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Translational Research on Rho-kinase in Cardiovascular Medicine

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Rho-kinase (ROCKs) is an important downstream effector of the small GTP-binding protein RhoA. There are 2 isoforms of Rho-kinase, ROCK1 and ROCK2, and they have different functions in several vascular components. The RhoA/Rho-kinase pathway plays an important role in various fundamental cellular functions, including contraction, motility, proliferation and apoptosis, whereas its excessive activity is involved in the pathogenesis of cardiovascular diseases. For the last 20 years, a series of translational research studies have demonstrated the important roles of Rho-kinase in the pathogenesis of cardiovascular diseases. At the molecular and cellular levels, Rho-kinase up-regulates several molecules related to inflammation, thrombosis and fibrosis. In animal experiments, Rho-kinase plays an important role in the pathogenesis of vasospasm, arteriosclerosis, hypertension, pulmonary hypertension and heart failure. Finally, at the human level, Rho-kinase is substantially involved in the pathogenesis of coronary vasospasm, angina pectoris, hypertension, pulmonary hypertension and heart failure. Furthermore, Rho-kinase activity in circulating leukocytes is a useful biomarker for the assessment of disease severity and therapeutic responses in vasospastic angina, heart failure and pulmonary hypertension. In addition to fasudil, many other Rho-kinase inhibitors are currently under development for various indications. Thus, the Rho-kinase pathway is an important novel therapeutic target in cardiovascular medicine.

Key Words: Rho-kinase; cardiovascular disease; inflammation