Throughput Screening Encyclopedia Article

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Throughput Screening

Throughput screening is the process whereby many compounds can be tested for their target activity in a single experiment. The experiments, also called assays, are automated both with respect to the performance of the assay and detection of activity. Such automated assays are also referred to as high throughput screening.

The technique of throughput screening has proved a particularly powerful tool in pharmaceutical research. Many compounds can be screened for activity in a short time. Promising candidates can then be analyzed with more vigor to assess their therapeutic and commercial potential.

Throughput screening was first done using animals. However, the expense of this procedure resulted in the development of a test tube-type of assay system. Now, in a typical assay each compound to be tested is put into a well in a plastic plate containing 96 wells. The assay reagent, a solution containing the molecules needed to stimulate a reaction for the test compounds, is added to each well. After a set time, each well is monitored for the target reaction. Inhibition or activation are two typical reactions. High throughput screening thus functions to rapidly weed out potentially useful compounds or cells--tens of thousands can be analyzed each day--from those that are not useful for the particular purpose.

The advent of laboratory automation and robotic technology in the mid-1990s made throughput screening possible. In a further **evolution**, the assay mixture now can incorporate cells that contain genetically modified genes. The well plates used in this technique contain over 1500 wells. The characteristic positive reaction, such as fluorescence, is easier to detect and requires a smaller volume of test substance. This advance, designated ultra-high throughput screening, permits up to 200,000 substances a day to be screened.

Typically, out of a million compounds tested by throughput screening, three to five candidates emerge. One in twenty candidates end up being developed into a new drug. Without the speed and economy of afforded by throughput screening, drug development would be extremely slow and extraordinarily expensive. In the human **genome**, estimates are that approximately three to then thousand genes may be potential targets of drug therapy. There are around 10^{63} chemical molecules that can potentially be used against these target genes. Without throughput screening, identification of therapeutic molecules would be virtually impossible.