AC XN000000006
XX
DT 1999-06-23 15:05:09.0(created); frs.
DT 2004-01-05 15:36:36.0(updated); mkl.
CO Copyright (c) Biobase GmbH.
XX
NA Raf --> MEK
XX
EF activation; phosphorylation; binding.
TY semantic; direct.
HP <XN000023295>; MEK + NTP --Ras:GTP:Raf{p}--> MEK{p} + NDP (phosphorylation).
XX
CC mechanism: for activation of MEKs by Raf a proline-rich sequence in MEKs is essential; this sequence is not found in other MAPKKs [1].
XX
MB <MO000000009>; Raf.
MA <MO000000018>; MEK.
XX
PW <CH000000038>; insulin ---> ERK (chain).
XX
RN [1].
RX <pubmed:10082509>.
RA Schaeffer H. J., Weber M. J.
RT Mitogen-activated protein kinases: specific messages from ubiquitous messengers.
RL Mol. Cell. Biol. 19:2435-2444 (1999).
XX
RN [2].
RX <pubmed:10209155>.
. . .
//

AC XN000000034
XX
DT 1999-06-28 10:37:23.0(created); frs.

DT 2011-09-30 16:26:32.0(updated); ili.

XX
NA p110 --> PIP3
XX
EF activation.
TY semantic; direct.
HP <XN000023595>; PIP2 + ATP --C3d:antigen:BCR{p}:CD19{p}:CD21:CD81:p85:p110--> PIP3 + ADP (phosphorylation).
HP <XN000023692>; PIP2 + ATP --IRS-1, IRS-2{pY}:p85:p110--> PIP3 + ADP (phosphorylation).
HP <XN000023733>; PIP2 + ATP --PDGF AA:(PDGFRalpha{pY731}{pY742})2:p85:p110--> PIP3 + ADP (phosphorylation).
HP <XN000023742>; PIP2 + ATP --PDGFBB:(PDGFRbeta{pY740}{pY751})2:p85:p110--> PIP3 + ADP (phosphorylation).
HP <XN000023842>; PIP2 + ATP --(VEGF-A:VEGFR-2{pY})2:p85{p}:p110--> PIP3 + ADP (phosphorylation).
HP <XN000024671>; PIP2 + ATP --(RANKL:RANK)3:Src:traf6:Cbl-b:p85:p110--> PIP3 + ADP (phosphorylation).
HP <XN000027999>; PIP2 + ATP --prolactin:(prlr)2:Fyn:c-Cbl{pY731}:p85:p110--> PIP3 + ADP (phosphorylation).
HP <XN000149121>; PIP2 + ATP --NRG:ErbB2{pY1139}{pY1222}{pY1248}:ErbB3{pY1054}{pY1197}{pY1222}{pY1260}{pY1276}{pY1289}:Sos:(Grb-2)2:Shc-1{pY}:p110:p85{pY}--> ADP + PIP3 (phosphorylation).
HP <XN000235029>; PIP2 + ATP --(IL-3:IL-3Ralpha:Jak2{pY1007}{pY1008})2:(IL-5Rbeta-isoform1{pS601}{pY}:Jak1)2:(14-3-3zeta)2:p85{pY}:p110--> ADP + PIP3 (phosphorylation).
HP <XN000242066>; PIP2 + ATP --(IL-3:IL-3Ralpha:Jak2{pY1007}{pY1008})2:(IL-5Rbeta-isoform1{pY}:Jak1)2:Fyn:Grb-2:c-Cbl{pY}:p85{pY}:p110--> PIP3 + ADP (phosphorylation).
HP <XN000274052>; PIP2 + ATP --EGF-ECD:(ErbB1-p170{pY1016}{pY1092}{pY1110}{pY1172}{pY1197})2:Grb-2:Sos1{pY}:H-Ras:GTP:p85{pY}:p110--> PIP3 + ADP (phosphorylation).
HE <XN000026403>; PDGFRbeta(m){p} + PI3K-C2beta(h) <==> PDGFRbeta(m){p}:PI3K-C2beta(h) (binding).
HE <XN000006624>; PIP2 + ATP --p110gamma(h):p101(pg)--> PIP3 + ADP (phosphorylation).
HE <XN000015409>; PIP2 + ATP --p101(pg):p110gamma(pg)--> PIP3 + ADP (phosphorylation).
HE <XN000149732>; Fyn(r) + PRLR-L(r) <==> Fyn(r):PRLR-L(r) (binding).
HE <XN000227869>; ATP + PIP2 --> PIP3 + ADP .
XX
MB <MO000016644>; p110.
MA <MO000017272>; PIP3.
XX
PW <CH000000050>; insulin ---> alphaENaC (chain).
PW <CH000000549>; PI3K ----/ Rheb (chain).

