

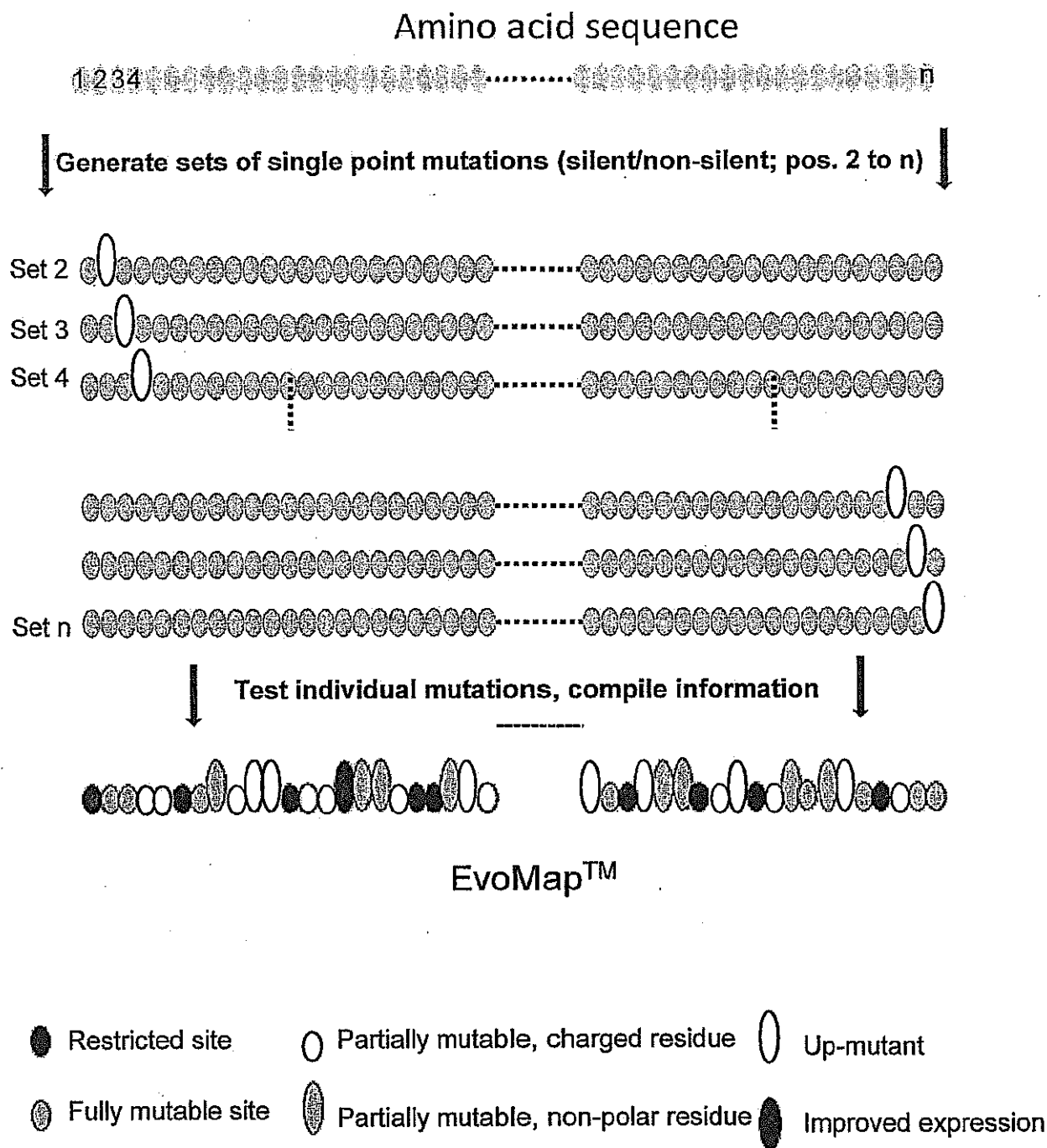
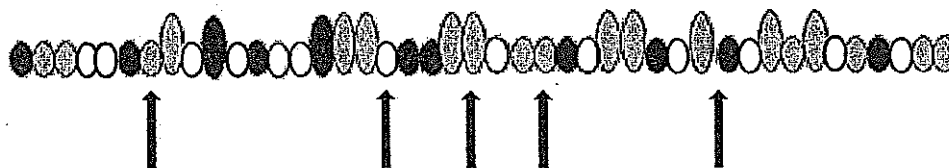


Figure 1: Comprehensive positional evolution (CPE) is used to generate a molecule specific database (EvoMap™).

