



Multisite Protein Evolution™ Services

Many proteins such as antibodies and large peptides depend both on the overall shape and on the physical properties (including rigidity, elasticity, adhesion, etc) for their structural or mechanical functions. Enzymes are additionally affected by the local geometry and chemistry of their catalytic site. Changing characteristics such as substrate specificity, K_n and K_{cat} , are only addressable through multiple simultaneous mutations and are not available through single site mutagenesis. BioAtla's Multisite Protein Evolution platforms are designed to deliver highly functional proteins that exhibit the desirable phenotypic traits and intellectual property for their commercial utilization.

Multisite Protein Evolution explores protein diversity by concurrently changing, recombining and assaying multiple amino acids to engineer highly complex molecules.

These studies are conducted with extreme precision and efficiency. Circumstances where these technologies may be useful are:

- 1) Tissue Targeting
- 2) Pharmacokinetics (PK)
- 3) Protein-protein aggregation
- 4) High assay variability
- 5) Other *in vivo* characteristics

BioAtla has developed two Multisite Protein Evolution platforms for next generation protein engineering:

Synergy Evolution™ OVERVIEW

- Testing all permutations of 2-20 distributed amino positions for complex combinatorial effects
- Does not require protein crystal structure
- Leverages comprehensive mapping approach (CPE) with combinatorial synthesis (CPS) capabilities
- Applications
 - Evolve complex molecular mechanistic changes
 - Evolve proteins with high assay variation
 - Evolve protein specificity
 - Apply to all protein therapeutic types (*e.g.* hormones, enzymes, cytokines, antibodies)

FlexEvolution™ OVERVIEW

- Leverages comprehensive mapping approach (CPE) with combinatorial synthesis (CPS) capabilities
- Prefers crystal structure of protein or related threaded protein structure
- Applications
 - Reduce protein-protein aggregation
 - Improve protein solubility
 - Optimize pharmacokinetic via glycosylation libraries (*in vivo*)
 - Deimmunize antigenic sites directly via mutation sets or indirectly through glycosylation masking
 - Apply to all protein therapeutic types (*e.g.* hormones, enzymes, antibodies)

BENEFITS

Evolve characteristics not possible with single site mutagenesis

Reduction of aggregation

Addresses high assay variation

