Docket #: S13-187

Personalized Cancer Treatment with Topoisomerase Inhibitors

Researchers in Prof. Gerald Crabtree's laboratory have developed a method for identifying cancer patients that are likely to benefit from treatment with topoisomerase IIa (TOP2A) inhibitors. This approach is based on the finding that BAF (BRG1- or HRBM-associated factor) complexes are required for proper function of TOP2A. In addition, this activity contributes to the role of BAF subunits as tumor suppressors. Therefore, testing tumor samples for BAF subunit activity could help determine which patients are likely to respond to specific topoisomerase inhibitor therapy. This could help physicians determine the best treatment option for their patients.

Stage of Research
The inventors have characterized the role of BAF in topoisomerase function. In related bioinformatics studies, they have identified BAF subunit mutations in approximately 20% of all human cancer (Kadoch, C., Hargreaves, D. C., Hodges, C., Elias, L., Ho, L., Ranish, J., & Crabtree, G. R. (2013). Proteomic and bioinformatic analysis of mammalian SWI/SNF complexes identifies extensive roles in human malignancy. *Nature Genetics* 45(6), 592-601. doi:10.1038/ng.2628.)

Applications

- **Personalized medicine** - identify and treat patients with tumors that are likely to respond to TOP2A inhibitors and avoid topoisomerase inhibitors that may not be effective

Publications

- E.C. Dykhuizen, D.C. Hargreaves, E.L. Miller, K. Cui, A. Korshunov, M. Kool, S. Pfister, Y-J. Cho, K. Zhao and G.R. Crabtree. "BAF complexes facilitate decatenation of DNA by topoisomerase IIα" *Nature*, May 30, 2013.

Patents

- Published Application: 20150185221
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