



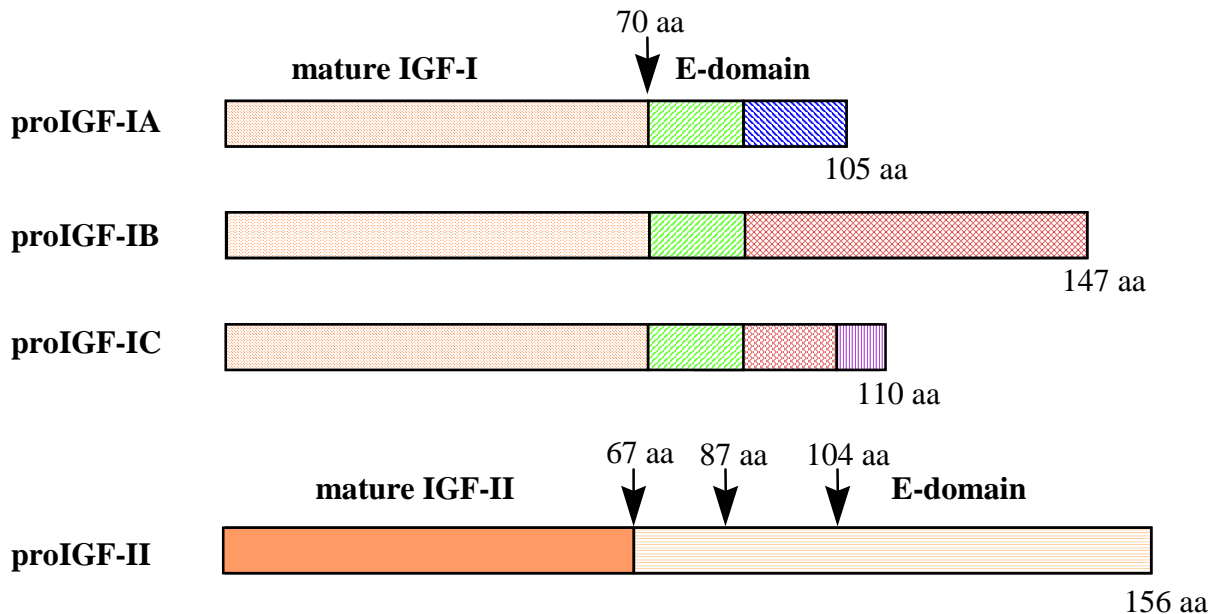
Insulin-like Growth Factor Precursors

The polypeptide growth factors IGF-I and IGF-II are synthesized as pre-pro-hormones which are subsequently processed by proteolysis to generate the mature 70 and 67 amino acid proteins (1). The proIGF proteins are characterized by the presence of C-terminal extensions known as E-domains.

IGF-I Precursors:

Alternative splicing of the IGF-I gene can generate three different proIGF-I proteins, designated proIGF-IA, proIGF-IB and proIGF-IC (Figure 1). These three forms contain 35 to 77 amino acid E-domains which share a common 16 amino acid N-terminal portion. IGF-IA has a further 19 amino acid extension not found in IGF-IB or IGF-IC. The E-domain of IGF-IB is 77 amino acids long, shares homology with part of the 40 amino acid IGF-IC E-domain and contains a potential heparin-binding domain and a consensus nuclear localization signal.

Figure 1: IGF Precursor Structure



IGF-II Precursors:

The IGF-II gene encodes a single transcript which results in a 156 amino acid protein including an 89 amino acid E-domain. ProIGF-II contains sites of O-linked glycosylation. ProIGF-II is converted to mature IGF-II by sequential cleavage after amino acids 104 and 87 (Figure 1) (2). Differential glycosylation and cleavage within the E-domain can therefore result in multiple proIGF-II isoforms.

Function:

The physiological significance of the proIGF proteins has not been completely defined. The three IGF-I precursors are differentially expressed in different tissues (3). However, the proIGF-I proteins have proven difficult to detect extracellularly. The proIGF-II proteins have been found in both normal human tissues and in serum (4). Overexpression of proIGF-II proteins has been observed in a variety of cancers and has been implicated in the development of non-islet cell tumor hypoglycemia (4,5). Other reports have linked elevated circulating proIGF-II levels with increased bone formation (6). An intriguing, although largely untested hypothesis is that the E-domain may have a role in targeting IGF proteins to specific tissues via interactions with the extracellular matrix. An IGF-independent role as a mitogen has been reported for the E-domain peptide derived from the cleavage of the IGF-I precursor (7).

For specifications on any of these reagents, click on the product titles below.

