

Combining MIAx-Based In-Silico-Peptide-Chips with Membrane-Support Peptide-Array-Chips Oriented to Novel Drug Discovery

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1 Introduction

Protein-protein interactions and polypeptide interaction in general play a central role in molecular recognition processes relevant to several cellular functions and triggering a diversity of biochemical processes, all of them at the realm of the natural, life sustaining endeavor. Moreover, unveiling disease generating mechanisms at the molecular level as well as the search for new chemical compounds to mimic, inhibit, or enhance determined molecular functions make knowledge of the principles governing polypeptide interaction crucial.

While data from large scale genome analysis projects are accumulating at high rates, tools for their rational analysis leading to reveal the principles governing polypeptide interactions have just started to be explored. Nevertheless, because of the intricacy of the problem which involves the yet completely solved problem of polypeptide 3D structure prediction and protein folding as well as consideration of the environment and conditions under which the interactions occur, approaching the problem requires both theoretical and experimental tools to deal with its intrinsic combinatorial chemical nature.

2 Method and Results

Del Carpio [1], has been involved in the development of a series of bioinformatic tools oriented to the analysis of protein-protein [1, 2], protein-ligand [3], and oligopeptide interaction [4], the result being the robust system for automatic bio-macromolecular interaction assessment in condensed phases MIAx [1, 2, 3]. MIAx is capable of assessing interaction among proteins, proteins-peptides and protein-small organic molecules at the sole input of the target receptor and the ligand. The system is endowed of binding site and epitope mapping capabilities that enhance the predictability of the configuration of the complex resulting from a determined interaction.

On the other hand, Kunimatsu [5] has been involved in the development of a robot machine for parallel synthesis of huge number of peptides, mixtures/pools and a growing range of other organic compounds with easy adaptation to a wide range of binding, enzymatic and cellular assays which allow in situ screening of compound libraries thanks to the special properties of the membrane supports.

The object of the present paper is to combine these two technologies and develop a bioinformatic-experimental system for analysis of the principles of peptide interaction as well as for discovery of novel chemical compounds with therapeutic characteristics.

We show that the newly developed combinatorial chemical/biological synthesis system can be applied to elucidate diverse mechanisms of molecular recognition and interaction underlying molecular biological, immunological and drug discovery processes.

Figure 1. illustrates the general scheme of the newly developed peptide-interaction learning engine involving the bioinformatic process based on MIAx-generated peptide chips and the membrane support peptide array chips.

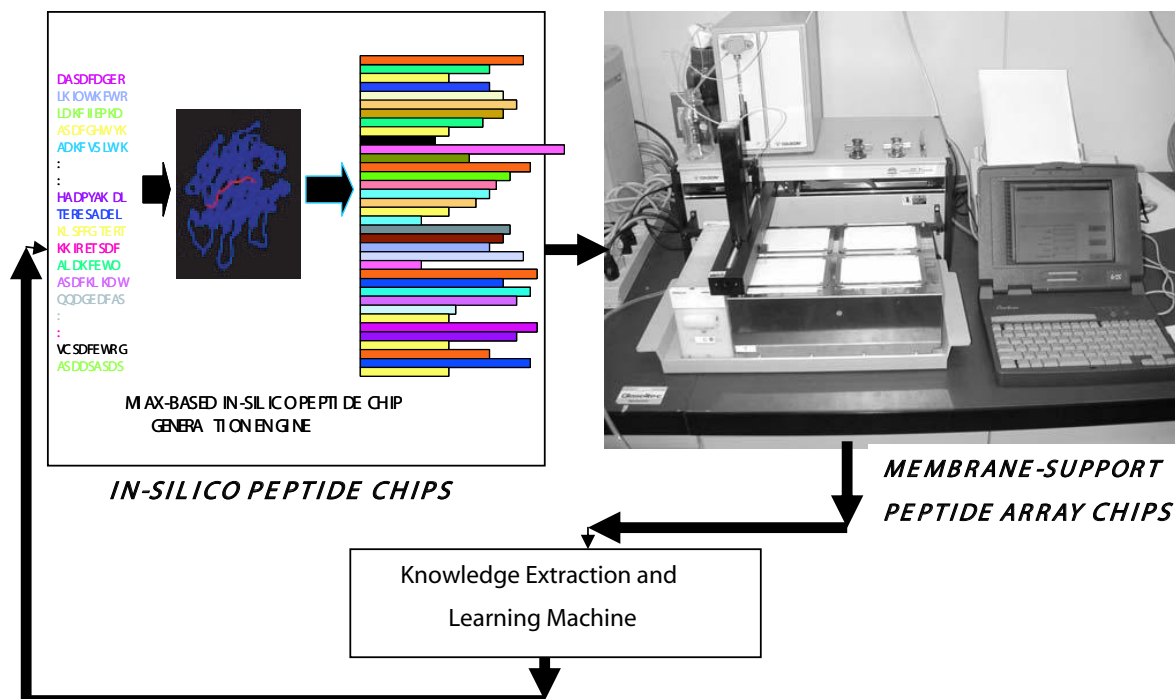


Figure 1: Novel technology for new drug discovery combining bioinformatic and experimental tools.

3 Discussion

As an example of the application of the newly developed learning machine we discuss the analysis of MHC-class I binding peptides.

References

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