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U.S. Kavli Frontiers of Science Symposium Series

Twenty-first Annual Kavli Frontiers of Science Symposium

National Academy of Sciences
November 12-14, 2009 - Irvine, California, USA

Community-Based Adaptation: From Revamping Drug Discovery Using Insights from Natural Product Molecules [-Presentation !\[\]\(3342c215b2a8b663596a81468d5dc314_img.jpg\)](#)
Derek S. Tan, Memorial Sloan-Kettering Cancer Center

Please click on the above link to watch the presentation - both slides and audio. This presentation file is in [Adobe Flash player](#) format, available free online.

The vast majority of pharmaceuticals are small molecules (non-oligomeric, low molecular weight, organic molecules) that bind to protein targets and alter their functions. Despite genomic sequencing efforts that have uncovered myriad new proteins, and an ever improving understanding of the molecular basis for disease, there is a current crisis in drug discovery, with fewer novel drugs being approved each year. This is particularly troubling in the antibacterial arena, where most major pharmaceutical companies have abandoned their efforts, making antibacterial drug resistance a growing threat to public health. One issue at the heart of this problem is an inability to identify small molecules that can address new potential therapeutic targets. Historically, drug discovery has focused on a very narrow range of biological targets, and a correspondingly narrow range of small molecules that can bind to those well-heeled targets. As a result, existing libraries (collections) of small molecules used in drug discovery are often ill-suited for interacting with new targets. To address this problem, we are engaged in a two-pronged approach to the discovery of small molecules that can be used to investigate fundamental questions in biology and to evaluate new potential therapeutic targets, involving both rational drug design and the synthesis of novel small molecule libraries for use drug discovery. In both cases, our approaches are influenced by insights from natural products, small molecules that are produced biosynthetically and are inherently compatible with binding to proteins. We leverage multidisciplinary collaborations with biologists to evaluate the molecules we synthesize with the long-term goals of probing key biological processes and exploring new therapeutic opportunities in cancer and infectious diseases.

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Introductory Review

Dobson, C. M. "Chemical space and biology." *Nature* 2004, 432, 824–828.

Technical Reviews

Payne, D. J.; Gwynn, M. N.; Holmes, D. J.; Pompliano, D. L. "Drugs for bad bugs: Confronting the challenges of antibacterial discovery." *Nat. Rev. Drug Discov.* 2007, 6, 29–40.

Cisar, J. S.; Tan, D. S. "Small molecule inhibition of microbial natural product biosynthesis – An emerging antibiotic strategy." *Chem. Soc. Rev.* 2008, 37, 1320–1329.

Tan, D. S. "Diversity-oriented synthesis: Exploring the intersections between chemistry and biology." *Nature Chem. Biol.* 2005, 1, 74–84.

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