Selection scheme for the directed evolution of novel and peptides with desired structural and binding properties

Technology #m08-033
Peptides are useful as a potential method of therapeutics due to their high potency, specificity, and low toxicity. However, their degradation in the presence of proteases severely limits their application. In addition, therapeutic peptides must also exhibit a high binding affinity for the desired target protein. Developing and screening for the peptide that has both of these properties has proven to be expensive and time consuming. This technology uses a directed molecular evolution method to screen for peptides with a high protease resistance and a strong affinity to proteins. It provides a combinatorial method to quickly engineer variations of peptides with the desired properties without loss in therapeutic potency.

Screening method allows for the engineering of useful therapeutic peptide candidates with desired properties and without a priori knowledge of the peptide’s or target’s structure.

This technology achieves the difficult task of coupling both a protease-based structural selection with a protein binding selection. While other related technologies also use directed evolution methodologies to select for peptides that exhibit desired structural properties, they do not couple this structural selection with binding selections. Therefore, this technology offers a method to screen for peptides that are therapeutically applicable. A batch of peptides known to show high binding affinity to a protein is diversified to express slightly different properties. The peptides undergo testing with proteases, with the non-resistant ones being removed from the system. Likewise, the peptides also undergo a reaction with the desired protein target, and the ones that do not bind tightly enough are removed from the system as well. Repetition of this general screening process affords the desired peptides. Because of the effective screening process, the structure-property relationship of the beginning peptide and targeted protein does not need to be known before the selection process, allowing for expedited and efficient screening new types of peptides.

To demonstrate the principle of this process, peptides underwent six rounds of structural and binding screening cycles. Four peptide variants were identified to interact strongly with the target protein E-selectin, while maintaining a high resistance to protease degradation.
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Applications:
• Generation of novel and robust peptides for therapeutic applications
• Generation of peptide based biomaterials with specific features
• Discovery of peptides with specific resistances to proteases or other enzymes
• Discovery of peptides with specific binding interactions with different types of proteins
• Efficient combinatorial method for research based discoveries of structural-property relationships of peptides and proteins
• Method to study the effects of environmental factors (pH, salt concentration, temperature, etc.) on structural and binding properties of peptide chains

Advantages:
• Dual screening method produces more robust peptide candidates than other screening methods
• Directed evolution of peptide strands produces a multitude of potential peptide candidates, which allows for a fast turnover of the discovery of novel peptides
• Quick and robust method reduces the screening time and cost

Patent information:
Patent Pending
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Related Publications:

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