

## *Natural Product Drug Discovery at the National Cancer Institute: New Approaches, New Targets, New Compounds*

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Natural products have a proven track record in use as anti-cancer and anti-infective agents. As of 2020 natural products and their derivatives represented >50% of small molecule-based anti-cancer and anti-microbial drugs. However, accessing the potential of natural products in high-throughput screening (HTS) campaigns has been challenging due to the complexity of the crude NP extracts and the time necessary for follow-up isolation efforts. This has resulted in NP-based libraries being significantly underrepresented in most recent large-scale HTS programs.

The US National Cancer Institute's Natural Product Extract Repository is one of the world's largest, most diverse collections of natural products containing ~ 230,000 unique extracts derived from plant, marine and microbial organisms. To address the challenges in screening NPs and encourage increased assay of NP chemical diversity, the NCI initiated the NCI Program for Natural Product Discovery (NPNPD) which has developed automated, high-throughput natural products chemistry platforms capable of generating a library of >1,000,000 partially purified extracts for screening. In addition, automated secondary purification and structure elucidation platforms have been created that significantly decrease costs and timelines. This presentation will discuss the progress of this new initiative, describe the use of natural products in targeted screens, and highlight recently identified novel natural products derived from these efforts.

