulated to direct adipocyte differentiation of human or mouse mesenchymal stem cells (MSCs). Additionally, we offer MSC Functional Identification Kits that contain differentiation supplements and a panel of antibodies for positive identification of differentiated adipocytes and other MSC lineages.



FABP4 in Differentiating Human Adipocytes. Human mesenchymal stem cells were differentiated using Human/Mouse StemXVivo Osteogenic/Adipogenic Base Media (Catalog # CCM007) supplemented with human/mouse StemXVivo Adipogenic Supplement (Catalog # CCM011). Adipocytes were stained using anti-mouse FABP4 polyclonal antibody provided in the Human Mesenchymal Stem Cell Functional Identification Kit (Catalog # SC006) followed by Rhodamine Red™-conjugated anti-goat secondary antibody. Cells were counterstained with DAPI (blue).

Product	Description	Catalog #
Human/Mouse StemXVivo™ Mesenchymal Stem Cell Expansion Media	Complete media for the expansion of MSCs.	CCM004
Human/Mouse StemXVivo Osteogenic/ Adipogenic Base Media	Base media used with the appropriate supplement for the differentiation of MSCs into adipocytes.	CCM007
Human/Mouse StemXVivo Adipogenic Supplement	Media supplement for the differentiation of human or mouse MSCs into adipocytes. For use with the Osteogenic/Adipogenic Base Media.	CCM011
Human Mesenchymal Stem Cell Functional Identification Kit	Contains adipogenic, chondrogenic, osteogenic, and ITS supplements for the differentiation of each lineage. A panel of antibodies for identification of the mature phenotypes are included: anti-Aggrecan, anti-Osteocalcin, & anti-FABP4.	SC006
Mouse Mesenchymal Stem Cell Functional Identification Kit	Contains adipogenic, chondrogenic, osteogenic, and ITS supplements for the differentiation of each lineage. A panel of antibodies for identification of the mature phenotypes are included: anti-Collagen II, anti-Osteopontin, & anti-FABP4.	SC010