

Simvastatin induces apoptosis by a Rho-dependent mechanism in cultured cardiac fibroblasts and myofibroblasts

Copaja, Miguel

Venegas, Daniel

Aránguiz, Pablo

Canales, Jimena

Vivar, Raúl

Catalán, Mabel

Olmedo, Ivonne

Rodríguez, Andrea E.

Chiong, Mario

Leyton, Lisette

Lavandero, Sergio

Díaz-Araya, Guillermo

Several clinical trials have shown the beneficial effects of statins in the prevention of coronary heart disease. Additionally, statins promote apoptosis in vascular smooth muscle cells, in renal tubular epithelial cells and also in a variety of cell lines; yet, the effects of statins on cardiac fibroblast and myofibroblast, primarily responsible for cardiac tissue healing are almost unknown. Here, we investigated the effects of simvastatin on cardiac fibroblast and myofibroblast viability and studied the molecular cell death mechanism triggered by simvastatin in both cell types. Methods: Rat neonatal cardiac fibroblasts and myofibroblasts were treated with simvastatin (0.1-10⁻⁶M) up to 72 h. Cell viability and apoptosis were evaluated by trypan blue exclusion method and by flow cytometry, respectively. Caspase-3 activation and Rho protein levels and activity were also determined by Western blot and pull-down assay, respectively. Results: Simvastatin induces caspase-dependent apoptosis