ROCK inhibitor for spinal cord injury

- Progress of researches on acupuncture treatment of spinal cord injury by promoting axonal regeneration
- The potential role of RhoA/ROCK-inhibition on locomotor recovery after spinal cord injury: a systematic review of in-vivo studies
- Preclinical characterization of a water-soluble low-impact ampakine prodrug, CX1942 and its active moiety, CX1763
- Development of Tissue-Engineered Model of Fibrotic Scarring after Spinal Cord Injury to Study Astrocyte Activation and Neurite Outgrowth In Vitro
- Schwann Cell-Derived Exosomes Induced Axon Growth after Spinal Cord Injury by Decreasing PTP-sigma Activation on CSPGs via the Rho/ROCK Pathway
- AMPA receptors play an important role in the biological consequences of spinal cord injury: Implications for AMPA receptor modulators for therapeutic benefit
- Axonal growth inhibitors and their receptors in spinal cord injury: from biology to clinical translation
- Covalent Fragment Inhibits RhoA Activation by Guanine Exchange Factors

Systematic reviews

A comprehensive search was conducted in Ovid MEDLINE, Embase, Scopus, and Web of Science Core Collection utilizing a combination of keywords. All in-vivo animal studies of acute or chronic spinal cord injury that evaluated the pharmacological effects of Rho/ROCK inhibitors in English literature were included in this study.

A total, of 2320 articles were identified, of which, 60 papers were included for further analysis. A total of 47 (78%) studies were conducted merely on rats, 9 (15%) on mice, 3 (5%) used both, and the remaining used other animals. Y-27632, Fasudil, C3 Transferase and its derivatives (C3-05/PEP-C3/CT04/C3bot154-182/C3bot26mer(156-181)), Ibuprofen, Electroacupuncture (EA), SiRhoA, miR-133b, miR-135-5p, miR-381, miR-30b, Statins, 17β-estradiol, β-elemene, Lentivirus-mediated PGC-1a, Repulsive guidance molecule (RGMa), Local profound hypothermia, Jisuikang (JSK), Hyperbaric oxygen (HBO), Lv-shRhoA (Notch-1 inhibitor), Anti-Ryk antibody, LINGO-antagonist, BA-210, p21Cip1/WAF1, ORL-1 antagonist, Epigallocatechin-3-gallate (EGCG), Tamsulosin, AAV.ULK1.DN, and Indomethacin were the 28 reported agents/procedures with anti-RhoA/ROCK effects. The pooled SMD for BBB scores was 0.41 ($p = 0.048$) in the first week, 0.85 ($p < 0.001$) in the second week, 1.22 ($p = 0.010$) in the third week, and 1.53 ($p = 0.001$) in the fourth week.

Of the 28 identified anti-RhoA/ROCK agents, all but two (C3bot and its derivatives and EGCG) demonstrated promising results. The results of the meta-analysis cautiously indicate a significant increase in BBB scores over time after SCI [1)].

Khavandegar et al. (2025) provide a valuable systematic review of RhoA/ROCK inhibitors in Spinal cord injury outcomes, highlighting the potential of various agents in enhancing locomotor function. The study benefits from a comprehensive search strategy and a meta-analysis of functional outcomes. However, limitations such as heterogeneity in included studies, absence of quality assessment, and potential publication bias should be addressed in future research. Moving forward,

standardized methodologies and rigorous risk-of-bias evaluations will be essential to strengthen the clinical relevance of these findings.

1)

Khavandegar A, Ahmadi NS, Mousavi MA, Ramezani Z, Khodadoust E, Hasan Zadeh Tabatabaei MS, Hasanpour Segherlou Z, Zeinaddini-Meymand A, Nasehi F, Moafi M, RayatSanati K, Masoomi R, Hamidi S, Pourkhodadad S, Rahimi-Movaghar V. The potential role of RhoA/ROCK-inhibition on locomotor recovery after spinal cord injury: a systematic review of in-vivo studies. Spinal Cord. 2025 Feb 16. doi: 10.1038/s41393-025-01064-2. Epub ahead of print. PMID: 39956860.