A Novel Anti-Cancer/Anti-Proliferation and Anti-Migration Compound—An Inhibitor to Dual Specificity Phosphatase Slingshot-2

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BACKGROUND

Cell growth and movement are controlled in part through the activation of a dual specificity phosphatase (DSP) called Slingshot-2 (SSH-2). SSH-2 is known to contribute to the progression of cancer and Alzheimer's disease. Therefore, finding a specific inhibitor for SSH-2 may have a profound impact in clinical treatments of these diseases.

TECHNOLOGY DESCRIPTION

Scientists at UC San Diego have found a family of small molecule inhibitors that specifically binds to SSH-2. These compounds represent the first inhibitors of a phosphatase that regulates the F-actin depolymerization.

The inventors used a molecular docking simulation software (DOCK 6.0) to virtually screen open-source chemical databases and determined the binding affinities to 18 of DSPs with known three-dimensional structures as determined by x-ray crystallography, including SSH-2, VHR (DUSP3), VHY (DUSP15), VHZ (DUSP23), VH1 (DUSP12), VH3 (DUSP5), PTEN (phosphatase and tensin homolog), KAP (Cdk2 associated protein phosphatase), MKP3 (rVH6, Pyst1), MKP4, MKP5, MTMR2, DUSP18, PRL3, CDC14b, Pac-1, Jsp-1, and TMPD. Five compounds with similar chemical structures have the highest affinity for SSH-2, but lowest affinity for the other DSPs, among the best 100 SSH-2 binding compounds.

Figure 1. Diagram illustrating the role of phosphorylation and SSH-2 in actin filament assembly.

ADVANTAGES

Highly specific SSH-2 inhibitor that regulates F-actin depolymerization.

APPLICATIONS

New therapeutics, targeting actin filament dynamics and signaling pathways, for the treatment of cancer, Alzheimer's, and other diseases.

STATE OF DEVELOPMENT

Virtual screening yielded a compound with high binding affinity to SSH-2 and very low binding affinity to other DSPs.

RELATED MATERIALS

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OTHER INFORMATION

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Disease: Central Nervous System
  - New Chemical Entities, Drug Leads

RELATED CASES

2010-247-0

▶ Mui MK , Levesque MJ, Chien S, and Haga JH. In-Silico Identification of High Potential SSH-2 Specific Inhibitors. The FASAB J. (1_MeetingAbstracts) Apr 2010; 24 No. 1060.3.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,487,522	11/08/2016	2010-247

Additional Patent Pending

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