

USING FURAN TECHNOLOGY TO STUDY PROTEIN-PROTEIN INTERACTIONS

We are seeking partners interested in selective crosslinking of peptides and proteins for the identification of PPI's. Further characterization of PPI interfaces potentially allows defining new drug targets and potential new modes of action.

INTRODUCTION

Proteins are essential in controlling biological systems in a cell, and while many proteins perform their functions independently, the vast majority of proteins interact with others for proper biological activity. Chemical cross-linking results in the formation of a covalent bond between close interacting partners and is a powerful tool to lock together receptors and their ligands which are normally associated only by weak and transient interactions. This enables a wide range of analytical techniques that would usually disrupt non-covalent bonds. The identification of unknown binding partners, new protein-protein interactions (PPIs) and elucidation of the specific interaction sites is currently a hot area of research.

Most modern cross-linking techniques take advantage of functional groups of which the intrinsic reactivity is only triggered by an external signal, such as light irradiation. However, currently used functional groups are normally very bulky, often disrupting the protein-protein interaction of interest or cannot be easily incorporated into a protein. Moreover, photo-activation-based cross-link techniques result on average in low cross-link yields and damage of the peptides and surrounding tissue under study.

TECHNOLOGY

At Ghent University, in the research group of Prof. Madder a method has been developed that allows cross-linking of a peptide/protein with a known or unknown second peptide/protein, with high efficiency and specificity. In this method a peptide comprising a furan amino acid, can be cross-linked to a second peptide upon selective activation of the furan moiety (Fig 1).

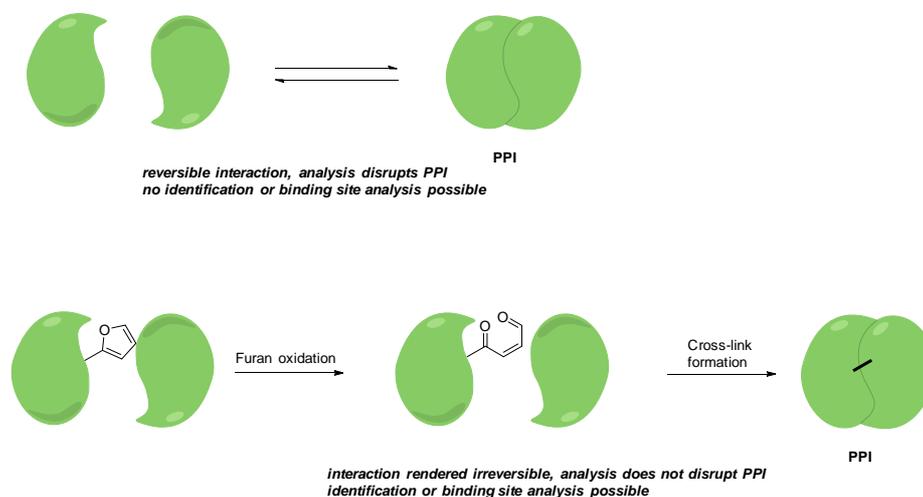


Figure 1. Furan-oxidation based crosslinking of peptide/protein complexes.

This method allows cross-linking of a peptide/protein with a known or unknown second peptide/protein to which it is bound. This enables to identify unknown binding partners in a specific PPI and further allows defining the interaction region between both partners of the complex. Moreover, the methods of the invention allow activation of the cross-link through the addition of a non-destructive activation signal, thereby advantageously preventing damage to the peptides under study.

APPLICATIONS

“Diagnostic assays in different application markets” or “Identification of unknown protein-protein interactions” or “Activity Based proteomics”.

ADVANTAGES

- Furan technology allows for site specific/selective cross-linking and is distance dependent: unspecific bond formation is minimized
- Allows activation of the cross-link through the addition of a nondestructive activation signal
- Furan crosslinking technology for peptides is part of a large furan-crosslinking and bioconjugation platform within our research group
- Ample knowledge in peptide synthesis and protein chemical modification present in OBCR research group

STATUS OF DEVELOPMENT

Furan crosslinking has been developed within Prof. Madder's group in a nucleic acid as well as a peptide/protein context. Furthermore, recent industrial collaborations have resulted in further proof of concept for in vitro cross-linking between peptides and relevant biomaterials.

PARTNERSHIP

We are looking for new collaborations with partners with an interest in selective modification of their peptides or proteins or in studying protein interactions.

INTELLECTUAL PROPERTY

W02012/085279 Method for cross-linking Peptides, Patent pending.

US9,290,539 Patent granted

REFERENCES

(1) Deceuninck, Madder et al. Chem. Comm. 2009, 21(3), 340 (2) Hoogewijs, Madder et al. Org. Biomol. Chem. 2012, 10 (20), 3999 (3) Hoogewijs, Madder et al. Chem. Comm. 2012, 49(28), 2927 (4) Op De Beeck, Madder et al., J Am Chem Soc. 2011, 133,796 (5) Op de Beeck, Madder et al., J Am Chem Soc. 2012, 134, 10737

KEYWORDS

Cross-linking, furan peptides, protein-protein interactions, target identification

CONTACT

Dr. AN VAN DEN BULCKE
Business Developer - CHEMTECH FOR LIFE SCIENCES
GHENT UNIVERSITY – Belgium
a.vandenbulcke@ugent www.chemtech.UGent.be
T +32 9 264 44 62 M +32 474 812381