FOSL1

Fos-related antigen 1 (FRA1) is a protein that in humans is encoded by the FOSL1 gene.

The Fos gene family consists of 4 members: c-Fos, FOSB, FOSL1, and FOSL2. These genes encode leucine zipper proteins that can dimerize with proteins of the JUN family, thereby forming the transcription factor complex AP-1. As such, the FOS proteins have been implicated as regulators of cell proliferation, differentiation, and transformation.

FOSL1 has been shown to interact with USF1 (human gene) and C-jun.

Marques et al. identified the AP-1 transcription factor FOSL1 as a key regulator of the mesenchymal glioblastoma subtype.

They provided a mechanistic basis to the role of the neurofibromatosis type 1 gene (NF1), a negative regulator of the RAS/MAPK pathway, in Glioblastoma mesenchymal transformation through the modulation of FOSL1 expression. Depletion of FOSL1 in NF1-mutant human BTSCs and Kras-mutant mouse neural stem cells results in loss of the mesenchymal gene signature and reduction in stem cell properties and in vivo tumorigenic potential. This data demonstrates that FOSL1 controls Glioblastoma plasticity and aggressiveness in response to NF1 alterations [1)].

Neuronal apoptosis is an important process of secondary brain injury that is induced by neurochemical signaling cascades after traumatic brain injury (TBI). The present study was designed to investigate whether FOS-like antigen 1 (Fra-1) is involved in neuronal apoptosis. Western blot analysis and immunohistochemistry in a rat TBI model revealed a significant increase in the expression of Fra-1 in the ipsilateral brain cortex, which was in parallel with increase in the expression of active caspase-3. With immunofluorescence double-labeling, Fra-1 was colocalized with active caspase-3 and with NeuN, a neuronal marker. In an in vitro cell injury model, H2O2 exposure induced cell apoptosis and reduced cell viability and at the same time, a similar increased expression of active caspase-3, p53, and Fra-1 was found in PC12 cells. Down-regulation of Fra-1 through transfection with Fra-1 siRNA remarkably elevated cell viability reduced the expression of active caspase-3 and p53 and decreased apoptosis of PC12 cells after H2O2 exposure. Taken together, present findings suggest that Fra-1 may be involved in the induction of neuronal apoptosis through up-regulating p53 signaling pathway and that this action may contribute to the secondary neuropathological process after TBI [2)].

1)
Marques C, Unterkircher T, Kroon P, Oldrini B, Izzo A, Dramaretska Y, Ferrarese R, Kling E, Schnell O, Nelander S, Wagner EF, Bakiri L, Gargiulo G, Carro MS, Squatrito M. NF1 regulates mesenchymal glioblastoma plasticity and aggressiveness through the AP-1 transcription factor FOSL1. Elife. 2021 Aug 17;10:e64846. doi: 10.7554/eLife.64846. PMID: 34399888.

2)
Xu X, Jiang R, Gong P, Liu Q, Chen Y, Hou S, Yuan D, Shi J, Lan Q. Up-regulation of FOS-like antigen 1 contributes to neuronal apoptosis in the cortex of rat following traumatic brain injury. Metab Brain Dis. 2017 Oct 27. doi: 10.1007/s11011-017-0129-7. [Epub ahead of print] PubMed PMID: 29080084.