# Article information:

Fragment-Based Drug Discovery: Advancing Fragments in the Absence of Crystal Structures - ScienceDirect  
<https://www-sciencedirect-com.docelec.univ-lyon1.fr/science/article/pii/S2451945618303337>

# Article summary:

1. Fragment-based drug discovery typically relies on X-ray crystallography to obtain three-dimensional structures of ligand/protein complexes, but this can be challenging for low-affinity fragment hits.

2. In the absence of crystal structures, alternative structural techniques such as NMR spectroscopy and molecular modeling can be used to advance and evolve fragments.

3. NMR spectroscopy is particularly useful for characterizing complexes with low-affinity ligands, and it has been successfully used to determine the structure of protein-fragment complexes and guide fragment optimization.

# Article rating:

Appears moderately imbalanced: The article provides some useful information, but is missing several important points or pieces of evidence that would be required to present the discussed topics in a balanced and reliable way. You are encouraged to seek a more balanced perspective on the presented issues by exploring the provided research topics and looking at different information sources.

# Article analysis:

The article titled "Fragment-Based Drug Discovery: Advancing Fragments in the Absence of Crystal Structures" provides an overview of strategies to advance and evolve fragments in drug discovery when crystal structures of protein-fragment complexes are not available. While the article provides valuable information on alternative methods such as NMR spectroscopy and molecular modeling, there are several potential biases and limitations that need to be considered.

One potential bias in the article is the emphasis on the importance of X-ray crystallography as the method of choice for obtaining structural information on protein-fragment complexes. The article acknowledges that not all proteins are suitable for crystallography and that crystal structures may not be obtainable for initial fragment hits. However, it does not explore alternative structural techniques in depth or discuss their advantages and limitations compared to X-ray crystallography. This could create a biased view towards X-ray crystallography as the preferred method.

Another limitation is the lack of discussion on the challenges and limitations of NMR spectroscopy for structure determination. While NMR is mentioned as an alternative method, there is no mention of its limitations, such as size limitations for protein targets or difficulties in obtaining high-resolution structures. This omission could lead to an overestimation of the capabilities and applicability of NMR spectroscopy in advancing fragment hits.

Additionally, the article focuses primarily on successful examples and does not provide a balanced view by discussing cases where fragment-based drug discovery has failed or faced significant challenges. This one-sided reporting could create a misleading impression that fragment-based drug discovery is always successful and straightforward.

Furthermore, there is limited discussion on potential risks or drawbacks associated with advancing fragments without crystal structures. For example, relying solely on computational modeling or NMR data may introduce uncertainties in accurately predicting binding modes or optimizing fragment hits. The article does not address these risks or provide guidance on how to mitigate them.

Overall, while the article provides useful insights into advancing fragments in the absence of crystal structures, it has potential biases and limitations that should be considered. It would benefit from a more balanced discussion of alternative structural techniques, limitations of NMR spectroscopy, challenges in fragment-based drug discovery, and potential risks associated with advancing fragments without crystal structures.

# Topics for further research:

* Alternative structural techniques for protein-fragment complexes
* Limitations of NMR spectroscopy in structure determination
* Challenges in fragment-based drug discovery
* Risks of advancing fragments without crystal structures
* Computational modeling in fragment-based drug discovery
* Strategies to mitigate uncertainties in fragment hit optimization

# Report location:

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