Development of 3,4,5-Trisubstituted Oxazolidinones as Ligands for Stem-Loop RNA

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There is a highly conserved motif within the 3'-untranslated region (UTR) of a variety of corona- and astroviruses referred to as the s2m motif. It has a unique structure involving an asymmetric bulge, which creates a negatively charged pocket within the stem. This feature could be selectively targeted with small molecules. One of the challenges in the development of small molecules as RNA ligands is achieving specific binding affinity for certain hairpin motifs. Recently, oxazolidinones have shown promise as RNA ligands. Trisubstituted oxazolidinones were shown to have selective binding affinity for a stem-loop RNA motif containing an asymmetric bulge. Using computational methods, we created libraries of oxazolidinones and screened them *in silico* against the s2m motif. Potential hits were further explored through guided, diverse-oriented synthesis and screening. Herein, we report our efforts towards the design and synthesis of 3,4,5-trisubstituted oxazolidinones as potential small molecule ligands for the s2m motif.