

RNA Focused Library

RNAs have been unravelled as unique molecules playing critical roles in developmental and physiological processes in all living organisms. RNA is involved in the progression of diseases such as infectious diseases (e.g. HIV, AIDS, hepatitis C), metabolic diseases (e.g. diabetes, cancer) and triplet repeat disorders (e.g. myotonic dystrophy, Huntington's disease). Recently, a number of RNA-based molecular targets have begun to grow rapidly with detailed elucidation of their structural and functional relationship. Also, small molecule inhibitors have been successfully developed for various different RNA molecules.

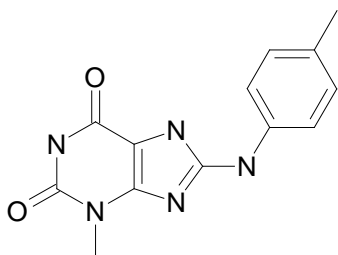
Life Chemical's RNA Focused Library comprises over 3,400 compounds with predicted RNA-binding activity. The library has been designed with two ligand-based approaches.

1. 2D Similarity Search

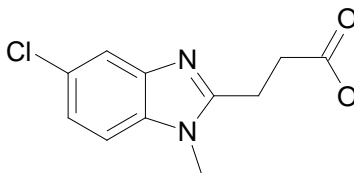
Initially, a set of about 750 known RNA-binding molecules has been collected from literature. It was narrowed down by binding activity via discarding compounds with low dissociation constant ($K_d > 10\mu\text{M}$). On the next step, 2D similarity search has been performed against Life Chemical's HTS Stock compound collection with Tanimoto and Tversky index values of ≥ 0.80 and ≥ 0.85 , respectively. Fragment Based\Chemical Hashed Fingerprints were used to compare the compound structures. Finally, PAINS compounds, as well as those with "bad" and reactive groups have been filtered out from the resulted compound set.

2. Bayesian Modeling

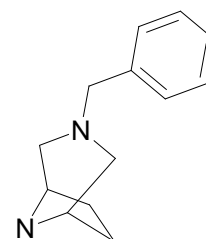
The same training set of known RNA-binding molecules has been used to build a Bayesian model (Bayesian categorization methodology) to learn "good" molecules from the compounds with known activity. Both molecular fingerprints (circular FCFP6 fingerprints) and molecular properties (MW, No. of HBA, No. of HBD, LogP, PSA, No. of rotatable bonds, No. of rings) were involved in the construction of Bayesian model. At the next step, the model has been applied to Life Chemical's HTS Stock compound collection in order to predict RNA-binding compounds. PAINS compounds, as well as those with "bad" and reactive groups have been filtered out from the resulted compound set.



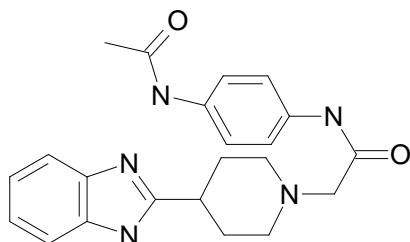
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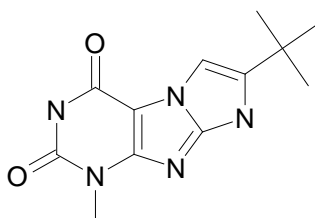
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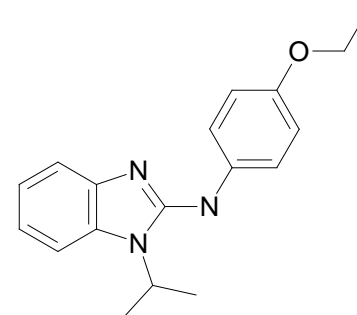
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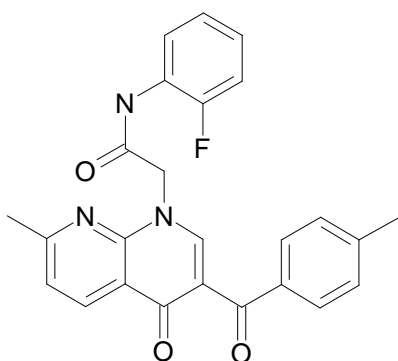
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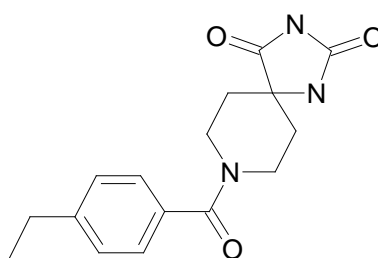
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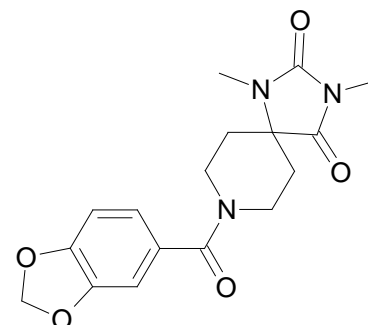
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F5047-0051



F5346-0141

Fig 1. Some representative compounds from Life Chemicals' RNA Focused Library.

To download a file with compound structures for this library, please follow this link:
http://www.lifechemicals.com/downloads/Screening_Libs/13062/RNA