



Combinatorial Peptide Library Protocols (Methods in Molecular Biology)

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During the course of evolution, an imbalance was created between the rate of vertebrate genetic adaptation and that of the lower forms of living organisms, such as bacteria and viruses. This imbalance has given the latter the advantage of generating, relatively quickly, molecules with unexpected structures and features that carry a threat to vertebrates. To compensate for their weakness, vertebrates have accelerated their own evolutionary processes, not at the level of whole organism, but in specialized cells containing the genes that code for antibody molecules or for T-cell receptors. That is, when an immediate requirement for molecules capable of specific interactions arose, nature has preferred to speed up the mode of Darwinian evolution in preference to any other approach (such as the use of X-ray diffraction studies and computergraphic analysis). Recently, Darwinian rules have been adapted for test tube research, and the concept of selecting molecules having particular characteristics from random pools has been realized in the form of various chemical and biological combinatorial libraries. While working with these libraries, we noticed the interesting fact that when combinatorial libraries of oligopeptides were allowed to interact with different selector proteins, only the actual binding sites of these proteins showed binding properties, whereas the rest of the protein surface seemed "inert." This seemingly common feature of protein-having no extra potential binding sites--was probably selected during evolution in order to minimize nonspecific interactions with the surrounding milieu.

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