Displays strong neuroprotective effect in brain ischemia

MGF

The C-terminal peptide of Mechano-Growth Factor, an alternatively spliced variant of insulin-like growth factor 1 (IGF-1)

Different roles of the IGF-I Ec peptide (MGF) and mature IGF-I in myoblast proliferation and differentiation
The physiological function of a recently cloned splice variant of insulin-like growth factor-I (IGF-I; mechano growth factor (MGF)) was studied using an in vitro cell model. Unlike mature IGF-I, the distinct E domain of MGF inhibits terminal differentiation whilst increasing myoblast proliferation. Blocking the IGF-I receptor with a specific antibody indicated that the function of MGF E domain is mediated via a different receptor. The results provide a basis for localized tissue adaptation and helps explain why loss of muscle mass occurs in the elderly and in dystrophic muscle in which MGF production is markedly affected.
Yang SY, Goldspink G. FEBS Lett. 2002 Jul 3;522(1-3):156-60.

The ischemic stroke is the third leading cause of death in developed countries. The C-terminal peptide of mechano-growth factor (MGF), an alternatively spliced variant of insulin-like growth factor 1 (IGF-1), was found to function independently from the rest of the molecule and showed a neuroprotective effect in vivo and in vitro. In vivo, in a gerbil model of transient brain ischemia, treatment with the synthetic MGF C-terminal peptide provided very significant protection to the vulnerable neurons. In the same model, ischemia evoked increased expression of endogenous MGF in the ischemia-resistant hippocampal neurons, suggesting that the endogenous MGF might have an important neuroprotective function. In an in vitro organotypic hippocampal culture model of neurodegeneration, the synthetic peptide was as potent as the full-length IGF-1 while its effect lasted significantly longer than that of recombinant IGF-1. While two peptides showed an additive effect, the neuroprotective action of the C-terminal MGF was independent from the IGF-1 receptor, indicating a new mode of action for this molecule. Although MGF is known for its regenerative capability in skeletal muscle, our findings demonstrate for the first time a neuroprotective role against ischemia for this specific IGF-1 isoform. Therefore, the C-terminal MGF peptide has a potential to be developed into a therapeutic modality for the prevention of neuronal damage.
Dluzniewska J, et al. FASEB J. 2005 Sep 6; [Epub ahead of print]

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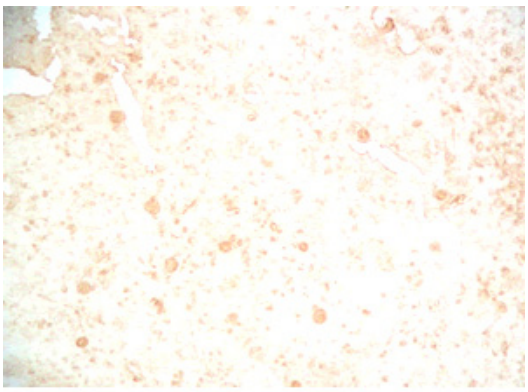
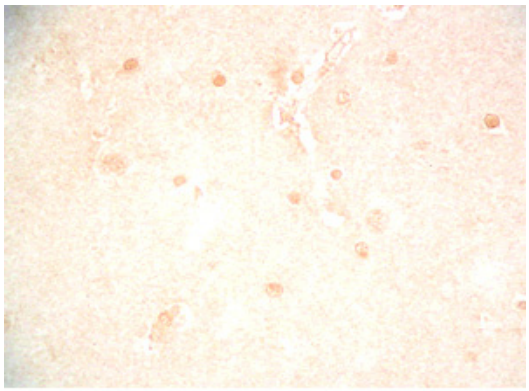


Mouse brain tissue was stained by Rabbit Anti-MGF (Human) Serum (Catalog No.: H-033-35)



Rat brain tissue was stained by Rabbit Anti-MGF (Human) Serum (Catalog No.: H-033-35)

