Protein-protein interactions

VCU Innovation Gateway

Stapled peptide discovery

Using mRNA display to create alpha-helical peptide libraries

VCU researchers have developed a more efficient method for discovering molecules that inhibit intracellular protein-protein interactions in human cells (PPIs). Intracellular PPI inhibitors are validated targets for many diseases including cancer, viral infections and neurodegenerative diseases. One class of molecules, known as hydrocarbon stapled peptides, is a promising therapeutic for inhibiting intracellular PPIs. Stapling of these peptides promotes the proper alpha helical orientation, which gives them a high affinity for binding to and inhibiting the alpha-helical interface of these PPIs. These stapled peptides are also resistant to proteolytic degradation and have a propensity to be cell permeable. However, the development of these stapled peptides is tedious and time consuming. The current development process requires extensive optimization and limits the ability to find a peptide with high affinity. The method developed by our researchers offers a significantly more streamlined approach, both shortening the time for discovery and the affinity of hydrocarbon stapled peptide hits.

The technology

The method developed by our researchers combines mRNA display and its ability to create large libraries of peptides (~10 trillion) with a unique stapling strategy. This strategy predisposes the created libraries to contain peptides that are both cell-permeable and alpha-helical. This greatly reduces the need for extensive optimization and will streamline the process for discovering stapled peptide inhibitors of many intracellular PPIs.

Benefits

- Libraries contain a vast number of unique peptides (~10 trillion)
- Reduces need for extensive optimization

Applications

- Discover possible treatment methods for diseases:
  - Cancer
  - Viral infections
  - Neurodegenerative

License status:
This technology is available for licensing to industry for further development and commercialization.

Category:
Biomedical

VCU Tech #:
18-097

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