Exploring a New Therapeutic Target Space: Can One Design Small Molecule Drugs for RNA?

Most of the human genome encodes RNAs that do not code for proteins. These non-coding RNAs may affect normal gene expression and disease progression, suggesting a new class of untapped targets for drug discovery.

We have plenty of structural information on RNA, we know there are drugable sites, yet developing small molecule drugs for RNA has been a tremendous challenge. RNA is inherently very flexible and very often due to this flexibility X-ray fails to provide the structural information required for RNA drug design and optimization. We have used NMR to detect binding and to derive a limited number of important structural constraints that have successfully guided modeling and chemistry optimization. We will present examples where, using this approach, small molecule selective RNA binders have been identified.