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CONNECTIVE TISSUE GROWTH FACTOR (CTGF) FROM BASICS TO CLINICS

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Abstract

Connective tissue growth factor, also known as CCN2, is a cysteine-rich matricellular protein involved in the control of biological processes, such as cell proliferation, differentiation, adhesion and angiogenesis, as well as multiple pathologies, such as tumor development and tissue fibrosis. Here, we describe the molecular and biological characteristics of CTGF, its regulation and various functions in the spectrum of development and regeneration to fibrosis. We further outline the preclinical and clinical studies concerning compounds targeting CTGF in various pathologies with the focus on heart, lung, liver, kidney and solid organ transplantation. Finally, we address the advances and pitfalls of translational fibrosis research and provide suggestions to move towards a better management of fibrosis.

Key words: Connective tissue growth factor, CCN2, matricellular protein, fibrosis, marker and therapeutic target

Abbreviations: AP1, activator protein 1; ASK1, apoptosis signal-regulating kinase 1; AT1R, angiotensin 2 type 1 receptor; AT2R, angiotensin 2 type 2 receptor; BCL-2, B-cell lymphoma 2; BMP4, bone morphogenic protein 4; BMP7, bone morphogenic protein 7; BMPs, bone morphogenic proteins; BMPs, bone morphogenic proteins; cAMP, cyclic adenosine monophosphate; CKD, chronic kidney disease; CTGF, connective tissue growth factor; CYR61, cysteine rich angiogenic inducer 61; c-Src, proto-oncogene c; DDR, DNA damage repair; DMD, Duchenne muscular dystrophy; DN, diabetic nephropathy; ECM, extracellular matrix; EGF, epidermal growth factor; EGF, epidermal growth factor; EGFR, epidermal growth factor receptor; EMT, epithelial-to-mesenchymal transition; ET-1, endothelin-1; Ets1, ETS proto-oncogene 1; FAK, focal adhesion kinase; FGF-2, fibroblast growth factor 2; FGFB, fibroblast growth factor 2; FOXO1/3a, forkhead box protein O1/forkhead box protein O3a; FZD7, frizzled 7; HIF1α, hypoxia- inducible factor 1α; HSC, hepatic stellate cells; HSPGs, heparan sulfate protoglycans; IGF, insulin-like growth factor IL-1R, interleukin 1 receptor; IL1β, interleukin 1 β; IPF, idiopathic pulmonary fibrosis; ITGs,