

AMPK, Insulin and Leptin Signaling

The enzyme 5'-AMP-activated protein kinase (AMPK) plays a major role in the regulation of cellular lipid and protein metabolism and is a mediator of the metabolic effects of hormones such as leptin, ghrelin, adiponectin, glucocorticoids and insulin. Both leptin and insulin are known to act as adiposity signals. Insulin is a hormone that regulates the energy and glucose metabolism in the body and causes cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle. Leptin, one of the most important adipose derived hormones, is a 16 kDa protein hormone that plays a key role in regulating energy intake and energy expenditure, including appetite and metabolism. In general, AMPK stimulates catabolism (glycolysis, fatty acid oxidation and mitochondrial biogenesis) while inhibiting anabolic pathways (gluconeogenesis, glycogen, fatty acid and protein synthesis) and has a direct effect on the hypothalamus to regulate appetite. AMPK activation is believed to upregulate insulin receptor substrate-1 through inhibition of the mTOR pathway, which has been implicated in the pathogenesis of insulin resistance and many types of cancer. Insulin has been shown to inhibit AMPK's hypothalamic activity. Insulin can also inhibit AMPK in fat by activating the Akt complex leading to phosphorylation of α -AMPK at S^{485/491} which causes a reduction of phosphorylation at T¹⁷² (required for AMPK activation). Furthermore, AMPK and insulin differ with respect to anabolic and catabolic processes. One of leptin's many metabolic roles includes the upregulation of fatty acid oxidation in skeletal muscle via the AMPK pathway. Recent studies indicate that abnormalities in cellular lipid metabolism are involved in the pathogenesis of the metabolic syndrome, possibly because of dysregulation of AMPK and malonyl-CoA, a closely related molecule. Leptin and insulin also modulate one another. Although there is some controversy on mechanism, it appears that leptin inhibits insulin secretion from pancreatic β -cells, either indirectly or directly. In addition, recent studies suggest that leptin down-regulates insulin by mediating the phosphorylation of IRS-1 through a JAK2, IRS-2 and PKC δ dependent pathway. This serine site is known to reduce the coupling of IRS-1 to the insulin receptor. In contrast, insulin is a potent stimulator of leptin secretion from white adipocytes.

Assay Kits

| Name | Cat. # |
|---|-----------|
| CTRP5 (human) Competitive ELISA kit | K4925-100 |
| Glucose Colorimetric Assay Kit II | K686-100 |
| Glucose Colorimetric/Fluorometric Assay Kit | K606-100 |
| PicoProbe™ Glucose Fluorometric Assay Kit | K688-100 |
| Glucose and Sucrose Colorimetric/Fluorometric Assay Kit | K616-100 |
| Glucose Dehydrogenase Activity Colorimetric Assay Kit | K786-100 |
| Glucose Uptake Colorimetric Assay Kit | K676-100 |
| Glucose Uptake Fluorometric Assay Kit | K666-100 |
| Glucose-1-Phosphate (G1P) Colorimetric Assay Kit | K697-100 |
| Glucose-6-Phosphate Colorimetric Assay Kit | K657-100 |
| PicoProbe™ Glucose-6-Phosphate Fluorometric Assay Kit | K687-100 |
| Glucose-6-Phosphate Dehydrogenase Activity Colorimetric Assay Kit | K757-100 |
| Glycogen Colorimetric Assay Kit II | K648-100 |
| Glycogen Colorimetric/Fluorometric Assay Kit | K646-100 |
| Hexokinase Colorimetric Assay Kit | K789-100 |
| Insulin (human) ELISA Kit | K4742-100 |
| Maltose and Glucose Colorimetric/Fluorometric Assay Kit | K618-100 |
| Phosphofructokinase (PFK) Activity Colorimetric Assay Kit | K776-100 |
| Phosphoglucomutase Colorimetric Assay Kit | K774-100 |
| Phosphoglucose Isomerase Colorimetric Assay Kit | K775-100 |
| PhosphoSeek™ PTP1B Fluorometric Assay Kit | K707-400 |
| PhosphoSeek™ Sphingosine Kinase-1 Fluorometric Assay Kit | K708-400 |

Proteins/Enzymes

| Name | Cat. # |
|----------------------------|-------------------|
| insulin, human recombinant | 4772-5, 25 |
| Leptin, human recombinant | 4366-02, 1, 5, 10 |
| Leptin, murine recombinant | 4367-02, 1, 5 |
| MAPKAPK2, Active | 7737-5 |
| MAPKAPK3, Active | 7755-5 |
| p38 beta, Active | 7763-5 |
| p38alpha, Active | 7756-5 |
| P38delta, Active | 7754-5 |
| p70 S6K, Active | 7725-5 |
| PDK1, Active | 7706-5 |
| PKC iota, Active | 7705-5 |
| PKCzeta, Active | 7718-5 |
| PTEN, human recombinant | 4838-5 |
| RAF1, Active | 7726-5 |
| RSK1, Active | 7721-5 |
| RSK2, Active | 7768-5 |
| RSK3, Active | 7774-5 |
| SGK1, Active | 7748-5 |
| SGK2, Active | 7749-5 |