XX
RN [1].
RX <pubmed:9696882>.
RA Malumbres M ., Pellicer A.
RT RAS pathways to cell cycle control and cell transformation.
RL Front. Biosci. 3:d887-912 (1998).
XX
RN [2].
RX <pubmed:9739761>.
. . .
//

AC XN000004410
XX
DT 2001-04-05 11:54:42.0(created); spi.
DT 2011-12-15 05:41:57.0(updated); shs.
CO Copyright (c) Biobase GmbH.
XX
QU low reliability (5).
XX
NA Cdc42(h) + GTP <==> Cdc42(h):GTP
XX
EF binding; reversible.
TY molecular evidence; direct.
HP <XN000023492>; Cdc42 + GTP <==> Cdc42:GTP (binding).
XX
CP (F1, M4) {Affinity precipitation in solution/batch (e.g. with sepharose or magneto beads) e.g. immunoprecipitation, pull-down assay} [2].
CP HEK 293(embryonal kidney cell line, adenovirus 5-infected; synonyme: 293 (hu-HEK)); human, Homo sapiens; <HyperCLDB:cl46.html>; <HyperCLDB:cl5008.html>; <HyperCLDB:cl45.html>; (D1, M4) {Affinity precipitation in solution/batch (e.g. with sepharose or magneto beads) e.g. immunoprecipitation, pull-down assay} [71727].
MB <MO000000007>; GTP.
MB <MO000016582>; Cdc42(h).
MA <MO000020593>; Cdc42(h):GTP.

XX
RN [1].
RX <pubmed:20890305>.
RA Zhan Y., Modi N., Stewart A. M., Hieronimus R. I., Liu J., Gutmann D. H., Chadee D. N.
RT Regulation of mixed lineage kinase 3 is required for Neurofibromatosis-2-mediated growth suppression in human cancer
RL Oncogene 30:781-789 (2011).
XX
RN [2].
RX <pubmed:9422512>.
RA Miki H., Sasaki T., Takai Y., Takenawa T.
RT Induction of filopodium formation by a WASP-related actin-depolymerizing protein N-WASP.
RL Nature 391:93-96 (1998).
XX
. . .
//

AC XN000004810
XX
DT 2001-06-27 16:21:07.0(created); spi.
DT 2011-11-29 05:06:39.0(updated); pos.
CO Copyright (c) Biobase GmbH.
XX
QU high reliability (2).
XX
NA EGFR(h) + ATP --> EGFR(h){pY} + ADP
XX
EF phosphorylation.
TY molecular evidence; direct.
HS <XN000000071>; EGF --> ErbB1 (activation; binding).
HP <XN000023636>; EGF:(ErbB1)2 + ATP --> EGF:(ErbB1{pY})2 + ADP (phosphorylation).
XX
CC mechanism: Kinase not shown; [11].
CC mechanism: Endogenous EGFR was phosphorylated in a ligand (EGF) dependant manner; [10].

