

Unstructured Protein : A New Approach for Drug Discovery

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There are many successful examples in drug discovery of developing enzyme inhibitors and receptor agonists/antagonists. However, attempts to develop modulators of protein/protein interaction have largely been unsuccessful. This is especially true in developing modulators for transcription factors and for doing so with small molecules.

Helix structures are prevalent and are often observed in intracellular protein/protein interactions. PRISM has designed novel compounds based on helix structures and has developed small to middle size molecules exhibiting strong activity in modulating critical intracellular protein/protein interaction. In case of intracellular protein/protein interaction, unstructured (intrinsic disorder) region plays an important role for their binding. The 50% of intracellular protein was estimated to have unstructured region. Intrinsic disorder region is highly abundant among proteins associated with various human diseases such as cancer, metabolic diseases, and cardiovascular diseases. However, systematic approach to target unstructured/structured protein/protein interaction has not been done in drug discovery area, to the best of our knowledge. PRISM focused on the protein/protein interaction to explore drug candidates. PRISM platform has resulted in a clinical-stage program based on targeting the CBP/beta-catenin complex, as well as other preclinical drug development programs.

We would like to discuss here PRISM's platform technology that focused on unstructured/structured protein/protein interaction to explore drug candidates.