Medical Xpress

Team reaches milestone in development of Kinase Chemogenomic Set

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The Structural Genomics Consortium at the University of North Carolina at Chapel Hill (SGC-UNC), in partnership with the DiscoverX Corporation, has reached the milestone halfway point in its development of the Kinase Chemogenomic Set, a potent group of inhibitors which allow deeper exploration of the human kinome, a family of enzymes critical to understanding human disease and developing new therapies.

By building this selective set of compounds and making it freely available, UNC-Chapel Hill and its partners are offering the scientific community a better understanding of the roles the kinome plays in human disease and the ability to collaborate on the discovery and advancement of new therapies.

The kinome, made up of enzymes called kinases, provides a tremendous opportunity for drug discovery. While more than 30 kinase inhibitors have been approved for the treatment of disease, the kinome has been largely unexplored until SGC-UNC, DiscoverX and other SGC partner companies embarked on this project.

"Through our collaboration with DiscoverX, we screened a large set of compounds that we call Published Kinase Inhibitor Set 2, and these results allowed us to reach the halfway point in constructing the KCGS" said David Drewry, a research associate professor at the UNC Eshelman School of Pharmacy and SGC-UNC principal investigator who is leading the project to develop the Kinase Chemogenomic Set. "To mark this milestone and in keeping with our mission of open science, we are

releasing these results into the public domain. We sincerely thank all of our co-author partners whose vision, generosity and hard work makes the construction of this set possible."

A publication describing the team's strategy and progress toward achieving a comprehensive KCGS is available online in the journal *PLOS ONE*. The manuscript also contains the results of screening each compound in PKIS2 against the DiscoverX panel of more than 400 kinase assays.

PKIS2 is a collection of more than 500 kinase inhibitors donated by GSK, Pfizer and Takeda Pharmaceuticals that SGC-UNC makes available to the scientific community. The kinome wide annotation of inhibition profiles allows users of the set to interpret their results more readily.

"We have shown how well each of the PKIS2 compounds inhibits each of the kinases DiscoverX screens," said Drewry. "Researchers to whom we have given access to PKIS2 can use that information. They will know that compound X inhibits kinases A, B and C, but compound Z inhibits kinases D and E. With such a big data set people can easily find compounds of particular interest to them and know that the compounds are annotated with near full-kinome inhibition data."

This collaborative project between industrial and academic scientists will continue to expand the KCGS with the goal of fully covering all human protein kinases. Drewry and his fellow scientists aim to ensure the therapeutic potential of as many protein kinases as possible will be uncovered. The expansion of the KCGS, combined with its use in diverse disease-relevant phenotypic screens and the sharing of the resulting data in the public domain, is the best mechanism for reaching this goal.