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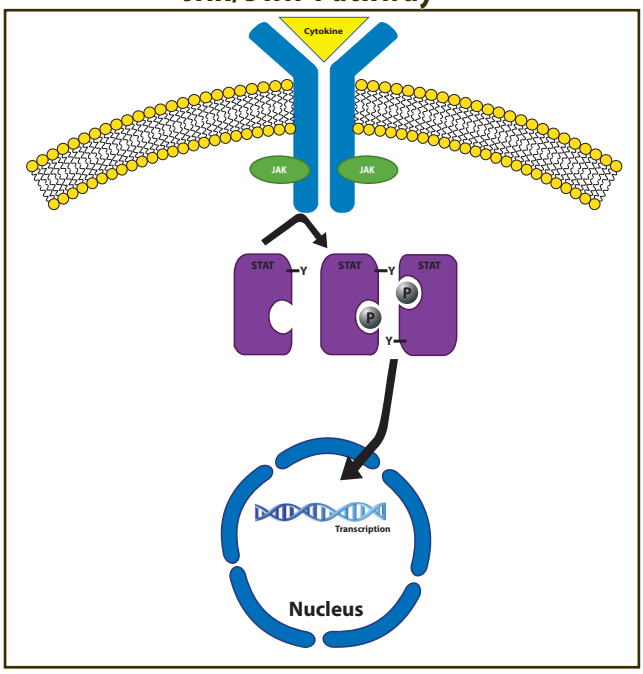
JAK/STAT Signaling

The JAK/STAT signaling pathway transmits a signal from outside the cell eventually resulting in DNA transcription and activity in the cell. Leptin (a product of the obese gene) can induce a cascade of events through its receptor (LRb; also known as Ob-Rb or the long isoform) and the JAK/STAT pathway. Siginificantly, Leptin mediated signaling through the JAK2/STAT3 pathway affects appetite and has been implicated in various carcinomas. Constitutively associated with the LRb is the Janus kinase 2 (JAK2) whose association and subsequent activation requires the so called Box 1 proline-rich motif found on all LRb receptors. Upon leptin binding, the receptor homodimerizes bringing two JAK2 in proximity to allow trans-phosphorylation of the JAK2's which activates them and leads to their phosphorylation of the receptor which creates binding opportunities for proteins that possess phosphotyrosine-binding SH2 domains. The signal transducer and activator of transcription (STAT) proteins possess such SH2 domains. Hence STAT3 recruitment via its SH2 domains results in STAT3 phosphorylation followed by its dimerization and translocation to the nucleus. Within the nucleus, STAT3 can bind promoters and affect expression of DNA sequences which control basic cell functions such as cell growth, differentiation and death. In addition, the activated JAK2 phosphorylates and activates numerous other STATs and proteins, such as IRS-1, PI3K and AkT. This LRb/JAK2/STAT3 signaling pathway is widely expressed in the brain and can control appetite by affecting the production of the anorexigenic peptide α-MSH.

Obesity also greatly influences the risk of many common forms of cancer with hepatocellular carcinoma exhibiting the highest relative-risk (4.52X) increase for obese men compared with all the cancers studied. Studies have shown that treatment with leptin increased the proliferation of HepG2 and Huh7 cells and involved the activation of STAT3, PI3K, Akt and Erk via JAK2. Temporally, studies demonstrated that JAK2/STAT3 activation followed leptin treatment and was upstream of PI3K, Akt and ERK phosphorylation. In addition, leptin was found to increase the migration capability of hepatocellular carcinoma cells and correlated with JAK2/STAT3 activation demonstrated by using the JAK/STAT inhibitor AG490.

JAK/STAT Pathway



Antibodies

Name	Cat. #
GH (Growth Hormone) Antibody	5769-100
GM-CSF Antibody	5100-100
GM-CSF Antibody	5101-100
IFN alpha Antibody	5596-100

Antibodies Continued...

Name	Cat. #
IFN gamma Antibody	5117-100
IL-1 beta Antibody	5128-100
IL-1 beta Antibody	5129-100
IL-2 Antibody	5133-100
IL-2 Antibody	5131-100
IL-3 Antibody	5134-100
IL-4 Antibody	5137-200
IL-6 Antibody	5143-100
IL-6 Antibody	5144-100
IL-6 Antibody	5145-100
IL-7 Antibody	5148-100
IL-12 Antibody	5162-100
IL-12p40 Antibody	5732-100
IL-13 Antibody	5165R-100
IL-13 Antibody	5164-100
IL-13 Antibody	5165-100
Leptin Antibody	5366-100
Leptin Antibody	5367-100
Leptin Antibody	5368-100
Leptin Receptor Antibody	5582-100
Prolactin Antibody	5688-100
Prolactin Antibody	5689-100
SOCS1 Antibody	3861-100

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Antibodies Continued...

