Fluvastatin inhibits AGE-induced cell proliferation, migration, and ECM accumulation in VSMC by targeting CTGF

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Connective tissue growth factor (CTGF) is a novel fibrotic mediator, which is implicated in fibroblast proliferation, cellular adhesion, angiogenesis and extracellular matrix (ECM) synthesis. Recent studies have demonstrated that advanced glycation end products (AGE) and their receptor-ligand interactions play a key role in neointimal formation and renal fibrosis after vascular injury. However, the potential link between CTGF and AGE has not been investigated. Based on this, we aimed to examine whether Fluvastatin could protect AGE induced vascular smooth muscle cell (VSMC) fibrosis and its putative transduction signals. In the present study, we have shown that AGE stimulated CTGF mRNA and protein expression time-dependent manners. The CTGF induction signal mediated by AGE was demonstrated via ERK1/2, JNK, and Egr-1 but not p38, consequently cell proliferation, migration, and ECM accumulation were regulated by CTGF signal pathway. And AGE also stimulated VSMC proliferation, migration, and ECM accumulations were blocked by Fluvastatin. In addition, the inhibitory effect of Fluvastatin was restored by administration of CTGF recombinant protein. Furthermore, AGE-induced VSMC proliferation was dependent on cell cycle arrest, increasing G1/G0 phase. Fluvastatin repressed cell cycle regulatory genes, cyclin D1 and CDK4 and augmented cyclin-dependent kinase inhibitors, p27 and p21 in AGE-induced VSMC. Taken together, Fluvastatin suppressed AGE-induced VSMC proliferation, migration, and ECM accumulation in by targeting CTGF signaling mechanism. Therefore, it might be recent evidence for CTGF as a potential therapeutic target in diabetic vasculature complication.

Biography

Young Jin Kang has completed her PhD degree from Gyeongsang National University in 2000 and she is working at Yeongnam University since 2005 as a Professor. Her major subject is what kind of signal gene regulates vascular fibrosis and how to modulate vascular smooth muscle cell proliferation in diabetes or hypertension?

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