Figure 1

EvoMap™



Select up to 20 residues in vicinity to restricted sites for simultaneous mutation, include only allowed changes according to EvoMap™ information

- Simultaneous mutations (5-20 a.a.) for combinatorial effects
- Does not require protein crystal structure
- Useful for proteins with high assay variation and other multi-site effects

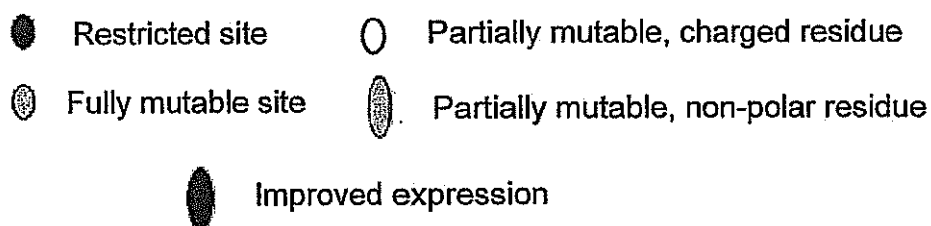


Figure 2: Synergy Evolution: Optimization of proteins with insensitive assays for in situations where multiple changes are needed

Figure 2

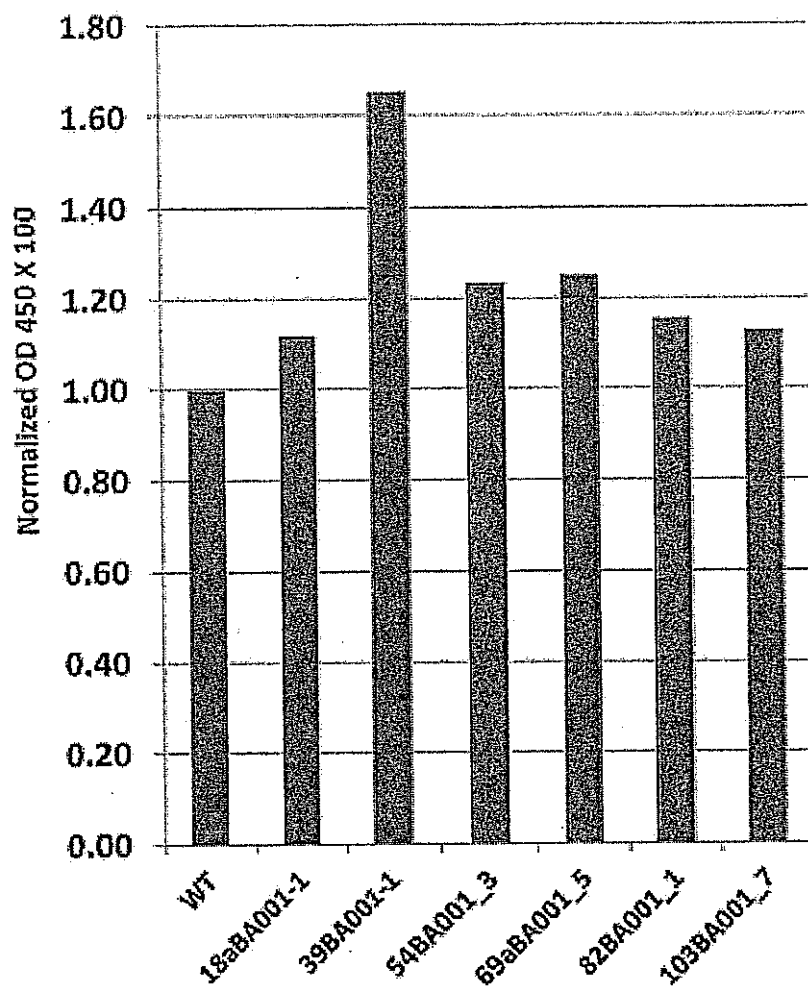


Figure 3

CPI™ - Comprehensive Positional Insertion Evolution
Inserts up to 20 individual amino acids at every
single amino position throughout the protein

