The total synthesis of antimicrobial peptides and proteins

Oleg Melnyk,[1] Vangelis Agouridas,[1,2] Vincent Diemer,[1] Jérôme Vicogne,[1] Muriel Pichavant,[1] Gemma Bogard,[1] Florent Kerdraon,[1] Marine Cargöet,[1] Thomas Toupy,[3] Jean-Christophe Monbaliu,[3] Nathalie Ollivier[1]

[1] *Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, U1019 - UMR 9017; Center for Infection and Immunity of Lille, F-59000 Lille, France.*
[2] *Centrale Lille, F-59000 Lille, France.*
[3] *Department of Chemistry, University of Liège, B-4000, Liège (Sart Tilman), Belgium.*

Mots-Clés : (5 max) : Chemical protein synthesis, chemoselective ligation, microfluidics, antibacterial

Doctorant/post-doctorant ☐ Oui ☒ Non

Résumé (10-15 lignes max, calibri 12, interligne 1,5) :

We are interested by the discovery of practical means for assembling proteins by chemical synthesis from shorter unprotected peptide segments using water as the solvent. For that purpose, we take inspiration from chemical processes taking place in nature for designing novel reactions enabling high yielding chemoselective transformations at the protein level under extremely mild conditions.[1-3]

Using this approach and during the last decade, we developed powerful peptide segment assembly methods through the engineering of functional groups, whose reactivity was placed under the control of disulfide, selenosulfide or diselenide bonds acting as redox-switches.[1]

I will show how such methods can be implemented to facilitate the access to challenging antibacterial peptides or proteins.[4,5]

Références :

[1] Agouridas, V.; Ollivier, N.; Vicogne, J.; Diemer, V.; Melnyk, O. Redox-controlled chemical protein synthesis: Sundry shades of latency. Acc Chem Res 2022, 55, 2685-2697.
[2] Diemer, V.; Bouchenna, J.; Kerdraon, F.; Agouridas, V.; Melnyk, O. *N,S*- and *N,Se*-acyl transfer devices in protein synthesis. In Total chemical synthesis of proteins, Brik, A., Liu, L., Dawson, P. Eds.; Wiley, 2021; 59-85.
[3] Diemer, V.; Ollivier, N.; Leclercq, B.; Drobecq, H.; Vicogne, J.; Agouridas, V.; Melnyk, O. A cysteine selenosulfide redox switch for protein chemical synthesis. Nat. Commun. 2020, 11, 2558.
[4] Kerdraon, F.; Bogard, G.; Snella, B.; Drobecq, H.; Pichavant, M.; Agouridas, V.; Melnyk, O. Insights into the mechanism and catalysis of peptide thioester synthesis by alkylselenols provide a new tool for chemical protein synthesis. Molecules 2021, 26 (5), 1386.
[5] Ollivier, N.; Toupy, T.; Hartkoorn, R. C.; Desmet, R.; Monbaliu, J.-C. M.; Melnyk, O. Accelerated microfluidic native chemical ligation at difficult amino acids toward cyclic peptides. Nat. Commun. 2018, 9, 2847.

****Correspondance :*** *Oleg.melnyk@ibl.cnrs.fr*