CC mechanism: The ROS mediated phosphorylation of EGFR activates the ERK and Akt downstream signaling pathways to reach the ubiquitin-dependent degradation of the pro-apoptotic protein Bim; [55112].
CC experimental inhibitor: NDGA and NAC: inhibitors of adhesion induced EGFR phosphorylation; [55112].
CC experimental inhibitor: AG1478; Selective EGFR inhibitor; [55112].
CC mechanism: The activation of EGFR depends upon the activation of Rac-1; [55112].
CC mechanism: The adhesion induced activation of EGFR requires the redox dependent activation of Src; [55112].
CC mechanism: phosphorylation detected with antibody that recognizes EGFR phosphorylated at Tyr 1173 [67812].
CC mechanism: the phosphorylation of EGFR was detected with an antibody that recognizes EGFR phosphorylated at the Tyr-1068 residue position [69912].
CC mechanism: the EGF-stimulated EGFR tyrosine phosphorylation was enhanced by the Serine phosphorylation of IQGAP1 [69912].
CC mechanism: phosphorylation detected with antibody that recognizes EGFR phosphorylated at Tyr 1068 residue [70045].
XX
CP A-431(carcinoma, squamous cell); human, Homo sapiens; <HyperCLDB:cl155.html>; <HyperCLDB:cl160.html>; <HyperCLDB:cl159.html>; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [11].
CP A-431(carcinoma, squamous cell); human, Homo sapiens; <HyperCLDB:cl155.html>; <HyperCLDB:cl160.html>; <HyperCLDB:cl159.html>; (C1, M16) {In vitro modification of a substrate (e.g. phosphorylation or dephosphorylation (e.g. Kinase-assay), ubiquitination)} [23836].
CP (X2, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [36095].
CP 293T cells; human, Homo sapiens; (D1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [10].
CP ECV304(spontaneously-transformed Japanese human umbilical vein endothelial cells (HUVEC)); human, Homo sapiens; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [55112].
CP HMEC(Human mammary epithelial cell.); human, Homo sapiens; (B3, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [55206].
CP MCF-7(epithelial carcinoma); human, Homo sapiens; <HyperCLDB:cl3372.html>; <HyperCLDB:cl3373.html>; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [55676].
CP HaCaT(HaCaT keratinocyte cells); human, Homo sapiens; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [66650].
CP SCC-9(human squamous cell carcinoma); human, Homo sapiens; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [66650].
CP SCC-9(human squamous cell carcinoma); human, Homo sapiens; (D1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [66650].

CP RPMI 7951(Peripheral blood myeloma cells); human, Homo sapiens; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [66650].
CP C8161(Human melanoma cell line derived from an aggressive form of subcutaneous melanoma); human, Homo sapiens; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [66650].
CP T47D(mammary cell line); human, Homo sapiens; <HyperCLDB:cl4455.html>; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [12].
CP HBE(human bronchial epithelium); human, Homo sapiens; (B4, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [67812].
CP A-431(carcinoma, squamous cell); human, Homo sapiens; <HyperCLDB:cl155.html>; <HyperCLDB:cl160.html>; <HyperCLDB:cl159.html>; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [69912].
CP HeLa(epitheloid cervical carcinoma cell line); human, Homo sapiens; <HyperCLDB:cl1601.html>; <HyperCLDB:cl1598.html>; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [69912].
CP HeLa(epitheloid cervical carcinoma cell line); human, Homo sapiens; <HyperCLDB:cl1601.html>; <HyperCLDB:cl1598.html>; (D1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [69912].
CP keratinocytes(human primary keratinocytes); human, Homo sapiens; (B3, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [70045].
CP Scc-12F(human keratinocyte cell line); human, Homo sapiens; (C1, M13) {Modification of proteins in living cells (e.g. proteinphosphorylation and -dephosphorylation, ubiquitination, farnesylation; detection of the modified proteins, e.g. from cell extracts)} [71593].
MB <MO000000327>; ATP.
MB <MO000021355>; EGFR(h).
MA <MO000000328>; ADP.
MA <MO000021356>; EGFR(h){pY}.
XX
PW <CH000000152>; CH000000152 (evidence chain).
XX
RN [1].
RX <pubmed:21349850>.
RA McNulty D. E., Li Z., White C. D., Sacks D. B., Annan R. S.
RT Map kinase scaffold IQGAP1 binds the EGF receptor and modulates its activation

