Novel Specific Inhibitor of Cdc42 GTPase for Cell Biology and Human Disease

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Technology description

Researchers at the University of New Mexico have discovered a compound that is novel in that it is directly binding to the enzyme and prevents nucleotide binding.
Usually aberrant regulation or expression of Rho GTPases is linked to tumorigenesis or other disorders. For this reason the novel specific inhibitor of Cdc42 GTPase, capable of regulation of Rho GTPases activity, is extraordinarily useful, particularly since it is specific and acts reversibly. The identified novel small molecule specifically inhibits GTP binding to Cdc42. There are limited pharmacological tools targeting individual small GTPases, and most efforts have been focused on inhibiting post-translational GTPase modification by lipids, which is necessary for their membrane localization and activation.

Background

During the past few years, Rho GTPases and their effector proteins have been recognized as major regulators of a wide range of signaling pathways that control various biological processes. Among different mammalian Rho GTPases, the most extensively characterized members are RhoA, Rac1, and Cdc42. Reorganization of the actin cytoskeleton is the most characterized function for Rho GTPases. Mammalian Rac1, Cdc42 and RhoA are implicated in lamellipodia, filopodia and stress fibers formation, respectively. Besides this, there is growing evidence that Rho-family GTPases are regulating cell-cycle progression, gene transcription, and have been implicated in cellular processes such as adhesion, migration, phagocytosis, cytokinesis, neurite extension and retraction, cellular morphogenesis and polarization, growth and cell survival. Despite the fact that Cdc42 specific inhibitors would be very useful and interesting for pharmacological use, up to date there is very little success in development of such drugs.

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Publications

Distillery: Therapeutics - Various. Cell division cycle 42 (CDC42). SciBX 6(9); doi :10.1038/scibx.2013.225

About STC.UNM

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STC has filed intellectual property on this exciting new technology and is currently exploring commercialization options. If you are interested in information about this or other technologies, please contact Arlene Mirabal at amirabal@stc.unm.edu or 505-272-7886.

Application area

Inhibitor of Cdc42 GTPase is specific and acts reversibly
Prevents nucleotide binding
Inhibitor works in RhoGDI-dependent manner
Specific inhibitor of CDC42 GTPase works by regulatory proteins-independently and for this reason might be more effective
May be used to inhibit rejection (graft host response) in transplant patients (pursuant to transplantation), to promote immunosuppression, anti-inflammatory response and to mobilize stem cell (migration) in patients in need

Treats diseases including cancers, metastatic cancers especially B-cell lymphoma, stomach cancer including gastric adenocarcinoma, leukemias including myeloid and B-call leukemias, breast, cervical, testicular, and prostate cancer
Other applications where Cdc42 GTPase is overexpressed or hyperactivated include to treat neurodegenerative diseases including Alzheimer’s disease, Huntington’s disease, Parkinson’s disease, amyotrophic lateral sclerosis, rheumatoid arthritis, atherosclerosis, diabetes type I, autosomal polycystitis kidney disease, cystic kidney disease, precystic kidney disease, microbial infections, including Chlamydia infections, E. coli infections, H. pylori infections and its secondary effects including gastric ulcers, Coxiella Brunetti (Q-fever) infections and Streptococcus pneumonia infections, fungal infections including Paracoccidiodes brasiliensis and Candida albicans and their secondary effects including lung edema

Institution

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