Antibodies

| Name | Cat. # |
|--|---------------|
| Alpha-Amylase Antibody | 3925-100 |
| AMPK α Antibody | 3113-100 |
| AMPK α 1 Antibody | 3110-100 |
| AMPK α 2 Antibody | 3169-100 |
| AMPK α 2 Antibody | 3117-100 |
| AMPK β Antibody | 3108-100 |
| AMPK γ Antibody | 3109-100 |
| AMPK1 Antibody | 3112-100 |
| AMPK2 Antibody | 3118-100 |
| ASK1/MAPKKK5 Antibody | 3128-100 |
| ATGL Antibody | 3814-100 |
| C-Peptide Antibody (Clone HCP-B2) | 3103-100 |
| cAMP Antibody | 3567-100 |
| Elk-1 Antibody | 3387-100 |
| Erk1/2 MAPK Antibody | 3085-100 |
| Erk2 Antibody | 3442-100 |
| Erk5 Antibody | 3397-100 |
| GAPDH Antibody | 3777R-100 |
| GLP-1 Antibody (Clone HGL-B5) | 3104-100 |
| GLUT4 Antibody | 3945-200 |
| HK2 (Hexokinase II) (Center) Antibody | 3145-100 |
| HK2 (Hexokinase II) (NT) Antibody | 3144-100 |
| HK3 (Hexokinase III) (CT) Antibody | 3143-100 |
| HK3 (Hexokinase III) (NT) Antibody | 3198-100 |
| HNF-4 Antibody | 3688-100 |
| HNF4A Antibody | 3119-100 |
| HNF4A Antibody | 3121-100 |
| IGF-I Antibody | 5119-100 |
| IGF-I Antibody | 5120R-100 |
| IGF-II Antibody | 5122-100 |
| Insulin Antibody | 5772-100 |
| IRS-1 Antibody | 3424-100 |
| Leptin Antibody | 5366-100 |
| Leptin Antibody | 5367-100 |
| Leptin Receptor Antibody | 5582-100 |
| MAPKAPK-2 Antibody | 3100-100 |
| Mek1 Antibody | 3196-100 |
| Mek1/2 Antibody | 3518-100 |
| p38 MAP Kinase Antibody | 3114-100 |
| p42/44 MAPK Antibody | 3542-100 |
| p70S6 Kinase Antibody | 3485-100 |
| PDK1 Antibody | 3449-100 |
| Perilipin A Antibody | 3543-100 |
| Phospho-ATF-2 Antibody | 3359-100 |
| Phospho-Elk-1 Antibody | 3388-100 |
| Phospho-Erk1/2 Antibody | 3441-100 |
| Phospho-IRS (Ser616) Antibody (Clone HIR-B1) | 3105-100 |

Antibodies Continued...

| Name | Cat. # |
|--|---------------|
| Phospho-JKK/SEK1/MKK4 Antibody | 3478-100 |
| Phospho-MAPKAPK-2 Antibody | 3434-100 |
| Phospho-Mek1/2 Antibody | 3519-100 |
| Phospho-p38 MAPK Antibody | 3438-100 |
| Phospho-p70 S6 Kinase Antibody | 3505-100 |
| Phospho-Raf Antibody | 3504-100 |
| PKA Antibody | 3115-100 |
| Proinsulin Antibody (Clone HPI-B5) | 3106-100 |
| PTEN Antibody | 3479-100 |
| PTP1B Antibody | 3171-100 |
| PTP1B Antibody | 3174-100 |
| PTP1B Antibody (Clone 107AT531) | 3122-100 |
| Raf1 Antibody | 3116-100 |
| RasGAP Antibody | 3311-100 |
| Rat Pancreatic Amylase Antibody (Clone RPA-B5) | 3102-100 |
| RSK2 Antibody | 3546-100 |
| SGLT-1 Antibody | 3711-100 |
| SGLT-2 Antibody | 3690-100 |
| Sphingosine Kinase 1 (SPK1) Antibody | 3883-100 |
| Sphingosine Kinase 2 (SPK2) Antibody | 3884-100 |
| Tau Antibody | 3549R-100 |

AMPK Activators

| Name | Cat. # |
|--------------------------|----------------|
| AICAR | 1687-50, 250 |
| A-769662 | 1719-5 |
| Metformin, Hydrochloride | 1691-5G |
| Phenformin hydrochloride | 1889-100, 1000 |

AMPK Inhibitors

| Name | Cat. # |
|--------------|---------------|
| Dorsomorphin | 1686-5 |

PTEN Inhibitors

| Name | Cat. # |
|----------------------|---------------|
| bpV(phen) | 1793-5 |
| bpV(pic) | 1794-5 |
| VO-OHpic, Trihydrate | 1801-5, 25 |

TGR5 Receptor Agonist

| Name | Cat. # |
|-----------------------|---------------|
| Oleanolic Acid | 1731-100, 500 |
| TGR5 Receptor Agonist | 1722-5 |