

84. Armstrong, R.A., et al., *Br. J. Pharmacol.*, **79**, 953-964 (1983).
85. Katsura, M., et al., *Adv. Prost. Thromb. Leukot. Res.*, **11**, 327-332 (1983).
86. Jones, R.L., et al., *Br. J. Pharmacol.*, **96**, 875-887 (1989).
87. Morinelli, T.A., et al., *J. Pharmacol. Exp. Ther.*, **251**, 557-562 (1989).
88. Armstrong, R.A., et al., *Br. J. Pharmacol.*, **84**, 595-607 (1985).
89. Narisada, M. et al., *J. Med. Chem.*, **31**, 1847-1854 (1988).
90. Lumley, P., et al., *Br. J. Pharmacol.*, **97**, 783-794 (1989).
91. Ogletree, M.L., et al., *J. Pharmacol. Exp. Ther.*, **234**, 435-441 (1985).
92. Hall, S.E., *Med. Res. Rev.*, **11**, 503-579 (1991).
93. Ogletree, M.L., et al., *J. Pharmacol. Exp. Ther.*, **264**, 570-578 (1993).
94. Armstrong, R.A., et al., *Br. J. Pharmacol.*, **110**, 548-552 (1993).
95. Wilson, T.W., Quest, D.W., *Cardiovasc. Drug Rev.*, **18**, 222-231 (2000).
96. Sugimoto, Y., et al., *Prog. Lipid. Res.*, **39**, 289-314 (2000).
97. Nitta, M., et al., *Scand. J. Immunol.*, **56**, 66-75 (1995).
98. Yoshida, K., et al., *Proc. Natl. Acad. Sci. USA*, **99**, 4580-4585 (2002).
99. Hong, M. et al., *Circulation*, **104**, 1176-1180 (2001).
100. Nantel, F. et al., "Altered bronchodilation and pulmonary inflammation in prostanoid EP2 receptor knockout mice". In: *Advances in Prostaglandin and Leukotriene Research* (Eds. Samuelsson, B. et al.) pp 99-101; Kluwer Academic, The Netherlands (2001).

Monoclonal Anti- γ Parvin: Focal adhesion protein

Prod. No. **P 5746**

Clone γ parvin 40, developed in mouse
Purified mouse immunoglobulin in phosphate-buffered saline
Immunogen: peptide corresponding to the C-terminal region of human γ parvin (amino acids 314-328)
Isotype: mouse IgG1
Species Reactivity: The antibody recognizes human, monkey and bovine γ parvin; it does not react with mouse or rat γ parvin

Cell adhesion to the extracellular matrix (ECM) is an important process that controls cell morphology, proliferation, migration, differentiation and survival. The engagement of integrin molecules on the cell surface during cell adhesion to the ECM is accompanied by recruitment of multiple cytoskeletal and signaling proteins to focal adhesion sites [1-4]. These proteins link the cytoskeleton to the ECM and mediate signal transduction between the ECM and the intra-cellular compartment.

The parvin protein family belongs to the focal adhesion proteins which comprises three members referred to as α , β , and γ parvin [5]. α Parvin is ubiquitously expressed, β parvin is expressed in heart and skeletal muscle, and γ parvin is expressed in lymphoid tissues. Development studies have shown that α parvin is expressed throughout mouse development, while β parvin is gradually up-regulated and γ parvin is down-regulated at day 11. In cancer cells, the levels of the three parvins are down-regulated compared to normal tissues [5].

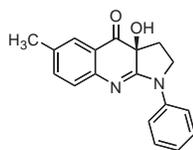
Immunoblot using a total extract from 293T cells detected a band at 42 kDa. Monoclonal antibodies specific for γ parvin are an important tool for studying the biology of focal adhesion proteins.

References

1. Turner, C.E. and Burridge, K., Transmembrane molecular assemblies in cell-extracellular matrix interactions., *Curr. Opin. Cell Biol.*, **3**, 849-853 (1991).
2. Turner, C.E., Paxillin and focal adhesion signaling., *Nature Cell Biol.*, **2**, E231-E236 (2000).
3. Turner, C.E., Paxillin interactions., *J. Cell Sci.*, **113**, 4139-4140 (2000).
4. Giancotti, F.G. and Rouslahti, E., Integrin signaling., *Science*, **285**, 1028-1032 (1999).
5. Korenbaum, E., et al., Genomic organization and expression profile of the parvin family of focal adhesion proteins in mice and humans., *Gene*, **279**, 69-79 (2001).

