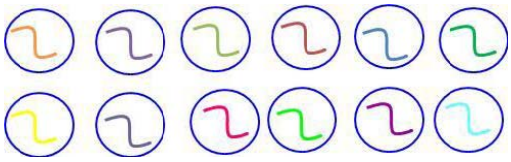
Peptide Library Synthesis

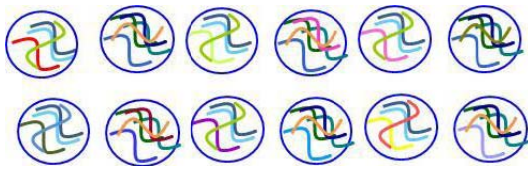
CHINESE PEPTIDE
The Peptide Quality Standard

Peptide library: A group of large number of peptides typically ranging from tens to several millions or more with a systematic arrangement of amino acids in their sequence. *Combinatorial chemistry (CC) combined with high throughput screening (HTS) technique is an efficient method of synthesizing and screening large number of molecules rapidly.*

The simplest form a combinatorial peptide library is **parallel library** in which each peptide is synthesized in individual reaction chambers resulting in well characterized libraries. This method generates only a small set of peptides library though automation and microwave technology can be employed to increase productivity.

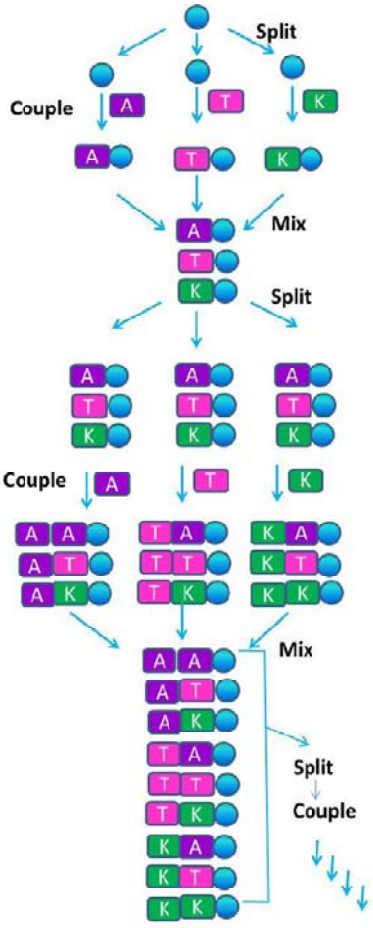


The second type of peptide libraries are **called random libraries** which generates a mixture (pool) of several thousand or millions of peptides in each reaction chamber thereby facilitating rapid screening of a large number of peptides.

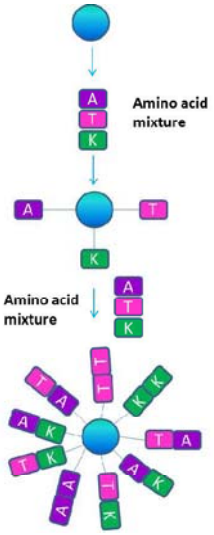


Synthesis of Random peptide libraries:

Split and Mix & Pre-mix methods



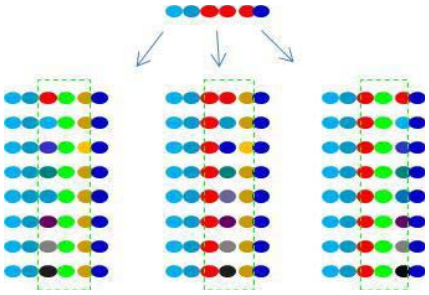
Two different methods are available for synthesizing random peptide libraries. The first technique is known as **Split and Mix method** which consists of three basic steps: splitting, coupling and mixing. Firstly, resin beads are split in a number of aliquots that equals the number of building blocks to be utilized in the synthesis (splitting). Then, to each resin aliquot one building block is coupled and the reactions are driven to completion (coupling). Following this step, beads are randomly and thoroughly mixed (mixing) and then re-splitted in the same number of aliquots, achieving a set of homogeneous and equimolar collections of compounds. Repetitive execution of these basic steps for "n" times will thus produce a rapid increase of newly generated molecules, while bead number remains constant. Resin beads encounter one reactant at a time, no more than one compound per bead can be generated (one-bead one-compound-OBOC-library). As reactions are driven to completion, all peptides are generated in equal ratios in the mixtures. After removing protecting groups, the peptides can be tested on the bead itself.



Pre-Mix Synthesis:

The synthesis of peptide mixture libraries using pre-mixed solutions of amino acids was introduced to overcome the limitations of OBOC approach to make larger libraries. Using this approach, the amino acids chosen for the library are pre-mixed and then coupled to a single resin batch. Before coupling the last amino acid, the resin is split in a number of aliquots that equals the number of building blocks and to each aliquot, one single amino acid is separately coupled. This procedure leads to the generation of sub-libraries that are labeled by the N-terminal residue. Every single bead contains all the ensemble of peptides of the sub-library, as any single bead encounters the reagents under the same conditions.

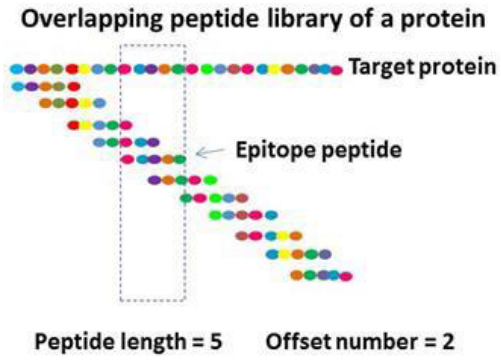
Positional Peptide Library:



A selected position in a peptide sequence is systematically replaced with different amino acid to show the effect on the substitute amino acid at certain position. This will determine the preferred amino acid residues at these positions, measured by corresponding increases in activity.

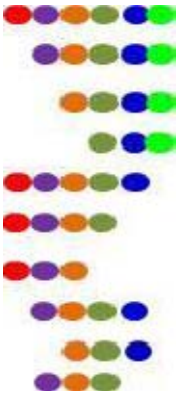
Overlapping Peptide Library:

A library of overlapping peptide sequences of specific length and specific offset, to cover the entire native protein sequence is designed in this strategy and is used for linear, continuous epitope mapping and T-cell epitope determination.



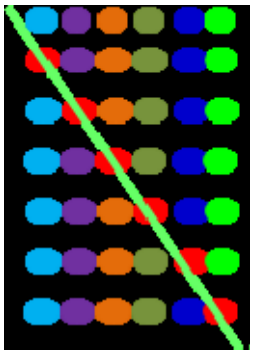
Truncation Peptide Library:

The truncation library is used to predict the minimum amino acid length required for optimum epitope activity. It is created by generating a set of peptides with systematic truncation of the flanking residues.



Alanine Peptide Scanning Library:

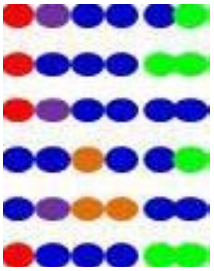
The generation of peptide library in which alanine (Ala, A) is systematically substituted into each of the amino in the identified epitope. This method is used to identify amino acids in the protein which are essential for activity.



: **Alanine**

Scrambled Peptide Library:

Scramble Library is constructed by carrying out permutation on the original peptide's sequence. It has the potential to give all possible alternatives and offers and represents the highest degree of variability for peptide library.



CPC has the capability to design and synthesize:

Peptide mixture combinatorial libraries comprising millions of peptides

Well characterized parallel peptide libraries in the desired formats