

-3- 2 (CHI3I2) ERK1/2 (HEK293)

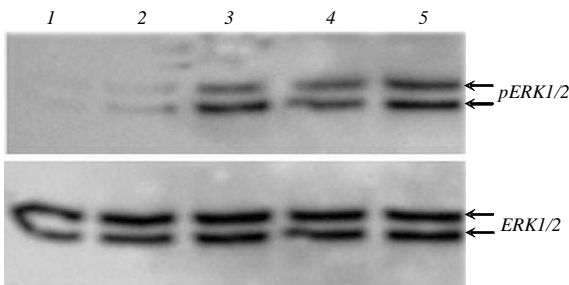
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• , 150, , 03680
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a. o a , *CHI3L2*, *CHI3L1*, *ERK1/2*.
CHI3L2 *ERK1/2* - -
-ERK1/2 a o - *-ERK1/2-a i a* .
ERK1/2 *CHI3L2*
DMEM. *o* *o* *CHI3L2* *ERK1/2*
(HEK293) i , *ERK1/2-MAP-*
-3- *1 (CHI3L1, HC gp-39, YKL-40)*, *-3-* *2*
(CHI3L2, YKL-39), MAP , *ERK1/ERK2*.

• , [3, 4]. *a i o* -
i e *CHI3L1* -
o , *i* - [5].
 - 18. *-3-* *o* 1 *CHI3L1* -
 (*CHI3L1, HC gp-39, YKL-40*), *o* ,
 , *a* 40 , *o o* - [6]. *e x*
 383 *i* *MAPK*
Met¹-Ala²¹ *AKT* ,
 . *N-* *x*
Y-K-L N- - *CHI3L1* [7].
Asn⁶⁰ [1]. *CHI3L2* *CHI3L1* -
CHI3L1 - *i* *CHI3L1*
 , , *P K* [8]. - -
x , *ax* [2]. *CHI3L2* *CHI3L1* [9],
CHI3L1 -
o o c e - *e o* *o o* *a* ,
oc i *CHI3L2 (YKL-39)*, *CHI3L1*
 (*YKL-40*), , -
 Institute of Molecular Biology and Genetics NAS of Ukraine, 2009 *ERK1/ERK2 i a* .

1 MGATTMDQKSLWAGVFFVILLIQGGSAIKLV YKL-39
 1 -----MGFKASQTGFVWLVLELQCCSAIKLV YKL-40
 51 CTFYNWEDRQEPGFFTFENIDPFLGSHLI YKL-39
 56 CTFYSWSDYREGDGSCTPFDALDRFLCTHII YKL-40
 61 YSFAISIEENKVIKDKSEVMEYQTINSEKT YKL-39
 56 YSFAISNDHIDIWEWNDFTLYQLNITLKN YKL-40
 91 ENPKKIILSRIGGGLFGSKGFHPMFDSSIT YKL-39
 86 RNPNKITLSPGGWNEGSQRFSKIASNTQS YKL-40
 121 RLEFINSLILFLRNHNFDGIDPFSWIYFDQK YKL-39
 116 RNTFIKSVPPFLRTHGFDGIDLAWLYPGR YKL-40
 151 ENTHFIVLHHLAEAFQKDFIKSTKERLLI YKL-39
 146 DEQHFITLKEEMKAEFIKEAQPGKQ-LLI YKL-40
 181 TAGVPSAGRQMIENSTQVERLAKDLDFINLI YKL-39
 175 SAALSAGKVTIDSSYDIARISQHLDFISIM YKL-40
 211 SFDFHGSWEKPLITGHNEPLSKGWFQDRGFS YKL-39
 205 TYDFHGAWRG--TIGHHSEPLFRGQEDASFD YKL-40
 241 STYNVEFAVGIWIHRGMPSEKVFVNGIPIYIG YKL-39
 235 RFSNTDYAVGYMLRLGARASKLVNGIPIYFG YKL-40
 271 HSFLLASAEITVGAFASSGPGAAAGPITESSG YKL-39
 265 RSFLLASS EIGVGAFASSGPGIPIGRFYKEAG YKL-40
 301 FLAYYEICQFIKGAKITRIQDQGFYAFEG YKL-39
 295 FLAYYEICDFLRGATVHRILGQGFPEATEG YKL-40
 331 NQWFGYDDVKSMETKVPFLKLNINEGGAMIV YKL-39
 325 NQWFGYDDQESVKSKEVQYERDRQLAGAMVW YKL-40
 363 IIDMDDFTGKSENQGP-IFIFQAFYRSEIGS YKL-39
 355 AIDLDDFQGSFCGQDLRFPITNAIKDAIAA YKL-40
 390 L YKL-39
 383 T YKL-40