S(-)-Blebbistatin: Selective inhibitor of non-muscle myosin II

Prod. No. **B 0560**



Cytokinesis is the final stage of mitosis when the two daughter cells separate. Much of the basic research identifying the components in the cytokinesis pathway has been performed on fission yeast and slime mold. However, less detail is known about the process in mammalian cells. For cytokinesis to occur, the cytoskeleton and membrane system of the cell must undergo a complex and rapid series of coordinated changes. A key structure, the contractile ring/cleavage furrow, consists of a complex of an actin-binding protein (anillin), septins, actins, myosin II and tyrosine phosphorylated proteins. It has been established that the non-muscle myosin II motor provides the force for furrow ingression and a second pathway positions anillin required for cell separation.

Blebbistatin, a selective inhibitor of non-muscle myosin II, was identified via a small molecule screen performed on HeLa cells [1-3]. It is cell-permeable and was found to arrest furrow ingression without blocking furrow assembly. Inhibition of myosin II by blebbistatin (IC₅₀ 2 μ M) is fast-acting and reversible and leads to the formation of binucleate HeLa cells in culture.

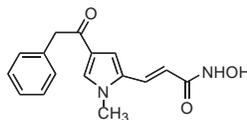
The selective, potent, fast and reversible action of blebbistatin makes it an important new tool for researchers investigating the temporal and spatial organization of the cellular machinery underlying cytokinesis.

References

1. Straight, A.F. et al., Dissecting temporal and spatial control of cytokinesis with a myosin II inhibitor. *Science*, **299**, 1743-1747 (2003).
2. Straight, A.F. et al., www.sciencemag.org/cgi/content/full/299/5613/1743/DC1
3. Duxbury MS, et al., Inhibition of pancreatic adenocarcinoma cellular invasiveness by blebbistatin: a novel myosin II inhibitor., *Biochem. Biophys. Res. Commun.* **313**, 992-997 (2004).

APHA Compound 8: Novel histone deacetylase inhibitor

Prod. No. **A 2478**



Mammalian histone deacetylase (HDAC) belongs to a large family of enzymes that work in opposition to the activities of histone acetyltransferases (HATs) thereby determining the acetylation state of histone/non-histone nucleosomal proteins and controlling chromatin structure, transcriptional activities and gene expression [1]. Hyperacetylation disrupts charge interaction between histones and the phosphate backbone of DNA leading to an open chromatin structure that is accessible to transcription factors, RNA polymerase and other regulatory complexes thereby leading to transcription activation.

APHA Compound 8 is a novel HDAC inhibitor belonging to the same structural class as SAHA (suberoylanilide hydroxamic acid), a compound currently in clinical trials. In a mouse assay for HDAC 1 using [³H]acetate-prelabeled chicken reticulocyte histones, APHA Compound 8 displayed an IC₅₀ value of 0.5 μ M [3]. In a separate study, significant inhibition was observed in the proliferation of MEL cells at 24 μ M and differentiation, assayed as the accumulation of hemoglobin, was observed at 5 μ M [4].

APHA Compound 8 represents a valuable tool for studying the role of histone acetylation in controlling gene transcription.

References

1. Thiagalingam, S, et al., Histone deacetylases: unique players in shaping the epigenetic histone code., *Ann N.Y. Acad. Sci.*, **983**, 84-100 (2003).
2. Marks, P, et al., Histone deacetylases and cancer: causes and therapies., *Nat. Rev. Cancer*, **1**, 194-202 (2001).
3. Mai, A., et al., 3-(4-Aroyl-1-methyl-1H-2-pyrrolyl)-N-hydroxy-2-alkylamides as a New Class of Synthetic Histone Deacetylase Inhibitors. 1. Design, Synthesis, Biological Evaluation, and Binding Mode Studies Performed through Three Different Docking Procedures., *J. Med. Chem.*, **46**, 512-524 (2003).
4. Mai, A, et al., 3-(4-Aroyl-1-methyl-1H-2-pyrrolyl)-N-hydroxy-2-propenamides as a new class of synthetic histone deacetylase inhibitors. 2. Effect of pyrrole-C2 and/or -C4 substitutions on biological activity., *J. Med. Chem.*, **47**, 1098-1109 (2004).