**Supporting Information S1. Manual editing of MC-Sym scripts to introduce specific GU base pairs in HDV ribozyme.**

//========== Sequence ==========

sequence( r A1 CUAAGGGUCGGCAGGGUCCACCUCCUCGCGGUCCGACCUGGGCAUGCGGCUUCGCAUGGCUAAGGGACCC )

// ....(((((((..[[[[[[(((.......))))))))))..((((((((..)))))))).....]]]]]]

// CCCCCCC aaaaaaAAAAAAAAAAAAACCCCCCC BBBBBBBBBBBBBBBBBB aaaaaa

// | | | | | | | | | | | | | |

// 5 10 15 20 25 30 35 40 45 50 55 60 65 70

***trans* Watson-Crick/Hoogsteen U23G28 base pair with G28 in *anti* conformation**

//========== Relations ==========

relation(

//this constraint will define the trans watson hoogsteen U23G28

A23 A28 { pairing && 95} 10 )

// ========= Ribose / Restraints =========

//this restraint will define the anti conformation for the G28

ribose\_rst ( structure[A28]

method = ccm,

pucker = C3p\_endo,

glycosyl = anti,

threshold = 2.0 )

***trans* Watson-Crick U23G28 base pair with G28 in *syn* conformation**

//========== Relations ==========

relation(

//this constraint will define the trans watson watson U23G28

A23 A28 { pairing && XXVII} 10 )

// ========= Ribose / Restraints =========

// this restraint will define the syn conformation for the G28

ribose\_rst ( structure[A28]

method = ccm,

pucker = C3p\_endo,

glycosyl = syn,

threshold = 2.0 )