GroPep Rabbit antisera to proIGF-I proteins:

Antibody	Epitope	Product Code	IGF-I	proIGF-IA	proIGF-IB	proIGF-IC
anti-IGF-IE	aa 71 - 86	PAAV1	nd	+	+	+
anti-IGF-IEA	aa 92 - 105	PAAU1	nd	+	nd	nd
anti-IGF-IEB	aa 104 - 123	PAAT1	nd	nd	+	nd
anti-IGF-IEC	aa 104 - 110	PAAS1	nd	nd	nd	+

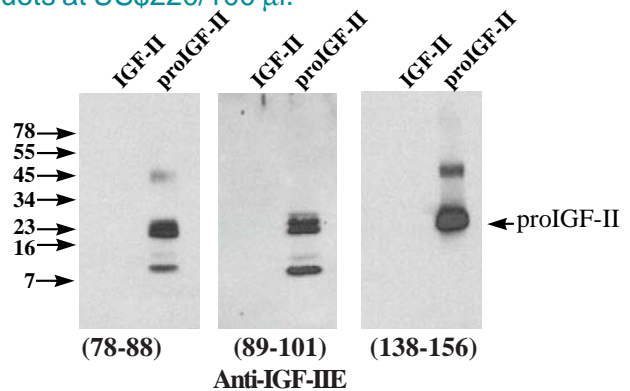
GroPep Rabbit antisera to proIGF-II proteins:

Antibody	Epitope	Product Code	IGF-II	proIGF-II
anti-IGF-IIIE	aa 78 - 88	PAAZ1	nd	+
anti-IGF-IIIE	aa 89 - 101	PAAAY1	nd	+
anti-IGF-IIIE	aa 138 - 156	PAAAX1	nd	+

nd = not detected; + = positive.

- ◆ Suitable for Western blotting and other applications.
- ◆ Supplied in 100 µl lyophilized aliquots at US\$220/100 µl.

Figure 2: Western Blot with GroPep IGF-IIIE Antisera against GroPep IGF-II and proIGF-II (aa 1 - 156)



Recombinant proIGF-II Proteins:

GroPep's proIGF-II:

- ◆ Produced recombinantly in *E.coli*.
- ◆ Available in both full-length (156 amino acid) and truncated (104 amino acid) forms.
- ◆ Has biological activity in the following assays:
 - * IGF Receptor binding.
 - * Stimulation of protein synthesis (rat L6 myoblasts).

GroPep's proIGF-II is useful for:

- ◆ Investigating the effects of the IGF-II precursor proteins.
- ◆ Detection and quantification of proIGF-II isoforms in normal and cancerous tissues (*reference standard*).

Human proIGF-II (aa 1 - 104) (Receptor Grade)

Code: AZU100 100 µg US\$570
 Code: AZM001 1 mg US\$4290

Human proIGF-II (aa 1 - 156)

Code: AHU020 20 µg US\$340
 Code: AHU100 100 µg US\$570

Useful References:

1. Duguay, S. J. (1999) Post-translational processing of insulin-like growth factors. *Horm. Metab. Res.*, **31**, 43-49.
2. Duguay, S. J., *et al.* (1998) Post translational processing of the insulin-like growth factor-2 precursor. *J. Biol. Chem.*, **273**, 18443-18451.
3. Lowe, W. L. *et al.* (1988) Distribution and regulation of rat insulin-like growth factor-I messenger ribonucleic acids encoding alternative carboxyterminal E peptides: Evidence for differential processing and regulation in liver. *Mol. Endocrinol.*, **2**, 528-353.
4. Daughday, W. H., *et al.* (1988) Synthesis and secretion of insulin-like growth factor II by a Leiomyosarcoma with associated hypoglycemia. *N. Engl. J. Med.*, **318**, 1434-1440.
5. Zapf, J., *et al.* (1992) Can big insulin-like growth factor II in serum of tumor patients account for the development of extra pancreatic tumor hypoglycemia. *J. Clin. Invest.*, **90**, 2574-2584.
6. Khosla, S., *et al.* (1998) Insulin-like growth factor system abnormalities in Hepatitis C-associated osteosclerosis. *J. Clin. Invest.*, **101**, 2165-2173.
7. Tian, X. C., *et al.* (1999) Recombinant E-peptides or pro-IGF-I have mitogenic activity. *Endocrinology.*, **140**, 3387-3390.



GroPep : Experience Quality

P.O. Box 10065, Adelaide BC, SA 5000, AUSTRALIA

Telephone: +61 8 8354 7700

E-mail: bioreagents@gropep.com.au

Facsimile: +61 8 8354 7788

Website: www.gropep.com.au