Title: **Biophysical studies of assembled peptide amphiphiles with possible application in the preexposure prophylaxis of HIV-1 infection**

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Date: January 2020

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Acquired Immunodeficiency Syndrome (AIDS) represents the final expression of the infection of the Human Immunodeficiency Virus (HIV), which causes the destruction of the immune system, facilitating the infection by many diseases that can cause the death of the patient. Several studies have established that, the co-infection of HIV and GB Virus-C (GBV-C), is related to a decrease in mortality in patients due to inhibition of HIV replication.

The USiBAP research group, from IQAC-CSIC, has demonstrated the antiviral properties of molecules formed by domains derived from the E1 membrane protein of GBV-C. The sequence 139-156 of the E1 protein, composed of 18 amino acids, is the region with the most anti-HIV activity and has been named E1P47 peptide. For this reason, numerous studies are being carried out to enhance this activity from the synthesis of amphiphilic peptides (AP), derived from E1P47, in order to be able to use them in the future as therapeutic agents against the HIV virus.

With this objective, the synthesis, purification and characterization of three new derivatives (AP10, AP11 and AP12) have been performed by adding different lipophilic moieties at the N-terminal end of the E1P47 peptide. In the case of AP10, the added compound is an alkyl tail and in AP11 it is a two-alkyl tails. In the latter case, AP12, firstly the union of a Cys residue and then a cholesterol molecule has been carried out.

These three compounds, together with E1P47, have been analysed by a vesicle content release assay, using liposomes as membrane models, to evaluate their capacity to destabilise cell membranes. It has been seen that E1P47, due to the high level of activity at membrane level, causes the rupture of the liposomes. On the other hand, the derivative that causes a lower destabilization is AP11.

The analysis, using the dynamic light scattering technique, of the size and charge of different APs (AP1-AP9) previously synthesized by the USiBAP research group, has also been

performed to evaluate the stability of the supramolecular aggregates that are formed, showing that the most stable compound of all is AP7, since it has provided the most suitable values, as well as sufficient charge to prevent particles in solution from being attracted.

Keywords: HIV, GBV-C, peptide synthesis, amphiphilic peptides, E1P47, dynamic light scattering, vesicle content release assay, liposomes