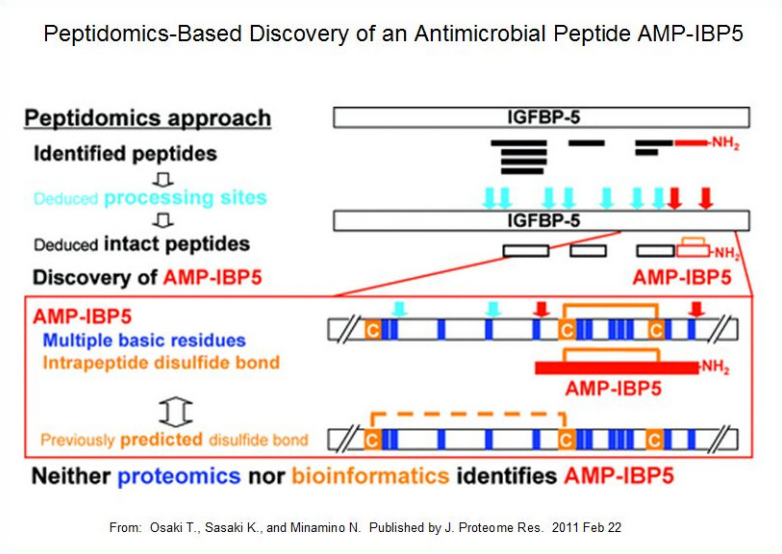
AMP-IGFB 5

Antimicrobial Peptide
Derived from Insulin-Like Growth Factor-Binding Protein



Insulin-like growth factor-binding protein-5 (IGFBP-5) inhibits TNF-α-induced NF-κB activity by binding to TNFR1.

IGFBP-5 is known to be involved in various cell phenomena such as proliferation, differentiation, and apoptosis. However, the exact mechanisms by which IGFBP-5 exerts its functions are unclear. In this study, we demonstrate for the first time that IGFBP-5 is a TNFR1-interacting protein. We found that ectopic expression of IGFBP-5 induced TNFR1 gene expression, and that IGFBP-5 interacted with TNFR1 in both an in vivo and an in vitro system. Secreted IGFBP-5 interacted with GST-TNFR1 and this interaction was blocked by TNF-α, demonstrating that IGFBP-5 might be a TNFR1 ligand. Furthermore, conditioned media containing secreted IGFBP-5 inhibited PMA-induced NF-κB activity and IL-6 expression in U-937 cells. Coimmunoprecipitation assays of TNFR1 and IGFBP-5 wild-type and truncation mutants revealed that IGFBP-5 interacts with TNFR1 through its N- and L-domains. However, only the interaction between the L-domain of IGFBP-5 and TNFR1 was blocked by TNF-α in a dose-dependent manner, suggesting that the L-domain of IGFBP-5 can function as a TNFR1 ligand. Competition between the L-domain of IGFBP-5 and TNF-α resulted in inhibition of TNF-α-induced NF-κB activity. Taken together, our results suggest that the L-domain of IGFBP-5 is a novel TNFR1 ligand that functions as a competitive TNF-α inhibitor.

Hwang J.R. et al., Biochem Biophys Res Comm:405(4)545-51. [Epub ahead of print]

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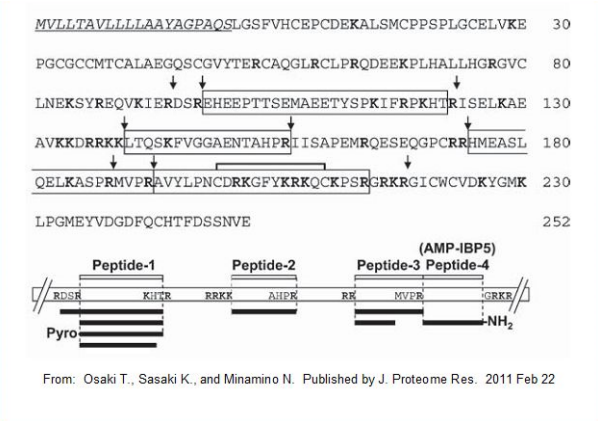
Peptidomics-Based Discovery of an Antimicrobial Peptide Derived from Insulin-Like Growth Factor-Binding Protein 5.

Antimicrobial peptides (AMPs) are effector molecules that are able to kill or inactivate microbial pathogens. However, most AMPs harbor multiple basic amino acids that hamper current proteomic identification. In our peptidomic survey of endogenous peptides, we identified a novel intramolecular disulfide-linked 22-residue amidated peptide. This peptide, designated AMP-IBP5 (antimicrobial peptide derived from insulin-like growth factor-binding protein 5), showed antimicrobial activity against six of the eight microorganisms tested at concentrations comparable to or lower than those for well-characterized AMPs cathelicidin and β-defensin-2. AMP-IBP5 is identical at the amino acid level between human, mouse, rat, pig, and cow. Natural occurrence of this peptide as the originally isolated form was demonstrated in the rat brain and intestine, using mass spectrometric characterization of major immunoreactivity. The peptide is flanked N-terminally by a single arginine and C-terminally by a common amidation signal, indicating that insulin-like growth factor-binding protein 5 (IGFBP-5) undergoes specific cleavage by a defined set of processing proteases. Furthermore, the intramolecular linkage C199-C210 reveals itself as a correct disulfide pairing in the precursor protein, the finding not inferred from closely related family members IGFBP-4 and -6. In principle, neither conventional proteomics nor bioinformatics would achieve the identification of this AMP. Our study exemplifies the impact of peptidomics to study naturally occurring peptides.

Osaki T, Sasaki K, Minamino N. et al., Proteome Res. 2011 Feb 22. [Epub ahead of print] PMID: 21210651



From: Osaki T., Sasaki K., and Minamino N. Published by J. Proteome Res. 2011 Feb 22

Determination of immunoreactive AMP-IBP5 levels in rat tissues by RIA

Tissues	Amounts in tissues (pmol/g)
Brain	2.0 ± 0.6
Pituitary gland	6.1 ± 1.1
Lung	0.51 ± 0.1
Heart	0.36 ± 0.05
Stomach	0.58 ± 0.1
Small intestine	1.41 ± 0.3
Liver	0.48 ± 0.1
Pancreas	0.44 ± 0.1
Kidney	0.3 ± 0.01
Uterus	0.46 ± 0.1

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Catalog Number	Name	Standard Size
033-72	AMP-IBP5 / prepro IGFBP-5 193-214 peptide 4 (Human, Bovine, Porcine, Mouse, Rat)	100ug
033-73	IGFBP-5, Prepro (98-122) (Peptide 1) (Human, Bovine, Porcine, Mouse, Rat)	100ug
033-74	IGFBP-5, Prepro (140-156) (Peptide 2) (Human, Bovine, Porcine, Mouse, Rat)	100ug
033-75	IGFBP-5, Prepro (175-192) (Peptide 3) (Human, Bovine, Porcine)	100ug
T-033-72	AMP-IBP5 / IGFBP-5, Prepro (193-214) (Peptide 4) (Human) - I-125 Labeled	10uCi