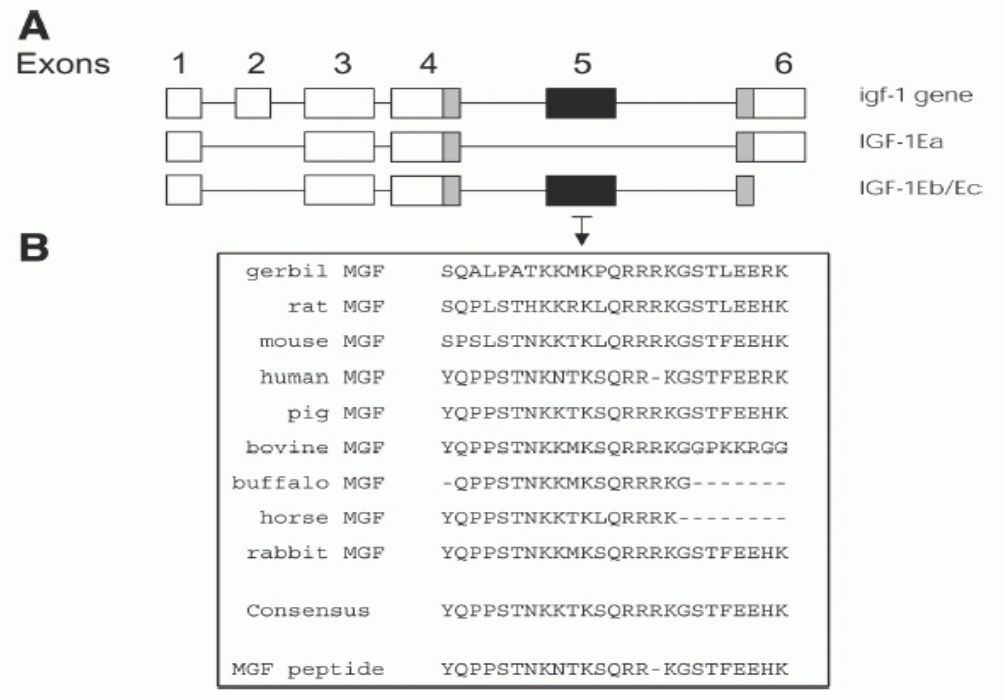


Figure 1. IGF-1: one gene, many proteins. A) A schematic representation of the IGF-1 gene and its locally produced splice variants. The black boxes denote the insert in exon 5 (49 bp in human, 52 bp in gerbil and other species studied), which gives rise to alternatively spliced MGF isoform. B) The gerbil C-terminal MGF peptide sequence shows a high degree of homology with E-domains from other species. Based on the consensus sequence, the C-terminal MGF peptide was synthesized.
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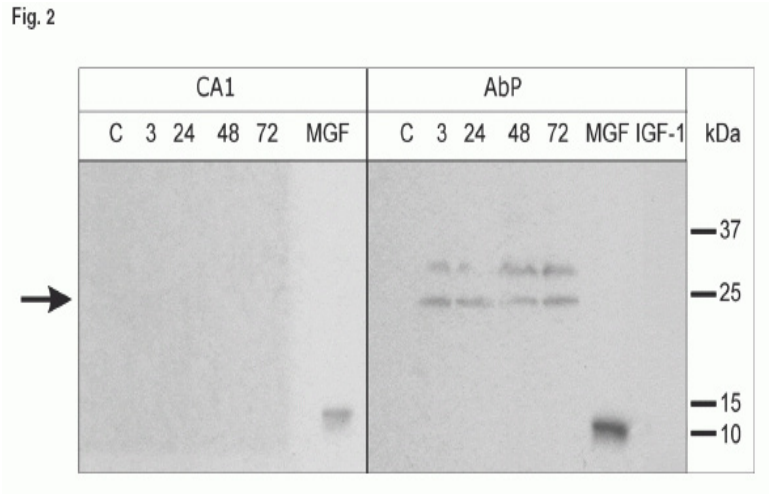