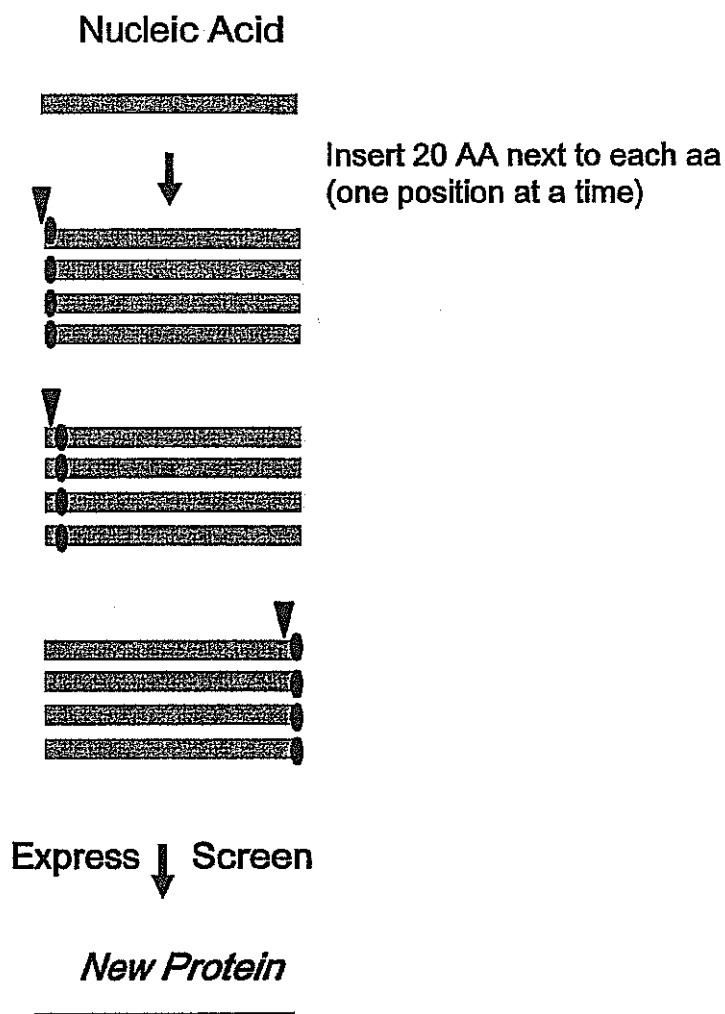


Figure 4

Comprehensive Positional Evolution (CPE™)

Lengthened Nucleic Acid from CPI

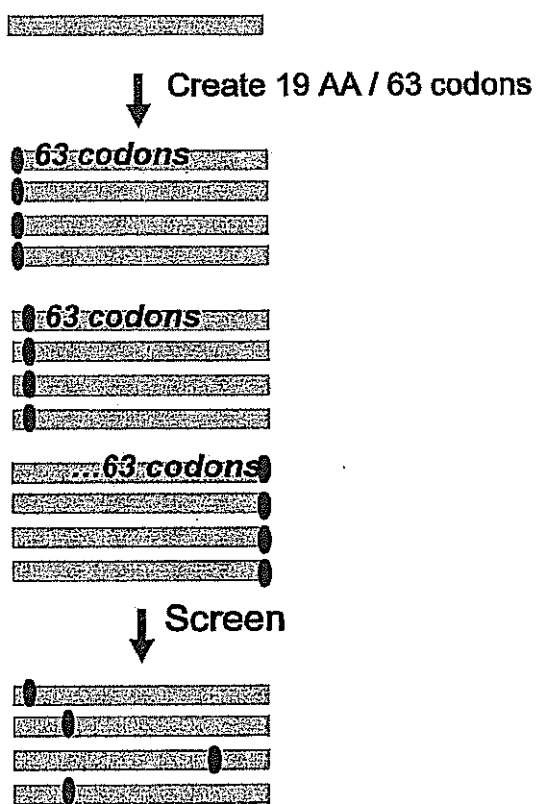


Figure 5

CPD™- Comprehensive Positional Deletion Evolution
Deletes every amino acid through a protein one position at a time

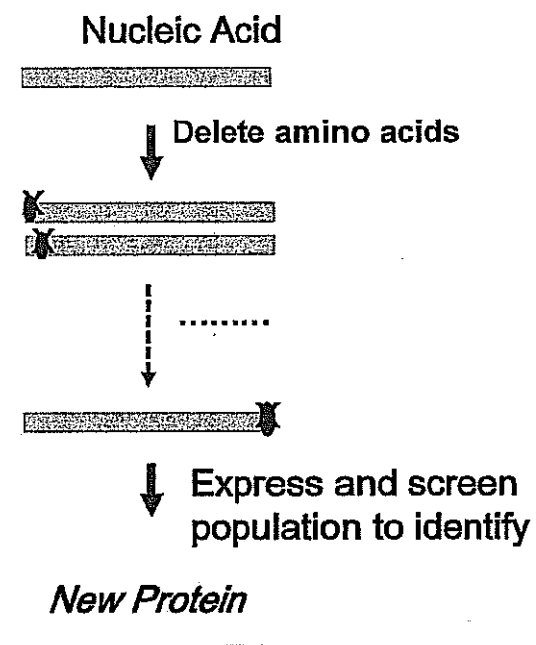


Figure 6

Comprehensive Positional Evolution (CPE™)