Name	Cat. #
Stat1 Antibody	3133R-100
Stat2 Antibody	3468R-100
Phospho-Stat2 Antibody	3469-100
Stat3 Antibody	3470R-100
Phospho-Stat3 Antibody	3474-100
Stat4 Antibody	3471R-100
Stat5 Antibody	3472-100
Phospho-Stat5 Antibody	3475-100
Stat6 Antibody	3473R-100
Phospho-Stat6 Antibody	3476-100
TPO Antibody	5352-100
TPO Antibody	5351R-100

Proteins/Enzymes

Name	Cat. #
EPO-alpha, human recombinant	4763-10, 1000
EPO-alpha, human recombinant	4764-500
EPO-beta, human recombinant	4766-500, 1000
GM-CSF, human recombinant	4100-10, 100, 1000
GM-CSF, murine recombinant	4101-10, 100, 1000
GM-CSF, rat recombinant	4102-10, 100, 1000
Growth Hormone, chicken recombinant	4771-50, 500
Growth Hormone, human recombinant	4769-100, 500, 1000, 5000
Growth Hormone, murine recombinant	4770-50, 1000
IFN-alpha 1, human recombinant	4596-10, 100, 1000
IFN-alpha 2a, human recombinant	4594-20, 100, 1000
IFN-alpha 2b, human recombinant	4595-20, 100, 1000
IFN-beta, human recombinant	4860-10, 50, 1000
IFN-gamma, human recombinant	4116-100, 1000
IFN-gamma, murine recombinant	4117-20, 100, 1000
IFN-gamma, rat recombinant	4118-20, 100, 1000
IL-2, human recombinant	4131-10, 50, 100
IL-2, murine recombinant	4132-20, 100, 1000
IL-2, rat recombinant	4133-20, 100, 1000
IL-3, human recombinant	4134-10, 50, 1000
IL-3, murine recombinant	4135-10, 50,1000
IL-3, rat recombinant	4136-10, 1000
IL-4, human recombinant	4137-10, 50, 1000
IL-4, murine recombinant	4138-10, 1000
IL-4, rat recombinant	4139-10, 1000
IL-5, human recombinant	4140-10, 1000
IL-5, murine recombinant	4141-10, 1000
IL-5, rat recombinant	4142-10, 1000
IL-6, human recombinant	4143-20, 100, 1000
IL-6, murine recombinant	4144-10, 50, 1000
IL-6, rat recombinant	4145-10, 1000
IL-6, rat recombinant	4145-10, 1000
IL-7, human recombinant	4146-10, 1000

Proteins/Enzymes Continued...

Name	Cat. #
IL-7, rat recombinant	4148-10,50, 1000
IL-11, human recombinant	4158-10, 1000
IL-11, murine recombinant	4159-10, 1000
IL-12, human recombinant	4161-10, 100
IL-12, rat recombinant	4163-10, 1000
IL-12p40, human recombinant	4732-10, 50, 1000
IL-13, human recombinant	4164-10, 50, 1000
IL-13, murine recombinant	4165-10, 50, 1000
IL-13, rat recombinant	4166-10, 1000
Leptin Receptor, human recombinant	4582-10, 50, 1000
Leptin, human recombinant	4366-02, 1, 5, 10
Leptin, murine recombinant	4367-02, 1, 5
Leptin, rat recombinant	4368-02, 1, 5
Prolactin Receptor, human recombinant	4989-50, 1000
Prolactin Receptor, rat recombinant	4991-50, 1000
Prolactin, human recombinant	4687-50, 100, 1000
Prolactin, murine recombinant	4688-10, 50, 1000
Prolactin, rat recombinant	4689-10, 50, 1000
TPO, human recombinant	4351-10, 50, 1000
TPO, murine recombinant	4352-10, 50, 1000

Inhibitors

JAK Inhibitors

Name	Cat. #
CP-690550	1622-5, 25
MS-1020	1911-1
Ruxolitinib, Free base	2139-5, 25
Tyrphostin AG 490	1570-5
WHI-P131	1853-5, 25
WP1066	1809-5, 25

Stat Inhibitors

Name	Cat. #
PathwayReady™ JAK/STAT Signaling Inhibitor Panel	K864-8
Lestaurtinib	1805-500, 1000
LLL12	1792-5, 25
Niclosamide	1826-500, 1000
Pimozide	1887-50, 250
Stat3 Activation Inhibitor, SPI	1813-2
Stat3 Inhibitor I, S3I-201	1775-5, 25
Stat3 Peptide Inhibitor, Cell-Permeable	1778-1, 5