



## **A new and efficient method for multivalent peptide assembly using scaffolded maleimide clusters.**

**The Challenge.** In recent years, there has been an increasing need for building drug delivery systems suitable for delivering peptides or peptide antigen drugs into intact cells. The existing protocols demand that the peptides either be linked to carrier proteins, core molecules or complex scaffold molecules for delivery into cells. One also has to keep in mind that the ratio of peptide molecules to the number of scaffold molecules delivered inside the cells should be greater in order to increase efficiency.

Currently, there are several methods which enable us to generate dual, tetrameric or octameric (multivalent) branches of a peptide using different types of scaffold molecules. These include cyclic peptides, porphyrin molecules, arena core and carbohydrates. However, each of them has certain drawbacks in that they may be using harsh conditions that can in turn affect the peptide drugs. Another method is to use the traditional step-wise solid phase peptide synthesis on an immobilized template. Nonetheless, purification of the multivalent peptide after cleavage from the immobilized template and de-protection pose an even bigger challenge. Therefore, the development of techniques in chemi-selective ligation of pre-assembled, unprotected peptide segments would significantly enhance the ability to synthesize large, complex, multivalent peptide segments and proteins.

**UMBI Solution.** A UMBI scientist has developed new scaffolded maleimide clusters as templates for multivalent peptide assembly. Multiple maleimide clusters were assembled on rigid scaffold molecules such as monosaccharides, cholic acid, or other acceptable carrier molecules, depending on the specific application. Any peptide that contains a cysteine residue is able to rapidly react with a maleimide moiety in a highly selective manner and form a covalent bond under neutral conditions at room temperature. This ligation method is extremely valuable for synthesizing large and complex multivalent peptides that may not be easily obtained by other conventional ligation methods.

### **Commercial Applications:**

- Development of therapeutic antibodies, vaccines, peptide inhibitors, protein hormones through homogeneous synthesis of scaffolded maleimide clusters for multivalent peptide assembly
- Building drug delivery systems
- Synthesis of artificial proteins to study the folding and structure of proteins

### **Advantages:**

- Synthesis of high titer of peptide-specific antibodies in the absence of any additional adjuvant
- Synthesized peptide inhibitors have enhanced inhibitory activities

- Avoid current difficulties in conjugation of hydrophobic or complex peptides to carrier proteins
- Deliver peptide antigens containing internal cysteine residues to reduce or eliminate the immunogenic response to carrier proteins

**Stage of Development:** Preclinical; tested in murine model system

**Patent Status:** Pending PCT and US patent applications

**Licensing Potential:** UMBI is seeking non-exclusive and exclusive licensees to all or part of this technology. The inventors welcome the opportunity to work with any licensee to further refine or extend the capabilities of this invention.

**Inventor & UMBI Reference:** Wang, 02-002

**Relevant Publications:**

1. Wei, Y., Li, C., Huang, W., Li, B., Strome, S. E., Wang, L. X., “Glyco-engineering of human IgG1-Fc through combined yeast expression and *in vitro* chemoenzymatic glycosylation”, *Biochemistry*, in press (2008).
2. Wang, L. X., “Chemoenzymatic synthesis of glycopeptides and glycoproteins through endoglycosidase-catalyzed transglycosylation”, *Carbohydr. Res.*, *343*, 1509-22 (2008).
3. Li, H, Li, B., Song, H., Breydo, L., Baskakov, I. V., Wang, L. X. “Chemoenzymatic synthesis of HIV-1 V3 domain glycopeptides carrying two N-glycans and effects of glycosylation on the peptide’s domain”. *J. Org. Chem.*, *70*, 9990-9996 (2005).
4. Li, B., Zeng, Y., Hauser, S., Song, H., Wang, L. X. “Highly efficient endoglycosidase-catalyzed synthesis of glycopeptides using oligosaccharide oxazolines as donor substrates”. *J. Am. Chem. Soc.*, *127*, 9692-9693 (2005).

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