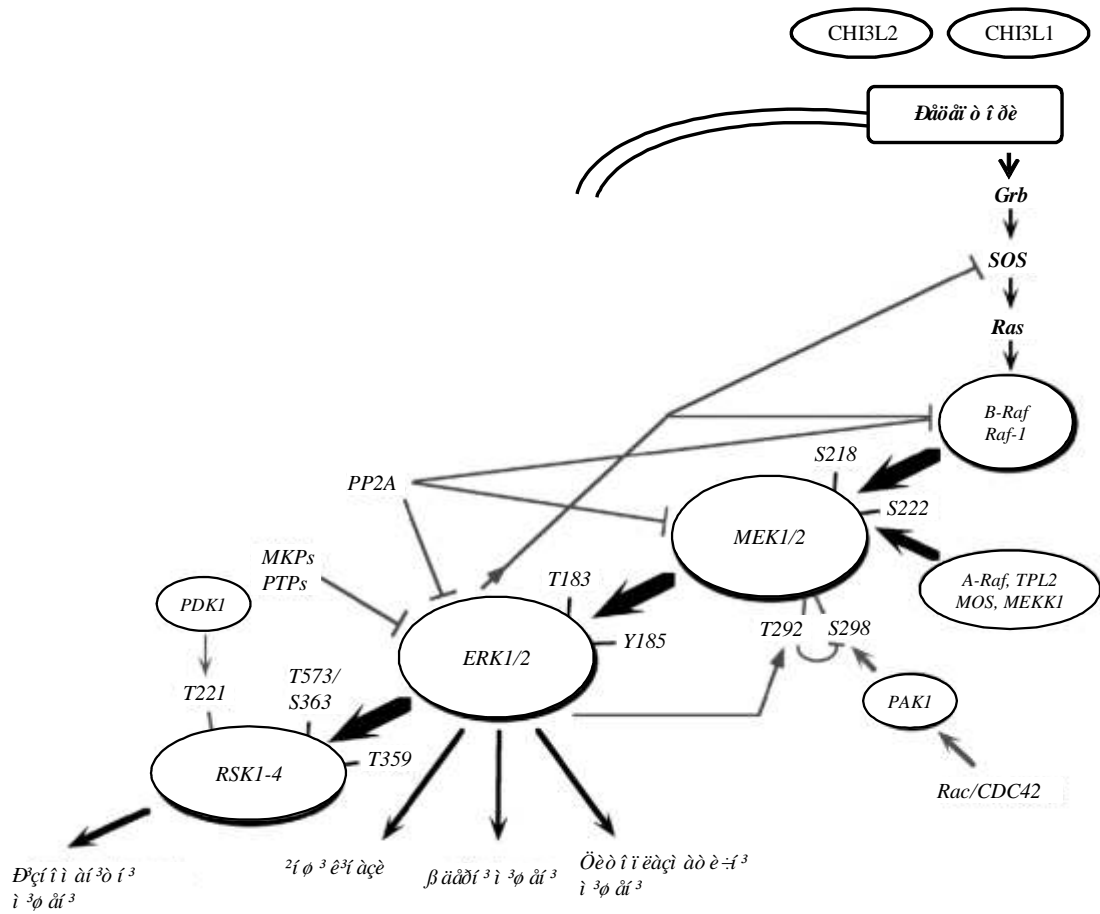
1. CHI3L2 CHI3L1.



2. - 293,
 c YKL-39 0 (2), 25 (3), 75 (4)
 100 (5) / - 150 / (1),
 pERK1/2 ERK1/2

-ERK1/2 (sc-7383)
 -ERK1/2 (sc-94)
 «Santa Cruz Biotechnology» ();
 , - «Promega» ().
 i o ea x c a i
 oc eo i i e i ECL («Amersham
 Pharmacia Biotechnology»,).
 NdeI/XhoI- pGemT-Easy-
 YKL-39 [9] pET-24a(+) («Novagen»,

Escherichia coli (BL21), pET-24a(+)-YKL-39,
 a 1
 IPTG. YKL-39,
 His C- , 8 M -
 i Ni-NTA («Qiagen»,). -
 12 %-
 SDS-PAGE. CHI3L2 MAP- -
 ERK1/ERK2 HEK293 ax, -
 6- 70 % ,
 24
 FBS, CHI3L2 -
 0-100 / (150 /).
 60 -
 -ERK1/2 -
 ERK1/2- .
 (SAGE)
 CHI3L2, CHI3L1, 44
 o o o
 YKL-39 -
 YKL-40 [9].
 CHI3L1, -
 [2],
 CHI3L2 .
 CHI3L1 CHI3L2 (. 1)
 cxo ic . ,
 - 18
 [6], -
 Drosophila melanogaster [10] c i ,
 i .
 CHI3L2 -
 ERK1/ERK2 ax HEK293, -
 - . -



. 3. ERK [11] CHI3L2 CHI3L1

. 2, TPL2 MEKK1.

ERK1/ERK2 CHI3L2.

ERK1/ERK2 CHI3L2 MAPK/ERK- (MEKs). A o i MEK

e ERK.

o ci . ERK- Elk1, Fos, p53, Ets1/2

, c-Jun.

MAPK/APK.

ERK1 ERK2 Ras- ERK-

Raf-ERK, S6 90 (RSKs)

G- (- (. 3).