Figure 2. Representative immunoblot analysis of the expression of endogenous MGF. The hippocampi (C-control) and postischemic at 3, 24, 48, and 72 h after reperfusion were divided into vulnerable (CA1) and the resistant (CA2-3, DGabdominal, AbP) parts. Note the rapid increase and sustained expression of MGF only in the abdominal part (arrow). There were always two immunopositive bands present; the identity of the larger-size band is not clear. Antibody was obtained by immunization with synthetic C-terminal MGF peptide shown on blots as a positive control (smaller band in MGF lane) and does not cross-react with the recombinant IGF-1 peptide (IGF-1 lane).
Dluzniewska J, et al. FASEB J.
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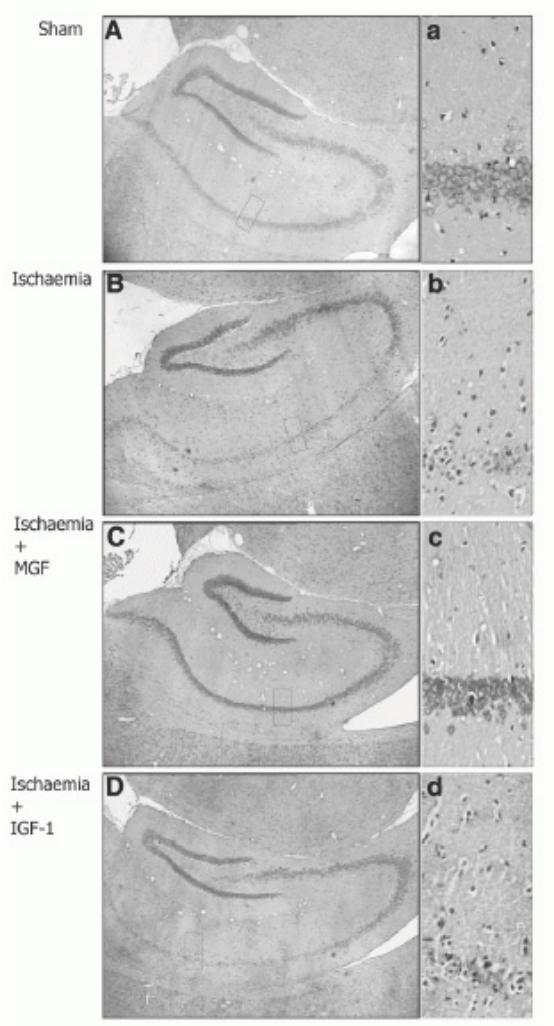

Figure 4. Neuroprotective effect of C-terminal MGF and IGF-1 peptides in global cerebral ischemia. Histological images of hematoxylin and eosin-stained coronal sections of the CA1 hippocampal regions from sham-operated (A), ischemic (B), and C-terminal MGF-treated (C) or IGF-1-treated (D) ischemic animals analyzed 7 days after the insult. Magnifications: ×2.5 or ×10 (a–d) . Note the well-preserved pyramidal neurones in the CA1 region in the ischemic animal treated with C-terminal MGF peptide (Cc).
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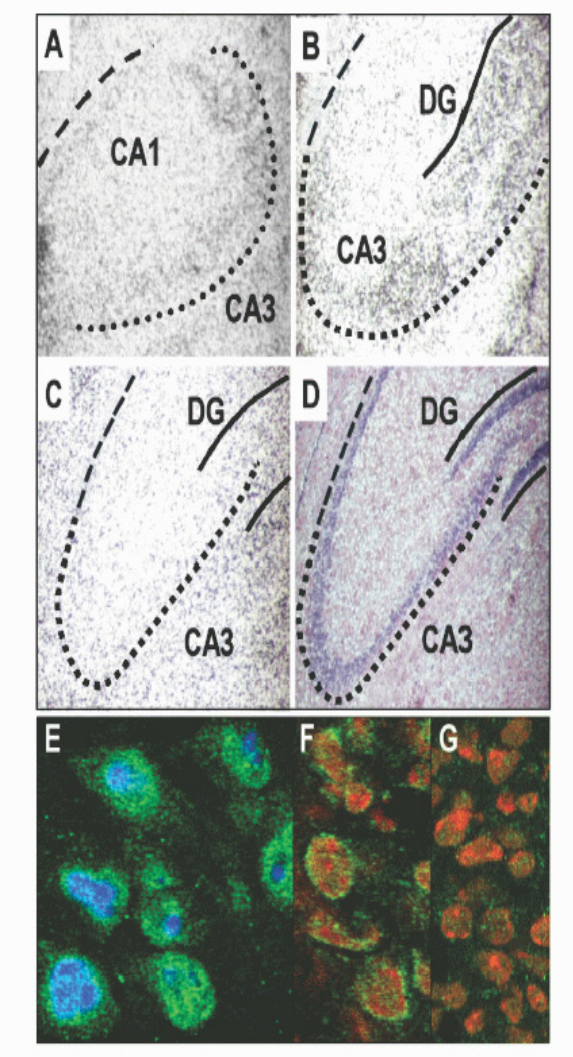

