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ACCEPTED MANUSCRIPT

Advancing Small Ligands Targeting RNA for Better Binding Affinity and Specificity: A Study of Structural Influence through Molecular Design Approach

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Highlights:

- The study demonstrated a molecular design approach for advancing small ligands targeting RNA for better binding affinity and specificity.
- The *in vivo* study of live cell imaging (human prostate cancer cells) indicated these small-sized molecules are able to provide strong interaction signal when binding with RNA in the region of nucleolus and cytoplasm.
- The structurally simple ligand shows much higher RNA-binding affinity than that of a well-studied RNA-selective dye **E36**.
- The advanced ligand shows much higher response (about 4 folds stronger) towards RNA than other types of nucleic acids like DNA in the *in vitro* assay.

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