Fragment Based Drug Discovery: A Paradigm Shift in Drug Development

Drug discovery is a complex and time-consuming process that has traditionally relied on laborious screening of large libraries of molecules. However, the advent of Fragment Based Drug Discovery (FBDD) has transformed the field by introducing a novel approach that focuses on identifying and optimizing small, fragment-sized molecules that bind to specific targets within the body.

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by Daniel A Erlanson

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FBDD has emerged as a powerful tool for drug discovery due to its ability to identify novel binding sites, overcome challenges associated with traditional drug-like molecules, and accelerate the lead optimization process. This article provides a comprehensive overview of FBDD, exploring its principles, techniques, and applications.

Principles of FBDD

FBDD is based on the concept that small, fragment-sized molecules can bind to specific targets with high affinity and selectivity. These fragments typically have molecular weights below 300 Da and contain a single functional group that interacts with the target. By targeting small binding sites that are often inaccessible to larger molecules, FBDD can identify novel leads that are not readily identified using traditional approaches.

FBDD relies on the principle of fragment assembly, where multiple fragments are combined to create larger, more complex molecules that retain the binding properties of the original fragments. This iterative process allows researchers to optimize the binding affinity and selectivity of their lead compounds, ultimately leading to the development of potent and specific drug candidates.

Techniques in FBDD

FBDD employs a variety of techniques to identify and optimize fragment-sized molecules. These techniques include:

- **Fragment screening:** This involves screening libraries of small molecules against a target protein to identify fragments that bind with high affinity.
- **X-ray crystallography:** Used to determine the precise binding mode of fragments and to guide the design of larger, more potent molecules.
- **NMR spectroscopy:** Provides detailed information about the structure and dynamics of protein-fragment interactions.
- **Virtual screening:** Used to identify potential fragments from large databases based on their predicted binding properties.

By combining these techniques, researchers can efficiently identify and optimize fragment-sized molecules that have the potential to be developed into effective drug candidates.

Applications of FBDD

FBDD has a wide range of applications in drug discovery. These include:

- **Target identification:** Identifying novel targets for drug discovery by screening fragments against libraries of proteins.
- **Lead optimization:** Optimizing the binding affinity and selectivity of lead compounds through fragment assembly.
- **Drug design:** Designing new drug molecules by combining fragments with known binding properties.
- **Overcoming drug resistance:** Identifying fragments that bind to novel sites on drug-resistant targets.

FBDD has been successfully applied to discover new treatments for a variety of diseases, including cancer, infectious diseases, and neurological disFree Downloads.

Fragment Based Drug Discovery has revolutionized the field of drug discovery by providing a novel approach to identifying and optimizing lead compounds. By focusing on small, fragment-sized molecules, FBDD has overcome the limitations of traditional drug-like molecules and opened up new avenues for drug development. As the field continues to advance, we can expect FBDD to play an increasingly important role in the discovery of new therapies for a wide range of diseases.

References

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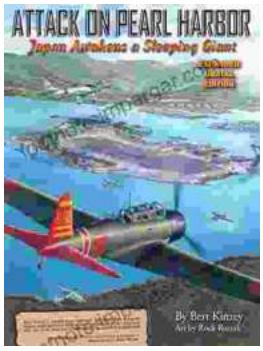

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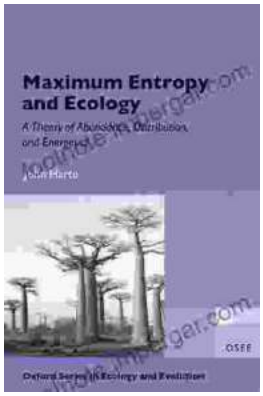

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