BIOTRANS
LA ROCHELLE 2023

N°429 / OC / PC
TOPIC(s) : (Chemo)enzymatic strategies / Biocatalytic cascade reactions

Enzymatic acylation of peptides

AUTHORS
Laura RODRIGUEZ PEREZ / UNIVERSITY OF MANCHESTER, 131 PRINCESS ST, MANCHESTER
William GOUNDRY / EARLY CHEMICAL DEVELOPMENT,PHARMACEUTICAL SCIENCES, R&D, ASTRAZENECA, CHARTER WAY, MACCLESFIELD
Christian SCHNEPEL / UNIVERSITY OF MANCHESTER, 131 PRINCESS ST, MANCHESTER
Sabine FLITSCH / UNIVERSITY OF MANCHESTER, 131 PRINCESS ST, MANCHESTER

PURPOSE OF THE ABSTRACT
Peptide modification is a field of interest due to its potential applications in the biomedical area, for example, in the manufacture of peptide-drug conjugates. Nevertheless, production of peptide conjugates is non-trivial, and chemical methods tend to display an array of shortcomings such as poor thermostability, low potency, or off-target toxicity.[1] Biocatalysis is an attractive alternative to chemical bioconjugation, as enzymes exhibit exceptional selectivity, fast kinetics, high yields and require mild conditions.[2] As a result, they can be considered to be superior to chemical methods in many aspects.

In this work, we developed an enzymatic method to acylate peptides, allowing the introduction of a range of bioorthogonal probes. The adenylation domain of the carboxylic acid reductase from Segniliparus rugosus was used to obtain in-situ the CoA derivative of the respective acids. The CoA substrates were employed by lysine acetyltransferase p300 for acylation, functionalizing a 20-mer peptide with bioorthogonal handles. Following the one-pot reaction, modification of up to five residues in peptide H4(1-20) was observed. Furthermore, peptide labelling with stable isotopes was also achieved via acetylation using the same enzymatic system.

FIGURES

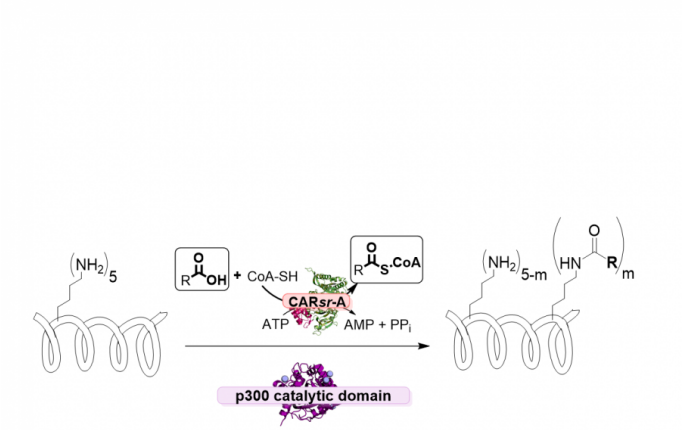

FIGURE 1

Scheme of the enzymatic modification of peptide H4(1-20)

CARsr-A was employed to form the CoA derivatives of the respective acids, which were used by enzyme p300 to functionalize peptide H4(1-20)

FIGURE 2

KEYWORDS

biocatalysis | click chemistry | peptide functionalization | lysine acetyltransferases

BIBLIOGRAPHY

[1] P. Hoppenz, S. Els-Heindl and A. G. Beck-Sickinger, Frontiers in chemistry, 2020, 8, 571.

[2] Y. Zhang, K.-Y. Park, K. F. Suazo, and M. D. Distefano, Chemical Society Reviews, 2018, 47, 9106.