Docket #: S10-155

Small-molecule inhibitors of dynein motor proteins

Stanford and Rockefeller researchers have identified and developed dynein-specific inhibitors that have significant medical applications involving mitotic spindle assembly, organelle transport, and primary cilia formation. The quinazolinones and structural analogs may be utilized as selective anti-mitotic cancer therapies, as they concurrently target cytoplasmic dynein-dependent primary cilia function, which would lead to the blockade of cilia-regulated processes such as oncogenic Hedgehog pathway activation. Though not confirmed of their effectiveness on axonemal dyneins, inhibitors of this dynein subfamily could in principle block movement of motile cilia and flagella, which could have significant implications for sperm immobilization, and the pharmacological modeling of human ciliopathies such as polycystic kidney disease, Baret-Biedl syndrome, Meckel-Gruber syndrome, and retinal degeneration.

Applications

- Cancer therapies involving anti-mitotic and/or anti-Hedgehog pathway activity
- Blockage of cilia and flagellar function
- Immobilization of sperm
- Pharmacological modeling of human ciliopathies

Advantages

- Cell permeable
- Dynein-specific
- Readily modifiable pharmacophore
- Improved potency and specificity with analog synthesis with respect to isoforms or cytoplasmic vs axonemal dynein

Publications

- A.J. Firestone, J.S. Weinger, M. Maldonado, K. Barlan, L.D. Langston, M. O'Donnell, V.I. Gelfand, T.M. Kapoor and J.K. Chen, Small-molecule inhibitors of the AAA+ ATPase motor cytoplasmic dynein, Nature, published online March 18, 2012.

Patents

- Published Application: WO2012099916
- Published Application: 20130296349
- Issued: 9,145,376 (USA)

Innovators

- James Chen
- Ari Firestone
- Tarun Kapoor
- Joshua Weinger

Licensing Contact

Kimberly Griffin

Technology Licensing and Strategic Alliances Manager

Email