Shortened Nucleic Acid from CPD

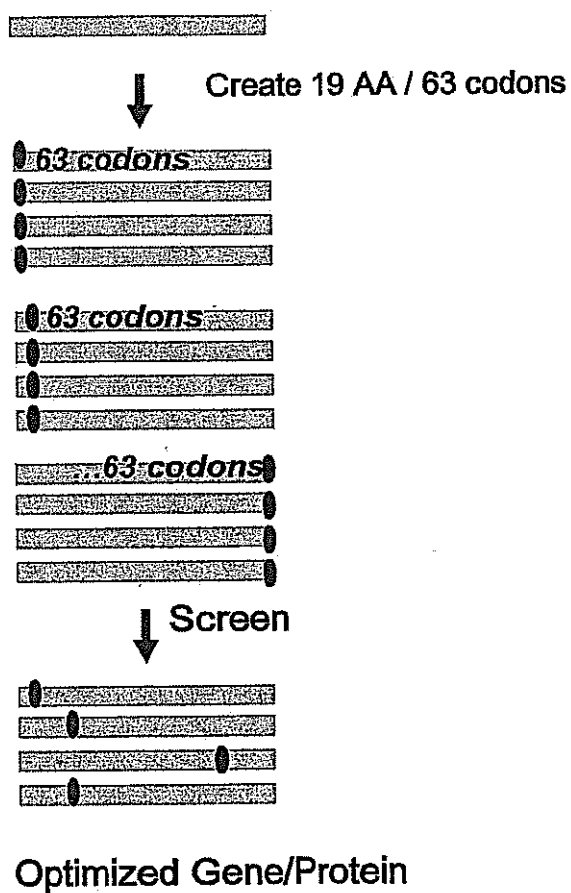


Figure 7

Combinatorial Protein Synthesis

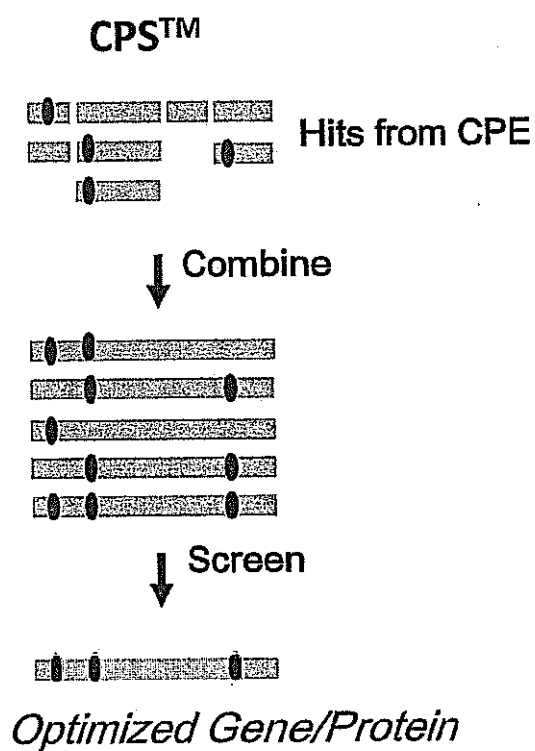
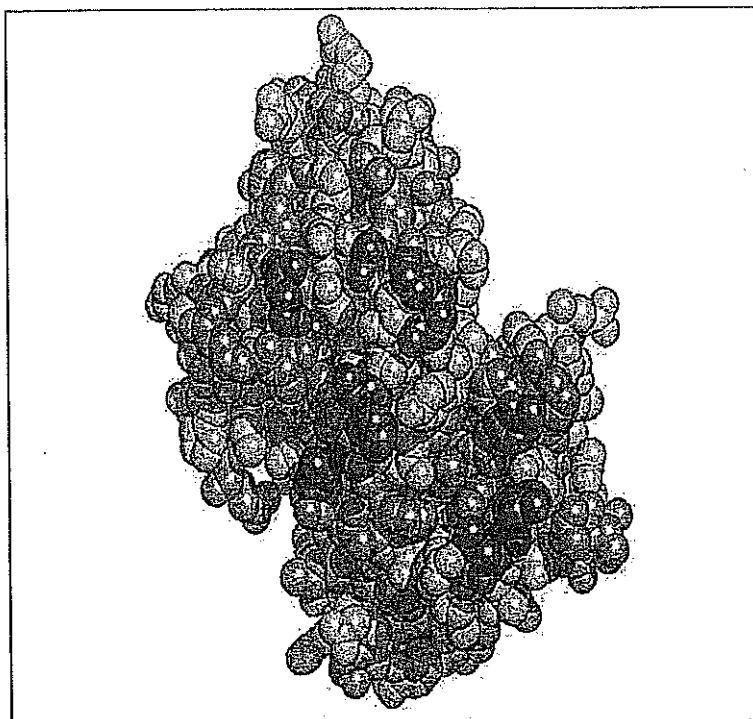


Figure 8



Comprehensive Positional Evolution Map
(Antibody LC/HC variable domains)

-  Up-mutants
-  Non-mutable sites
-  Partially mutable sites
-  Fully mutable sites

Figure 9