

# Recombinant Human Connective Tissue Growth Factor (rh CTGF)

**Synonyms:** CCN2, NOV2, HCS24, IGFBP8

**Introduction:** Connective Tissue Growth Factor belongs to the CCN family of proteins. The CCN family presently consists of six members in human also known as: Cyr61 (Cystein rich 61), CTGF (Connective Tissue Growth Factor), Nov (Nephroblastoma Overexpressed gene), WISP-1, 2 and 3 (Wnt-1 Induced Secreted Proteins). The CCN genes encode secreted proteins associated with the Extracellular Matrix (ECM) and cell membrane. CCN proteins are matricellular proteins which are involved in the regulation of various cellular functions including: proliferation, differentiation, survival, adhesion and migration. They are expressed in derivatives of the three embryonic sheets and are implicated in the development of kidney, nervous system, muscle, bone marrow, cartilage and bone. During adulthood, they are implicated in wound healing, bone fracture repair, and pathologies such as: fibrosis, vascular ailments and tumorigenesis. Full length secreted CCN proteins can show an antiproliferative activity, whereas truncated isoforms are likely to stimulate proliferation and behave as oncogenes. The full length protein consists of four modules:

**Module I** shares partial identity with the N-terminal part of the Insulin-like Growth Factor Binding Proteins (IGFBPs).

**Module II** includes a stretch of 70 amino acid residues – which shares sequence identity with the Von Willebrand Factor Type C repeat (VWC).

**Module III** contains sequences sharing identity with the Thrombospondin type 1 repeat (TSP1) (WSXCSXXCG), which is thought to be implicated in the binding of sulfated glycoconjugates and to be important for cell adhesion.

**Module IV**, also designated CT, is encoded by exon5. It is the least conserved one of the four domains at the level of nucleotide sequence, but it appears to be critical for several of the biological functions attributed to the CCN proteins. Module IV resembles the CT domain of several extracellular protein including, Von Willebrand's factor and mucins. Sequence similarities to heparin-binding motifs are also found within this domain. Proteolysis of the secreted full-length CCN proteins that has been reported in the case of CTGF and CCN3 might result in the production of CCN-derived peptides with high affinity for ligands that full-length CNN proteins bind only poorly. Amino-truncated CTGF isoforms were biologically active whereas no specific biological activity has been attributed to the truncated CCN3. Although the molecular processes underlying the production of these secreted isoforms is presently unknown, it is important to note that proteolysis occur at the same amino acid residues in both CTGF and CCN3. An elevated expression of CTGF has also been detected by Northern blotting in human invasive mammary ductal carcinomas, dermatofibromas, pyogenic granuloma, endothelial cells of angioliopomas and angioleiomyomas, and in pancreatic tumors. A study performed with chondrosarcomas representative of various histological grades established that CTGF expression was closely correlated with increasing levels of malignancy. In agreement with CTGF playing a role in brain tumor angiogenesis, immunocytochemistry studies indicated that both glioblastoma tumor cells and proliferating endothelial cells stained positive for CTGF. In astrocytomas, CTGF expression was particularly elevated in high grade tumors, with a marked effect of CTGF on cell proliferation. Downregulation of CTGF expression in these cells was associated with a growth arrest at the G1/S transition while over-expression of CTGF induced a two-fold increase of the number of cells in the G1 phase. Gene profiling analysis allowed to identify a set of about 50 genes whose expression might account for the proliferative activity of CTGF in these cells. CTGF was seen in a higher proportion of mononuclear cells of patients with acute lymphoblastic leukemia.

**Description:** Recombinant human CTGF produced in E.Coli is a single, non-glycosylated, polypeptide chain containing 98 amino acids and having a molecular mass of 11.2 kDa. The CTGF is purified by proprietary chromatographic techniques.

**Source:** *Escherichia Coli*.

**Physical Appearance:** Sterile filtered white lyophilized (freeze-dried) powder.

**Formulation:** Lyophilized from 1mg/ml solution containing 10mM NaAcetate buffer pH-6. The samples of 1µg contain Trehalose 5% (w/vol) for better recovery

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Gladiolenweg 2; 26169 Friesoythe; Germany  
phone:+49-(0)4491-400997, fax:+49-(0)4491-400998, [info@immunotools.com](mailto:info@immunotools.com)  
[www.immunotools.com](http://www.immunotools.com)

**Solubility:** Reconstitute at 0.1 mg/ml with 5mM NaAcetate, pH-6

**Stability:** Lyophilized rh CTGF, although stable at room temperature for 3 weeks, should be stored desiccated below  $-18^{\circ}$  C. Upon reconstitution rh CTGF should be stored at  $4^{\circ}$  C between 2-7 days and for future use below  $-18^{\circ}$  C. For long term storage it is recommended to add a carrier protein (0.1% HSA or BSA). Please prevent freeze-thaw cycles.

**Purity:** Purity of CTGF is greater than 95% as determined by SDS-PAGE.

**Amino acid sequence:** MGKKCIRTPK ISKPIKFELS GCTSMKTYRA KFCGVCTDGR CCTPHRTTTL PVEFKCPDGE VMKKNMMFIK TCACHYNCPG DNDIFESLYY RKMYGDMA

**Endotoxicity:** The endotoxin level is less than 1 EU /  $\mu$ g determined by LAL method.

**Biological Activity:** Determined by the dose-dependent stimulation of the proliferation of HUVEC cells the expected ED<sub>50</sub> for this effect is 1.0 - 2.0  $\mu$ g/ml.

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<i>small</i>	5 $\mu$ g	Cat.N°	11343480
<i>medium</i>	20 $\mu$ g	Cat.N°	11343484
<i>large</i>	100 $\mu$ g	Cat.N°	11343486
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 phone:+49-(0)4491-400997, fax:+49-(0)4491-400998, [info@immunotools.com](mailto:info@immunotools.com)  
[www.immunotools.com](http://www.immunotools.com)