**Supporting Information**

**Targeting the MicroRNA Binding Domain of Argonaute 2: Rational Inhibitor Design and Study of Mutation Effects on Protein-Ligand Interaction**

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\* 5' uuaaugcuaaucgugauagggguu 3'

**Fig. 1**' The generated model of the human Ago2 in complex with miR155 based on the crystal structure of miR-20a (PDB ID: 4F3T). The N domain is shown in blue, the PAZ domain in purple, the mid domain in pink, the PIWI domain in red, linker1in cyan and linker2 in yellow.

\* The sequence of the miR155 in the available crystal structure of Ago2.



**Fig. 2**' Representation of the last frame of MD simulation of the three complexes in which compound 1 binds to binding site of Ago2.



**Fig. 3'** DSSP analysis for the secondary structure fluctuations as a function of time from 0 to 200 ns for three complexes A, B and C.



**Fig. 4'** Hydrogen bond analysis from MD simulation study of interaction of compound **1** with Black: Complex A, Blue: Complex B, Pink: Complex C.

**Table 1'** 2D interaction diagram for the complex protein-ligand after docking interaction. violet: π-Sigma, pink: π-Alkyl, orange: π-Cation, light green: Van der Waals, green: Hydrogen bond, violet: π-π-stacked, cyan: Halogen.

|  |  |  |  |
| --- | --- | --- | --- |
| **No.** | Number of active torsions | CLogP | **Structure** |
| **1** | 4 | 5 |  |
| **2** | 2 | 3.3 |  |
| **3** | 3 | 4.6 |  |
| **4** | 2 | 3.3 |  |
| **5** | 3 | 4.7 |  |
| **6** | 3 | 3.1 |  |
| **7** | 2 | 3.3 |  |
| **8** | 2 | 2.8 |  |
| **9** | 2 | 3.1 |  |
| **10** | 2 | 3.26 |  |