Supporting Information

Efficient Synthesis with Green Chemistry Approach of Novel Pharmacophores of Imidazole-Based Hybrids for Tumor Treatment: Mechanistic Insights from In Situ to In Silico

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Table S1. The binding interactions of Compounds in the Active site of hCA-IX and hCA-II.

Compounds	Score	Ligand atom	Receptor atom	Bond type	Bond length (Å)
			hCA-IX		
1	-3.93	N10	ND1-HIS200	HBA	2.90
		O15	O-HOH603	HBA	2.87
		O17	NH2-ARG196	HBA	2.61
		O17	NH1-ARG196	Ionic	3.78
3	-3.49	N5	OE1-GLN203	HBD	3.14
		O14	HE2-GLN224	HBA	3.02
		O14	O-HOH603	HBA	2.00
		N7	O-HOH664	HBA	1.68
			O-HOH686	HBA	1.36
4	-3.77	S15	O-HOH664	HBA	3.87
		O14	ND1-HIS200	Ionic	3.45
		N13	NH2-ARG196	HBA	2.30
		O2	O-HOH603	HBD	2.19
7	-3.92	O18	NH2-ASN198	HBA	2.71
		O17	NE1-TRP141	HBA	2.87
		N1	OE2-GLN203	HBD	2.44
		O18	O-HOH664	HBD	1.98
		N1	O-HOH552	HBD	2.61
8	-3.74	N11	ND1-HIS200	HBA	3.16
		O18	NH2-ARG196	HBA	2.63
		O18	NH1-ARG196	Ionic	3.85
		O18	NH2-ARG196	Ionic	2.63
		6-ring	NE2-HIS140	π-H	2.89
9	-3.92	O8	NH2-ARG196	HBA	2.43
		O16	ND1-HIS200	HBA	2.96
		N11	HOH603	HBA	1.74
10	-3.93	O18	NH2-ARG196	HBA	2.66
		O18	NH1-ARG196	Ionic	3.94
		O18	NH2-ARG196	Ionic	2.66
11	-3.66	O7	ND1-HIS200	HBA	3.50

		O26	O-HOH664	HBA	3.14
		6-ring	NE2-GLN203	π-H	2.85
			hCA-II		
1	-4.97	O15	ZN-262	Metallic	2.37
		O3	HD2-ASN62	HBA	3.12
		O15	NE2-HIS94	HBA	3.01
2	-5.03	N-10	NE2-GLN92	HBA	3.39
		6-ring	ND2-ASN62	π-H	2.83
		O8	HG1-THR200	HBA	3.78
3	-4.35	N5	O-HOH370	HBD	3.64
		N10	N-THR199	HBA	3.13
		O15	ND2-ASN62	HBA	2.62
		O15	ND2-ASN67	HBA	2.98
4	-4.29	N12	OD1-ASN67	HBD	3.22
		O7	ND2-ASN62	HBA	3.19
		S15	N-THR199	HBA	3.14
		S15	OG1-THR199	HBA	4.02
9	-4.58	O16	O-PRO201	HBD	3.06
		S7	N-THR199	HBA	3.74
		O8	OG1-THR200	HBA	2.42

HBA = Hydrogen bond acceptor, HBD = Hydrogen bond donor.