RL J. Biol. Chem. 286:15010-15021 (2011).
XX
RN [2].
RX <pubmed:19864455>.
RA Xu Y., Baker D., Quan T., Baldassare J. J., Voorhees J. J., Fisher G. J.
RT Receptor type protein tyrosine phosphatase-kappa mediates cross-talk between transforming growth factor-beta and epidermal growth factor receptor signaling pathways in human keratinocytes
RL Mol. Biol. Cell 21:29-35 (2010).
XX
RN [3].
RX <pubmed:19112101>.
RA Kalari S., Zhao Y., Spannhake E. W., Berdyshev E. V., Natarajan V.
RT Role of acylglycerol kinase in LPA-induced IL-8 secretion and transactivation of epidermal growth factor-receptor in human bronchial epithelial cells
RL Am. J. Physiol. Lung Cell. Mol. Physiol. 296:L328-36 (2009).
XX
RN [4].
RX <pubmed:19003995>.
RA Singh B., Schneider M., Knyazev P., Ullrich A.
RT UV-induced EGFR signal transactivation is dependent on proligand shedding by activated metalloproteases in skin cancer cell lines
RL Int. J. Cancer 124:531-539 (2009).
XX
RN [5].
RX <pubmed:18259192>.
RA Giannoni E., Buricchi F., Grimaldi G., Parri M., Cialdai F., Taddei M. L., Raugei G., Ramponi G., Chiarugi P.
RT Redox regulation of anoikis: reactive oxygen species as essential mediators of cell survival
RL Cell Death Differ. 15:867-878 (2008).
XX
RN [6].
RX <pubmed:17525128>.
RA Song R. X., Zhang Z., Chen Y., Bao Y., Santen R. J.
RT Estrogen signaling via a linear pathway involving insulin-like growth factor I receptor, matrix metalloproteinases, and epidermal growth factor receptor to activate mitogen-activated protein kinase in MCF-7 breast cancer cells
RL Endocrinology 148:4091-4101 (2007).

XX
RN [7].
RX <pubmed:15467833>.
RA Abou-Rjaily G. A., Lee S. J., May D., Al-Share Q. Y., Deangelis A. M., Ruch R. J., Neumaier M., Kalthoff H., Lin S. H., Najjar S. M.
RT CEACAM1 modulates epidermal growth factor receptor--mediated cell proliferation
RL J. Clin. Invest. 114:944-952 (2004).
XX
RN [8].
RX <pubmed:14978035>.
RA Chen W. N., Woodbury R. L., Kathmann L. E., Opresko L. K., Zangar R. C., Wiley H. S., Thrall B. D.
RT Induced autocrine signaling through the epidermal growth factor receptor contributes to the response of mammary epithelial cells to tumor necrosis factor alpha
RL J. Biol. Chem. 279:18488-18496 (2004).
XX
RN [9].
RX <pubmed:11716761>.
RA Woodfield R. J., Hodgkin M. N., Akhtar N., Morse M. A., Fuller K. J., Saqib K., Thompson N. T., Wakelam M. J.
RT The p85 subunit of phosphoinositide 3-kinase is associated with beta-catenin in the cadherin-based adhesion complex
RL Biochem. J. 360:335-344 (2001).
XX
RN [10].
RX <pubmed:11094073>.
RA Zeng L., Sachdev P., Yan L., Chan J. L., Trenkle T., McClelland M., Welsh J., Wang L. H.
RT Vav3 mediates receptor protein tyrosine kinase signaling, regulates GTPase activity, modulates cell morphology, and induces cell transformation
RL Mol. Cell. Biol. 20:9212-24 (2000).
XX
RN [11].
RX <pubmed:9733788>.
RA Keilhack H., Tenev T., Nyakatura E., Godovac-Zimmermann J., Nielsen L., Seedorf K., Bohmer F. D.
RT Phosphotyrosine 1173 mediates binding of the protein-tyrosine phosphatase SHP-1 to the epidermal growth factor receptor and attenuation of receptor signaling.
RL J. Biol. Chem. 273:24839-24846 (1998).
XX

RN [12].
RX <pubmed:9652748>.
RA Fiddes R. J., Janes P. W., Sivertsen S. P., Sutherland R. L., Musgrove E. A., Daly R. J.
RT Inhibition of the MAP kinase cascade blocks heregulin-induced cell cycle progression in T-47D human breast cancer cells
RL Oncogene 16:2803-13 (1998).
XX
RN [13].
RX <pubmed:1315766>.
RA Rotin D., Honegger A. M., Margolis B. L., Ullrich A., Schlessinger J.
RT Presence of SH2 domains of phospholipase C gamma 1 enhances substrate phosphorylation by increasing the affinity toward the epidermal growth factor receptor.
RL J. Biol. Chem. 267:9678-9683 (1992).
XX
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