Raf- (MAP3K)

Raf, MAP3K c-Mos, ERK.

[11].

YKL-40

ERK1/2-MAP- (PI3K)

[6].

PI3K

CH13L2

ERK1/ERK2 (HEK293) i, ERK1/2 MAP

YKL-40

ERK1/2-MAP- (PI3K)

[6].

PI3K

CH13L2

ERK1/ERK2 (HEK293) i, ERK1/2 MAP

P. O. Areshkov, V. M. Kavsan

The chitinase 3-like human protein 2 (CHI3L2) activates ERK1/2 signaling pathway in human embryonic kidney cells (HEK293)

Summary

Aim. To show that CHI3L2 activates the extracellular signal regulated kinase (ERK1/ERK2) mediated cascade similarly to the homologous CHI3L1 protein. **Methods.** The involvement of CHI3L2 in ERK1/ERK2 phosphorylation was evaluated by Western blotting with either polyclonal anti-ERK1/ERK2 or monoclonal anti-phospho-ERK1/ERK2 antibodies. **Results.** The checking of CHI3L2 possibility to initiate MAPK cascade showed the phosphorylation of ERK1/ERK2 in HEK293 after addition of CHI3L2 to DMEM. **Conclusions.** Chitinase-like protein CHI3L2 activates phosphorylation of ERK1/ERK2 in human embryonic kidney cells (HEK293) and thus initiates the MAP kinase signaling cascade which may lead to increased cell proliferation or differentiation.

Keywords: chitinase 3-like protein 1 (CHI3L1, HC gp-39, YKL-40), chitinase 3-like protein 2 (CHI3L2, YKL-39), MAP kinase, ERK1/ERK2.

A.

-3-

ERK1/2 (HEK293)

CH13L2

CHI3L1, CHI3L2

ERK1/2

-ERK1/2

-ERK1/2-a

DMEM

1. Fusetti F., Pijning T., Kalk K. H., Bos E., Dijkstra B. W. Crystal structure and carbohydrate-binding properties of the human cartilage glycoprotein-39 // *J. Biol. Chem.*–2003.–**278**, N 39.–P. 37753–37760.
2. Johansen J. S. Studies on serum YKL-40 as a biomarker in diseases with inflammation, tissue remodelling, fibroses and cancer // *Dan. Med. Bull.*– 2006.–**53**, N 2.–P. 172–209.
3. Shostak K. O., Labunskyy V. N., Dmitrenko V. V., Malysheva T. A., Shamayev M. I., Rozumenko V. D., Zozulya Y. P., Zehetner G., Kavsan V. M. HC gp-39 gene is upregulated in glioblastomas // *Cancer Lett.*–2003.–**198**, N 2.–P. 203–210.
4. Dmytrenko V. V., Boyko O. I., Shostak C. O., Symyrenko O. E., Bukreyeva T. V., Rozumenko V. D., Malysheva T. A., Shamaev M. I., Zozulya Y. P., Kavsan V. M. Overexpression of genes at different stages of astrocytic glioma development // *Biopolymers and Cell.*–2006.–**22**, N 1.–P. 38–48.
5. Tanwar M. K., Gilbert M. R., Holland E. C. Gene expression microarray analysis reveals YKL-40 to be a potential serum marker for malignant character in human glioma // *Cancer Res.*–2002.–**62**, N 15.–P. 4364–4368.
6. Recklies A. D., White C., Ling H. The chitinase 3-like protein human cartilage glycoprotein 39 (HC-gp39) stimulates proliferation of human connective-tissue cells and activates both extracellular signal-regulated kinase- and protein kinase B-mediated signalling pathways // *Biochem. J.*–2002.–**365**, N 15.–P. 119–126.
7. Ling H., Recklies A. D. The chitinase 3-like protein human cartilage glycoprotein 39 inhibits cellular responses to the inflammatory cytokines interleukin-1 and tumour necrosis factor-alpha // *Biochem. J.*–2004.–**380**, N 15.–P. 651–659.
8. Kavsan V., Shostak K., Dmitrenko V., Zozulya Y., Rozumenko V., Demotes-Mainard J. Characterization of genes with increased expression in human glioblastomas // *Tsitology and Genetics.*–2005.–**39**, N 15.–P. 37–49.
9. Kavsan V., Dmitrenko V., Boyko O., Filonenko V., Avdeev S., Areshkov P., Marusyk A., Malysheva T., Rozumenko V., Zozulya Y. Overexpression of YKL-39 gene in glial brain tumors // *Scholarly Res. Exchange.*–2008.–doi: 10.3814/2008/814849.
10. Kawamura K., Shibata T., Saget O., Peel D., Bryant P. J. A new family of growth factors produced by the fat body and active on *Drosophila* imaginal disc cells // *Development.*–1999.–**126**, N 15.–P. 211–219.
11. Shaul Y. D., Seger R. The MEK/ERK cascade: From signaling specificity to diverse functions // *Biochim. et Biophys. Acta.*–2007.–**1773**, N 8.–P. 1213–1226.