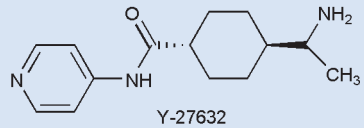
Y-27632: Selective inhibitor of the Rho-associated protein kinase p160ROCK

The small GTPase Rho and its downstream effectors, the Rho-associated coiled-coil forming protein serine/threonine kinase (ROCK) family, have been implicated in various cellular functions including actin cytoskeleton organization, cell adhesion, cell motility, vascular and smooth muscle contraction and cytokinesis [1,2]. It has been suggested that Rho/ROCK inhibition may be a novel therapeutic target in the treatment of various cardiovascular diseases, such as hypertension and arteriosclerosis [2], as well as bronchial asthma [4], cancer [5] and Alzheimer's disease [6]. In recent animal experiments, Rho-kinase inhibitors were reported to suppress coronary artery spasm [3,7]. In addition, they have been shown to inhibit the development of coronary arteriosclerotic lesions and promote the regression of coronary vascular lesions *in vivo* [3,7]. Recent clinical studies have demonstrated the inhibitory effect of the Rho-kinase inhibitor **HA-1077** (Prod. No. **H-139**) on coronary artery spasm in patients with vasospastic angina, and on exercise-induced myocardial ischemia in patients with stable effort angina [3,8].

Sigma-RBI is pleased to offer one of the best characterized ROCK inhibitors, **Y-27632** (Prod. No. **Y 0503**), which selectively targets p160ROCK from the family of Rho-associated protein kinases [1]. Y-27632 inhibits human p160ROCK displaying a K_i value of 140 µM vs rat brain **protein kinase C** (26 mM) (PLC, Prod. No. **P 7956**), bovine **cAMP-dependent protein kinase** (25 mM) (Prod. No. **C 8482**), and chicken myosin light chain kinase (>250 mM) and exhibits better potency than the Rho kinase inhibitor HA-1077 and the PKA/PKC inhibitor **H-7** (Prod. Nos. **I 6891**, **I 7016**) [1,9]. Y-27632 has also been shown to induce relaxation of rabbit aortic smooth muscle that has been contracted using **phenylephrine** (Prod. No. **P 6126**) displaying an IC_{50} value of 700 µM [1]. In addition, it inhibits the contraction of pig coronary artery strips and guinea-pig trachea induced by several agonists, including **histamine** (Prod. No. **H 7125**), **acetylcholine** (Prod. No. **A 5626**), **serotonin** (Prod. No. **H 9523**), **endothelin** (Prod. No. **E 7764**) and the thromboxane agonist **U-46619** (Prod. No. **D 8174**), exhibiting IC_{50} values in the range of 0.3 - 1 mM [1]. In various hypertensive rat models, Y-27632 significantly dose-dependently decreased blood pressure (30 mg/kg p.o.) while exhibiting little or no effect on blood pressure in control rats [1].

These results suggest that Y-27632 should serve as a useful tool for investigating the Rho/ROCK pathway *in vivo* and for studying its role in normal physiology and disease.



Y-27632
(Prod. No. Y 0503)

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