English

Combinatorial Library

Methods and Protocols



The continued successes of large- and small-scale genome sequencing projects are increasing the number of genomic targets available for drug d- covery at an exponential rate. In addition, a better understanding of molecular mechanisms—such as apoptosis, signal transduction, telomere control of ch- mosomes, cytoskeletal development, modulation of stress-related proteins, and cell surface display of antigens by the major histocompatibility complex m- ecules—has improved the probability of identifying the most promising genomic targets to counteract disease. As a result, developing and optimizing lead candidates for these targets and rapidly moving them into clinical trials is now a critical juncture in pharmaceutical research. Recent advances in com- natorial library synthesis, purification, and analysis techniques are not only increasing the numbers of compounds that can be tested against each specific genomic target, but are also speeding and improving the overall processes of lead discovery and optimization. There are two main approaches to combinatorial library production: p- allel chemical synthesis and split-and-mix chemical synthesis. These approaches can utilize solid- or solution-based synthetic methods, alone or in combination, although the majority of combinatorial library synthesis is still done on solid support. In a parallel synthesis, all the products are assembled separately in their own reaction vessels or microtiter plates. The array of rows and columns enables researchers to organize the building blocks to be c- bined, and provides an easy way to identify compounds in a particular well.

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