

Combinatorial Synthesis: An Introduction

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Combinatorial synthesis is a relatively recent innovation in medicinal and pharmaceutical chemistry. Essentially, it is an automated process by which large numbers of newer structure are synthesized on a small scale. There are two main approaches: Mix and Split method is also highly useful in the synthesis of mixture by combinatorial method. In this case each vial will contain different structures; structures will be physically distinct since each bead will only have a single product attached. Thus combinatorial libraries consist of structures that have been generated by combinatorial synthesis. Parallel combinatorial synthesis involves carrying out the same reaction sequence on series of reactions vials but using different reactant and reagent for each vial. This allows rapid synthesis of large number of analogs based on common skeleton. It is useful in providing a series of compounds for studies into SAR. It is also useful in fine-tuning or optimizing a lead compound in order to find a structure with improved activity or reduced side effects. Combinatorial synthesis is also used to deliberately synthesize a mixture of compounds in each vial. In this situation, the structure attached to each individual bead will be identical, but different beads in the same vial will contain different structures. This form of combinatorial synthesis is useful in drug discovery where one is searching for a lead compound. Such libraries provide a source of structures which can be tested for different activities and have the potential of providing useful lead compounds for future research programs [1-7].

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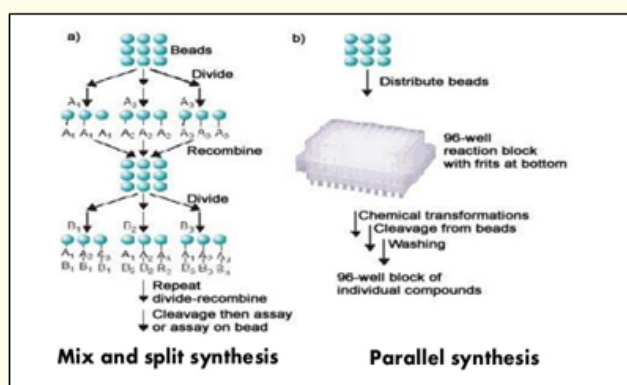


Figure 1: Alzheimer's disease culture cells. These cells have been genetically engineered to produce amyloid precursor protein (APP). (Figure is adapted from Simon Fraser).

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