OPEN ACCESS Freely available online

ISSN: 2153-0602
Journal of
Data Mining in
Genomics & Proteomics

Commentary

Application of PPIs Modulators to Treat Complex Diseases

Bridget Oberender *

Department of Epidemiology and Preventative Medicine, Monash University, Melbourne, Australia

DESCRIPTION

Protein-Protein Interactions (PPIs) are essential for many biological processes, such as signal transduction, cell cycle regulation, immune response, and gene expression. However, aberrant PPIs are often associated with various diseases, such as cancer, infectious diseases, and neurodegenerative diseases. Therefore, targeting PPIs is a promising strategy to develop new therapeutics for complex diseases. PPIs modulators are molecules that can interfere with or enhance the interaction between two or more proteins. PPIs modulators can be classified into three categories: small molecules, peptides, and antibodies.

Small molecules are organic compounds that have low molecular weight (usually less than 900 Da) and can bind to specific sites on the surface of proteins. Small molecules can act as inhibitors or activators of PPIs, depending on their binding mode and effect on the protein function. Small molecules have some advantages over other types of PPIs modulators, such as high specificity, high permeability, low immunogenicity, and ease of synthesis and optimization. However, small molecules also face some challenges in targeting PPIs, such as the large and flat interface of PPIs, the lack of suitable binding pockets or hotspots, the conformational flexibility and dynamics of proteins, and the potential off-target effects.

Small molecules that target PPIs for treating complex diseases

- Nutlin-3 is a small molecule that binds to the p53-binding pocket of MDM2 (a negative regulator of p53), preventing the interaction between MDM2 and p53 (a tumor suppressor protein). This leads to the stabilization and activation of p53, which induces cell cycle arrest and apoptosis in cancer cells.
- Bortezomib is a small molecule that inhibits the proteasome (a large protein complex that degrades ubiquitinated proteins), by binding to its catalytic subunit. This results in the accumulation of pro-apoptotic proteins and the inhibition of anti-apoptotic proteins, which trigger cell death in cancer cells.
- Raltegravir is a small molecule that inhibits the integrase (an enzyme that catalyzes the integration of viral DNA into host DNA) of Human Immunodeficiency Virus (HIV), by binding to its active site. This prevents the formation of a stable complex between integrase and viral DNA (Deoxyribonucleic Acid), blocking the viral replication cycle.
- Peptides are short chains of amino acids that can mimic or disrupt the interaction between proteins. Peptides can act as inhibitors or activators of PPIs, depending on their sequence and structure. Peptides have some advantages over small molecules in targeting PPIs, such as high affinity, high specificity, high diversity, and ease of design and synthesis. However, peptides also have some limitations in targeting PPIs, such as low stability, low bioavailability, low permeability, high immunogenicity, and high cost.

Examples of peptides that target PPIs for treating complex diseases

- SAH-p53-8 is a peptide that binds to the p53-binding domain of MDM2 (a negative regulator of p53), preventing the interaction between MDM2 and p53 (a tumor suppressor protein). This leads to the stabilization and activation of p53, which induces cell cycle arrest and apoptosis in cancer cells.
- TAT-CBD3 is a peptide that binds to the α1 subunit of Voltage-Gated Calcium Channels (VGCCs), inhibiting their activity. This reduces the calcium influx into neurons and protects them from excitotoxicity and neurodegeneration in Alzheimer's disease.
- T20 is a peptide that binds to the gp41 subunit of HIV Envelope Glycoprotein (Env), blocking its conformational change and fusion with host cell membrane. This prevents the entry of HIV into host cells and inhibits viral infection.

Antibodies are large proteins that can recognize and bind to specific antigens on the surface or inside of cells. Antibodies can act as inhibitors or activators of PPIs, depending on their binding mode and effect on the protein function. Antibodies have some advantages over small molecules and peptides in targeting PPIs.

Correspondence to: Bridget Oberender, Department of Epidemiology and Preventative Medicine, Monash University, Melbourne, Australia, E-mail: sanhartanu@gmail.com

Received: 03-Mar-2023, Manuscript No. JDMGP-23-20705; **Editor assigned:** 06-Mar-2023, JDMGP-23-20705 (PQ); **Reviewed:** 20-Mar-2023, QC No. JDMGP-23-20705; **Revised:** 27-Mar-2023, Manuscript No. JDMGP-23-20705 (R); **Published:** 03-Apr-2023, DOI: 10.4172/2153-0602.23.14.288

Citation: Oberender B (2023) Application of PPIs Modulators to Treat Complex Diseases. J Data Mining Genomics Proteomics. 14:288.