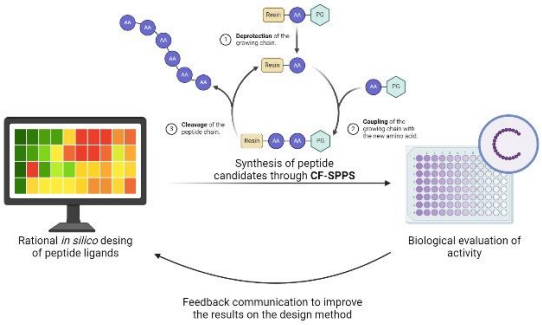
Most small molecule drug candidates being developed focus on their ability to bind to a protein's pockets to inhibit or block the binding of the natural substrates. However, they fail to inhibit protein-protein interactions, which have garnered significant attention in the pharmaceutical industry in recent years. Peptides' high structural compatibility with the targeted proteins have the ability to disrupt such protein-protein interfaces. Efficient *in silico* design of high-affinity peptide ligands is an ever-growing field that still demands the synthesis to confirm the desired activity.[1]

Batch-mode solid-phase peptide synthesis has been the standard for drug discovery; however, synthesizing a library of candidates is time- and resource-consuming.[2] In this work, we present our efforts for the rational design of two libraries of peptides targeting HLA-DR and Hsp90; as well as the use of CF-SPPS for synthesizing them to evaluate both the design model and their biological activity.



(1) Vanhee, P.; Rousseau, F.; Schymkowitz, J. Computational Design of Peptide Ligands. *Trends in Biotechnology*. May 2011, pp 231–239.

(2) Ruhl, K. E.; Schultz, D. M.; Lévesque, F.; Mansoor, U. F. Continuous-Flow Solid-Phase Peptide Synthesis to Enable Rapid, Multigram Deliveries of Peptides. *Org Process Res Dev*. 2024