Figure 3. Ischemia-induced changes in endogenous expression of MGF in gerbil hippocampi. A–C) In situ hybridization analysis of MGF mRNA expression. Bright-field autoradiographs of coronal brain sections hybridized with the MGFspecific oligo probe. The lines outline the external margins of the hippocampal areas. A) Control brain: very weak signal in the CA3 area of the hippocampus. B) Six hours after ischemia: increased MGF hybridization signal in the CA3 and the dentate gyrus (DG). C) Negative (background) control. D) Hematoxylin and eosin staining of the corresponding brain section showing histological organization of the specific hippocampal areas. E, F) Immunolocalization of the endogenous MGF in gerbil hippocampus postischemia. Polyclonal antibody against human (E) and rat (F) C-terminal MGF peptide was used to stain coronal sections of gerbil brains 72 h postischemia. E) Confocal image of MGF-specific signal visualized with Alexa 488 (green) conjugated secondary antibody merged with pseudo-DAPI nuclear counterstaining (×1000). F) A single optical section from a stack of confocal images: MGF-specific signal (green, Alexa 488) and cell nucleus (orange, ToPro) staining. Note the MGF-specific perinuclear reactivity with a granular appearance located in the CA3 pyramidal neurons. G) Negative (background) control in the CA1 region.
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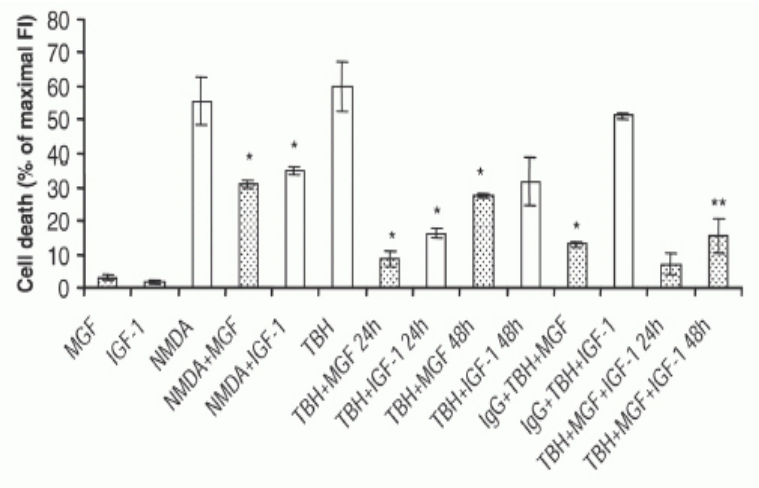

Figure 5. The neuroprotective effects of C-terminal MGF and IGF-1 peptides in vivo and in vitro. B) Analysis in organotypic hippocampal slices. Cell damage was quantified on fluorescence images as described in Materials and Methods and expressed as the percentage of maximal fluorescence (FI) produced by glutamate toxicity. Significant differences (*P<0.001) were observed in NMDA + Cterminal MGF peptide and NMDA + IGF-1 vs. NMDA-only group; TBH + C-terminal MGF peptide group after 24 h and 48 h and TBH + IGF-1 group after 24 h and IgG + TBH + C-terminal MGF peptide vs. TBH-only group. Note the additive effect seen at 48 h of TBH + C-terminal MGF peptide + IGF-1 vs. TBH + C-terminal MGF peptide (**P<0.001). Columns labeled MGF and IGF-1 show the effects of these compounds on control cultures without TBH or NMDA. Data are presented as mean ± SD.
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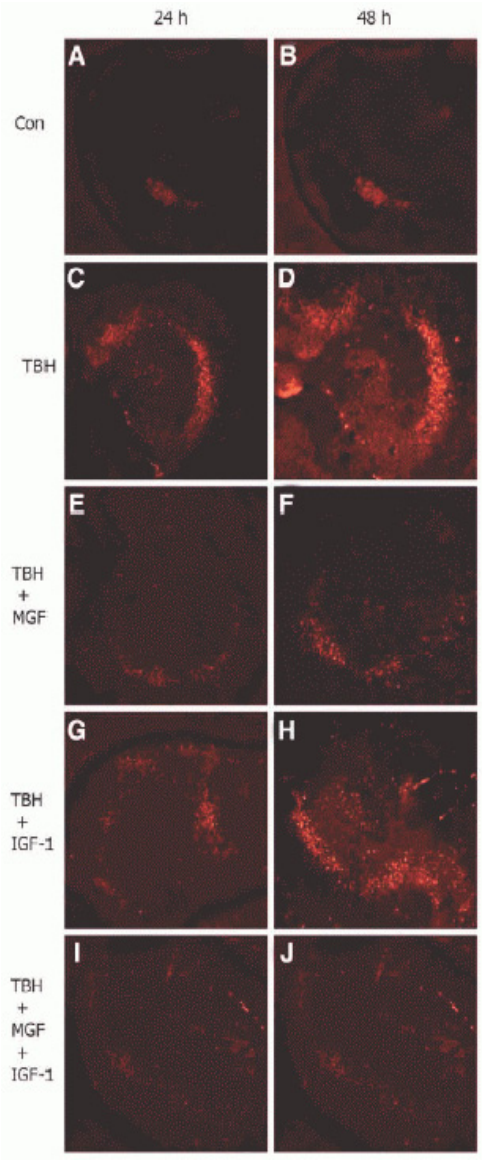

