Abstract

Nitric oxide (NO) produced by endothelial cells via nitric-oxide synthase (eNOS) conversion of L-arginine to L-citrulline represents an antifibrotic mechanism in the body. Studies suggest that nitric oxide (NO)-mediated signals does this role through regulating myofibroblast phenotypes. This work focused on the transcriptional regulation of NOS3 gene at promoter level .Rat and human NOS3 was used to transfect myofibroblast cells, promoter activity was assayed using the Dual Luciferase reporter gene assay technique. The results showed that rat NOS3 promoter was active in the rat pulmonary myofibroblasts with the human NOS3 promoter showing little or no activity. Determination of the effect of various compounds on promoter activity either as effectors or inhibitors and was carried out. NOS3 promoter activity was then assessed using Dual Luciferase Assay. The results showed that high concentrations of Phorbor-12-myristate-13-acetate (PMA), Calcium and S-nitroso-N-acetylpenicillamine (SNAP), a Nitric Oxide donor, down-regulated the expression of NOS3 gene. Conversely, high concentrations of transforming growth factor beta (TGFβ) up-regulated the expression of NOS3 gene. Calcium suppresses eNOS expression by the effect seen by 23187(Calcium ionophore) increasing the entry of calcium into the cells. From these results it can be concluded that down-regulation and up-regulation of the NOS3 promoter is therefore transcriptionally regulated. Inhibition of NO production has been seen to increase accumulation of myofibroblasts therefore an enhanced expression of eNOS in response to pharmacological interventions could provide protection against interstitial pulmonary fibrosis (IPF) emanating from altered characteristics of myofibroblasts..