

# Pepscan Therapeutics

## Shaping Peptides to Perfection



### Peptides

Peptides play an important role in life. Their role as mediator of key biological functions and their unique properties make them particularly attractive as therapeutic agents and as immunogens for identifying monoclonal antibodies against complex drug targets.

Major stumbling blocks for the use of peptides in drug discovery & development have been their inherent metabolic instability and their imperfect resemblance of functional protein surfaces. Both issues are caused by their inability, unlike native proteins, to adopt a well-defined spatial 3D-structure.

Pepscan has developed a generic technology for the structural fixation of linear peptides, both applicable to free peptides in solution, as well as to peptides on microarrays used e.g. for antibody-screening. Its technology, termed CLIPS (Chemical Linkage of Peptides onto Scaffolds), is unprecedented and unique in terms of mildness and efficiency.

The CLIPS technologies has solved the inherent problem of peptides, making them widely applicable in drug discovery. We have demonstrated that CLIPS technology improves the bio-activity of peptides by orders of magnitudes. Moreover, we have used CLIPS immunogens to generate antibodies against notoriously difficult drug targets, like GPCRs.

### Therapeutic Peptides

Peptides are highly attractive drug candidates due to their potentially high biological activities associated with high specificities and low toxicities. However, "ordinary" linear peptides often have as a drawback their inherent low metabolic stabilities, short half-lives, or high costs of manufacturing (compared to small molecules).

PEPSCAN's CLIPS technology can greatly increase the performance of peptides by locking the compound into the right biologically active conformation. For several targets we have shown that introduction of CLIPS stabilizes the linear peptide and increases the activity up to 5000-fold. This leads to lower cost of treatment and makes the peptides less susceptible to proteolytic degradation. In summary, this greatly enhances the therapeutic potential of peptides.

The CLIPS™ technology allows peptides to be locked into any desired conformation like  $\alpha$ -helix, loops, double loops, triple loops and sheets. This allows PEPSCAN to identify a therapeutic peptide that meets the requirements of your drug target.

### Anti-GPCR Monoclonal antibodies

Therapeutic antibody therapy is well established. Monoclonal antibodies are produced outside the body and administered parenterally. A major stumbling block in advancing therapeutic antibody therapies is often the inability to generate potent antibodies, especially when the target antigen is complex in nature (GPCR's, ion-channels). Pepscan's unique and proven technologies provide an elegant and effective way to arrive at superior immunogens for monoclonal antibodies especially against these complex targets.

Pepscan's approach for the generation of antibodies is based on gaining structural knowledge of the antigen and the subsequent synthesis of CLIPS peptide-based immunogens. Our successful development of antibody therapeutics relies on the ability to:

- define precisely the antigens at the level of single amino acids
- adequately mimic the native secondary and tertiary structure of the antigen
- translate these CLIPS peptides into active and potent immunogens that induce the desired antibodies

This approach is suitable for every protein target, but is unique for "difficult-to-target" proteins, like membrane-integrated receptors (GPCRs, ion-channels), or certain viral proteins such as HIV. Our cutting-edge platform technologies are specifically designed to reconstruct such structurally complex binding sites.

### For more information contact:

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