Figure 6. The C-terminal M images (×2.5) of propidium iodide-stained hippocampal cultures. Only dead cells are labeled (shown in red). Peptides were added to the culture medium at the time of insult (TBH exposure) and were present in the medium continuously. Twenty-four hours after insult, sections were stained with propidium iodide, and cell viability was assessed at 24 h (A, C, E, G, I) and 48 h (B, D, F, H, J). In control cultures, no cell death was seen (A, B), whereas TBH exposure induced neuronal cell death in the CA1 region (C, D). At 24 h, both C-terminal MGF peptide (E) and IGF-1 (G) reduced cell death. F) However, C-terminal MGF peptide protection was longer lasting and its neuroprotective effect was still apparent after 48 h. I, J) The protective effect of both C-terminal MGF peptide and IGF-1 was additive. L) The protective effect of C-terminal MGF peptide was not mediated via the IGF-1 receptor. Specific anti-IGF-1 receptor blocking antibody was included in the culture medium 1 h before the hippocampal slices were exposed to TBH (K) with either 100 ng/ml of Cterminal MGF peptide (L) or IGF-1 peptide (M). The presence of antibody significantly reduced the protection evoked by IGF-1 but did not affect that of C-terminal MGF peptide.
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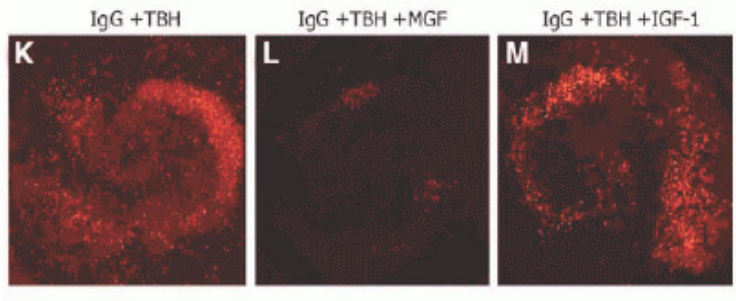

Available Products

Catalog Number	Description	Std. Size
033-20	IGF Binding Protein-3, Recombinant (IGFBP-3) (Human)	5 µg
033-23	IGF-II (Insulin-like Growth Factor-II), Recombinant (Human)	20 µg
033-26	IGF-I (Insulin-like Growth Factor-I), Recombinant (Human)	20 µg
033-34	MGF Peptide Amide [D-Arg14,15] / C-Terminal Peptide of IGF-1 Ec Amide	100 µg
033-35	MGF (Human)	100 µg
B-G-033-35	MGF (Human) - Purified IgG Biotin Labeled	100 µl
EK-033-19	IGF Binding Protein-1 (IGFBP-1) (Human), recombinant - ELISA Kit	1 kit
EK-033-20	IGF Binding Protein-3 (IGFBP-3) (Human), recombinant - ELISA Kit	1 kit
FC3-033-35	MGF (Human) - Cy3 Labeled	1 nmol
FC3-G-033-35	MGF (Human) - Cy3 Labeled purified IgG	100µl
FC5-033-35	MGF (Human) - Cy5 Labeled	1 nmol
FC5-G-033-35	MGF (Human) - Cy5 Labeled Purified IgG	100 ul
FG-033-35A	MGF (Human) - FAM Labeled	1 nmol
FG-G-033-35A	MGF (Human) - FAM Labeled Purified IgG	100 ul
FG-G-033-35B	MGF (Human) - FITC Labeled Purified Goat IgG	100 ul
FR-033-35	MGF (Human) - Rhodamine Labeled	1 nmol
FR-G-033-35	MGF (Human) - Rhodamine Labeled Purified IgG	100 µl
G-033-35	MGF (Human) - Purified IgG Antibody	200 µg
H-033-35	MGF (Human) - Antibody for Immunohistochemistry	100 µl
T-033-20	IGF Binding Protein-3 (IGFBP-3) (Human) recombinant - I-125 Labeled	10 µCi
T-033-21	IGF-II, recombinant (Mouse) - I-125 Labeled	10 µCi
T-033-23	IGF-II, recombinant (Human) - I-125 Labeled	10 µCi
T-033-26	IGF-I, recombinant (Human) - I-125 Labeled	10 µCi
T-033-35	MGF (Human) - Iodine 125 Labeled Tracer	10 µCi
T-G-033-35	MGF (Human) - Iodine 125 Labeled Purified IgG Tracer	10 µCi