SYNTHESIS AND EVALUATION OF ANTIVIRAL CYCLOPEPTIDES ISOLATED FROM A TROPICAL PLANT

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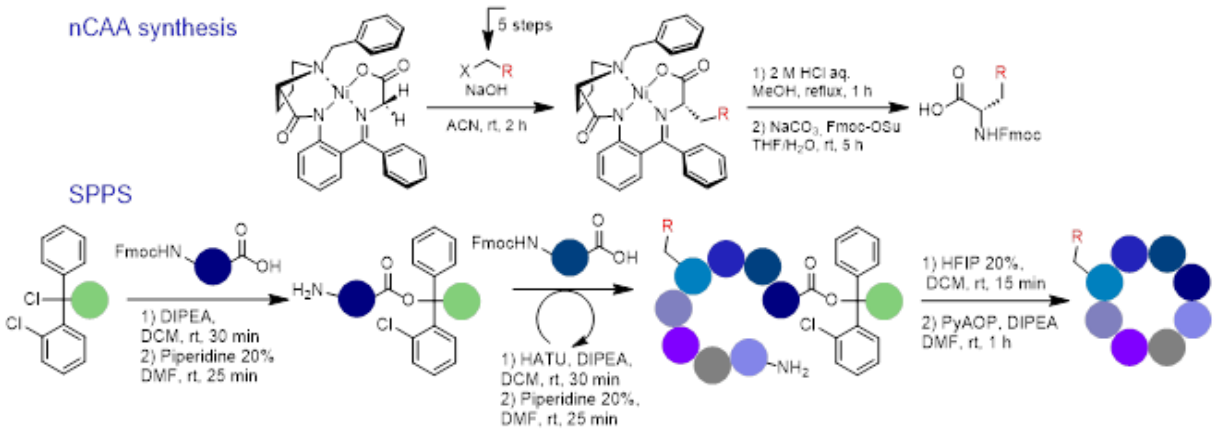
Arboviruses are viruses that are transmitted to humans and other animals through the bites of infected arthropods, such as mosquitoes, ticks, and sandflies. Some common arboviruses include dengue, Zika, and Chikungunya. These viruses can lead to significant epidemics with the potential for high human death rates.[1] In this context, a screening of 824 extracts of the ICSN extract library on the Zika virus replication inhibition was performed. From plant extract hits, we were able to isolate and identify a series of novel natural cyclopeptides bearing uncommon non-canonical amino acids (nCAA). This family of peptides has proven to show low toxicity to cells and strong antiviral activity against a panel of positive-sense single-stranded RNA viruses such as the Chikungunya, Dengue, Zika, Ross River, and SARS-CoV-2 viruses.

To go further in the development of antiviral agents, we've used a synthetic approach employing solid-phase peptide synthesis (SPPS). This technique proved reliable in integrating synthesised non-canonical amino acids (nCAAs)[2,3] facilitating access to the most potent isolated natural cyclopeptide and a diverse range of analogue compounds. The synthesised natural cyclopeptide confirmed the considerable potential of this compound series, as well as the target involved and the associated mechanism of action. These experiments highlighted the influence of peptides on both target degradation and RNA transcription or replication in arboviruses.



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