# 16th Iberian Peptide Meeting
# 4th ChemBio Group Meeting

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**PROGRAM & BOOK OF ABSTRACTS**

RSEQ

EPS

## P07 - Stereoselective S-Michael additions of sulphur nucleophiles to a chiral dehydroalanine. Synthesis of fluorescent peptides

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In the last few years, the study of new molecular labels is being of a great interest. Among these group of markers, cell penetrating peptides labelled with fluorophores have a large number of applications for biological studies. The usual way to obtain fluorescently labelled peptides involves the bioconjugation of a fluorescent dye to the corresponding peptide, once this peptide has been synthesized. This strategy is difficult to apply to peptides bearing more than one amine or thiol group, since several labelled species or mixtures can be generated. Therefore, the use of adequately amino acids incorporating fluorophores in their lateral chains could solve this drawback.

In this field and taking into account our previously works on stereoselective S-Michael additions to a bicyclic chiral dehydroalanine (Dha*), we envisioned the synthesis of two fluorescent amino acids, which have coumarin and dansyl dyes in their lateral chains. The key step involved a highly stereoselctive S-Michael addition of the corresponding dye, bearing a thiol group as an S-nucleophile, with the Dha* at room temperature. After acid hydrolysis of the unique Michael adduct obtained in each case, both free amino acids were Fmoc-protected to be incorporated, using SPPS, into two peptide sequences (VPALK and VPALR) of known activity as cell penetrating peptides. These fluorescent peptides have been used to perform a biological study that allowed us to observe their internalization in HeLa cells by fluorescent microscopy (Figure 1).

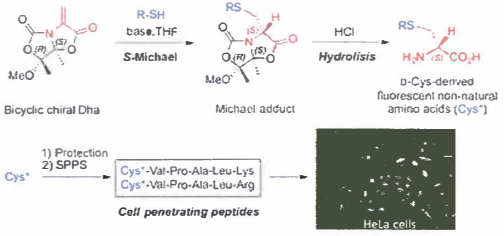


**Figure 1.** Synthesis of fluorescent amino acids, incorporation in cell penetrating peptides and internalization in HeLa cells.

### References

1. Gutiérrez-Jiménez, M. I.; Aydillo, C.; Navo, C. D.; Avenoza, A.; Corzana, F.; Jiménez-Osés, G.; Zurbano, M. M.; Busto, J. H.; Peregrina, J. M.; *Org. Lett.* **2016**, *18*, 2796.

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