RNA Targeted Library

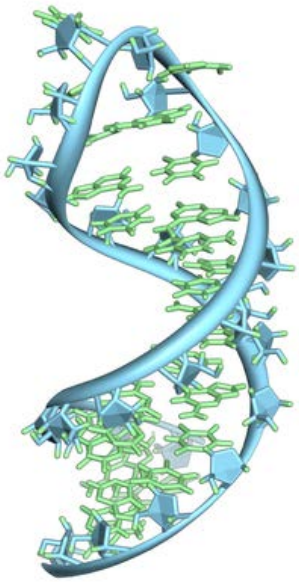
9,070 in-stock compounds

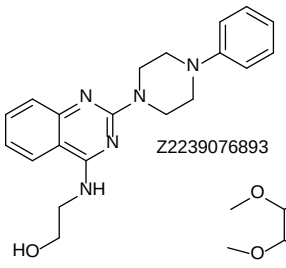
Ultimate library of compounds able to hit RNA; designed with versatile in silico screening approaches

The recent substantial progress in RNA biology underscores the importance of RNA in normal and aberrant cellular functions. RNA is essential for transcriptional regulation, translational regulation, protein function, and catalysis, responsibilities that have classically been reserved for proteins. It also highlights the potential of targeting RNA for treatment of a multitude of diseases including bacterial/viral infection and cancer.

Library Design

RNAs can form well-defined secondary structures, such as double helices, hairpins, bulges, internal loop, stems, which offer structural basis for designing therapeutic agents. These structural features have been taken into account in the design of our RNA Targeted Library. We focused on compounds which bind to RNA, forming interactions with different types of secondary structures.





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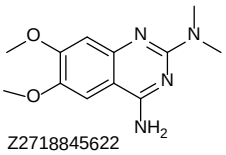

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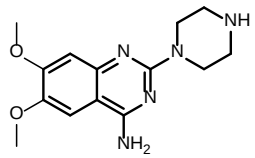
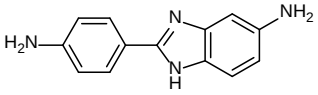


viral RNA binding, Kd=50.5 uM
Fragment fount to be effifient against
influenza A and B viral strains



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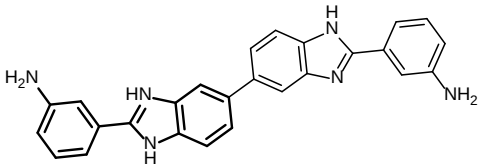


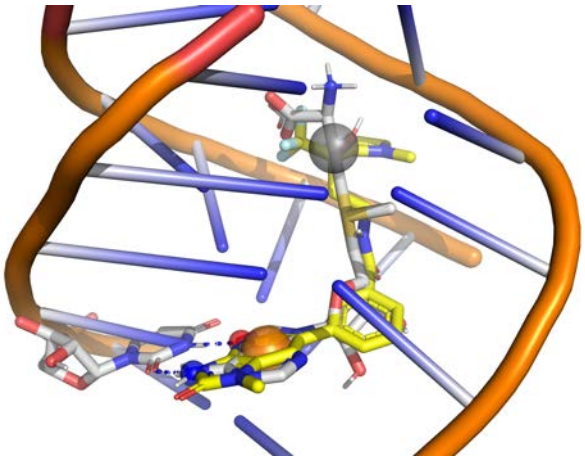
MBNL-poly(CUG) Ki=50uM
corrected splicing in cell

Reference Set of active compounds has been collected from public sources/databases (ChEMBL, PubChem, Drugs.com and other), then filtered to remove non selective binders and compounds with reactive moieties. Similarity search (chemical fingerprints) was carried out against MedChem filtered Enamine in-stock collection, 2.4 M compounds, to yield subset of 400 molecule.

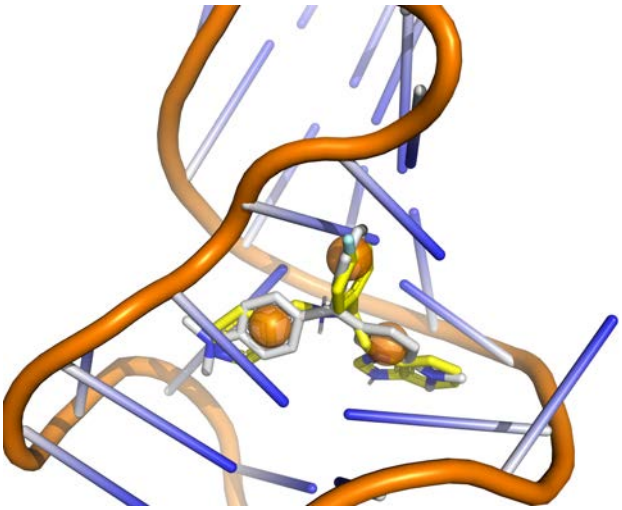
Pharmacophore search and **Shape similarity search** were used to enrich the library with new structures that can form same types of interaction as known ligand. Three 3D pharmacophore models were used for *in silico* screening based on the structure of most known binders. Additionally, **substructure search** was applied to find molecules bearing common structural moieties and cores known to be important for interaction with RNA (Inforna database was used for substructure selection).

Molecular modeling and Docking

Additionally, we analyzed all recorded in PDB RNA-ligand complexes. Four structures, which represent the most common types RNA-ligand interactions, have been selected for molecular docking and query generations – 1lvj, 1q8n, 4lvy, 6fz0 pdb entries. All query models were validated with the small sets of known active and non active ligands and subsequently corrected.



Example of molecular docking result (6fz0), native ligand is colored in grey, docked hit compounds (Z1723434664) is in yellow .



Example of molecular docking using 1qn8 pdb entry,
Docked ligand, identified as a hit compounds colored with yellow (Z1135145616).

The library comprises only drug-like compounds and provides an excellent basis for posttranscriptional gene regulation researches, antiviral and antibacterial drug discovery projects.