Supplementary Material for

X-ray crystallographic and kinetic studies of biguanide containing aryl sulfonamides as Carbonic anhydrase inhibitors

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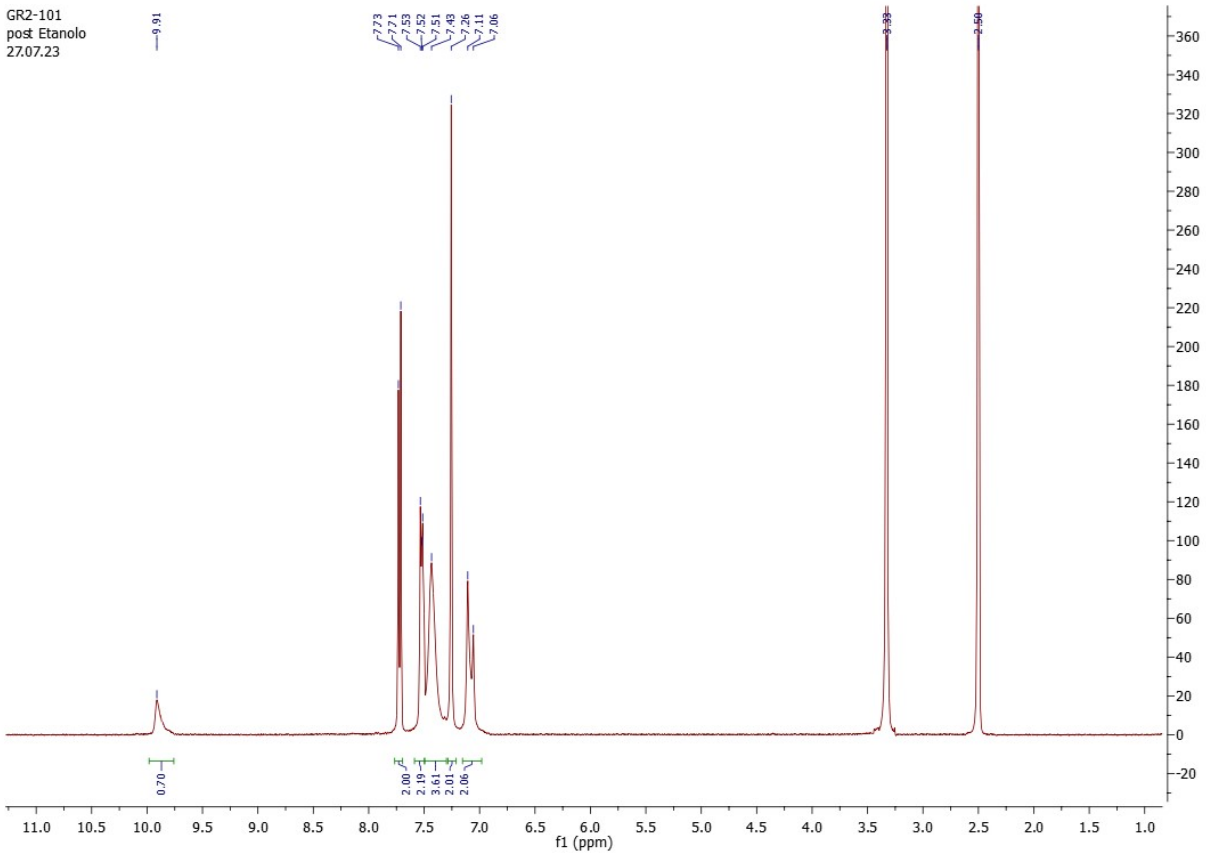
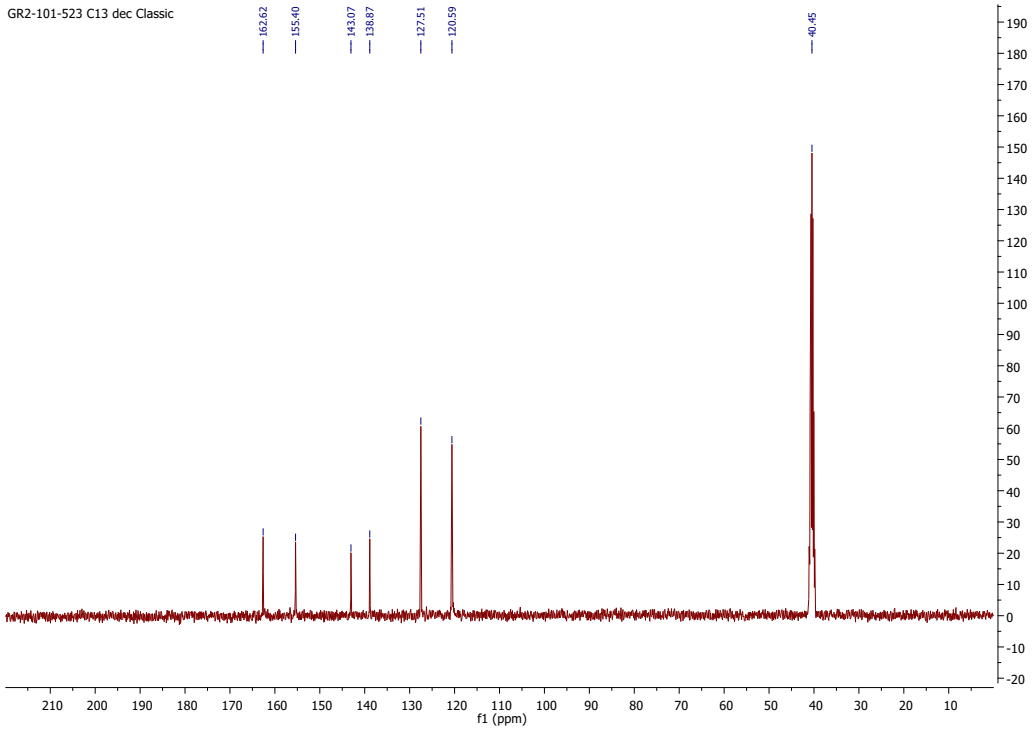
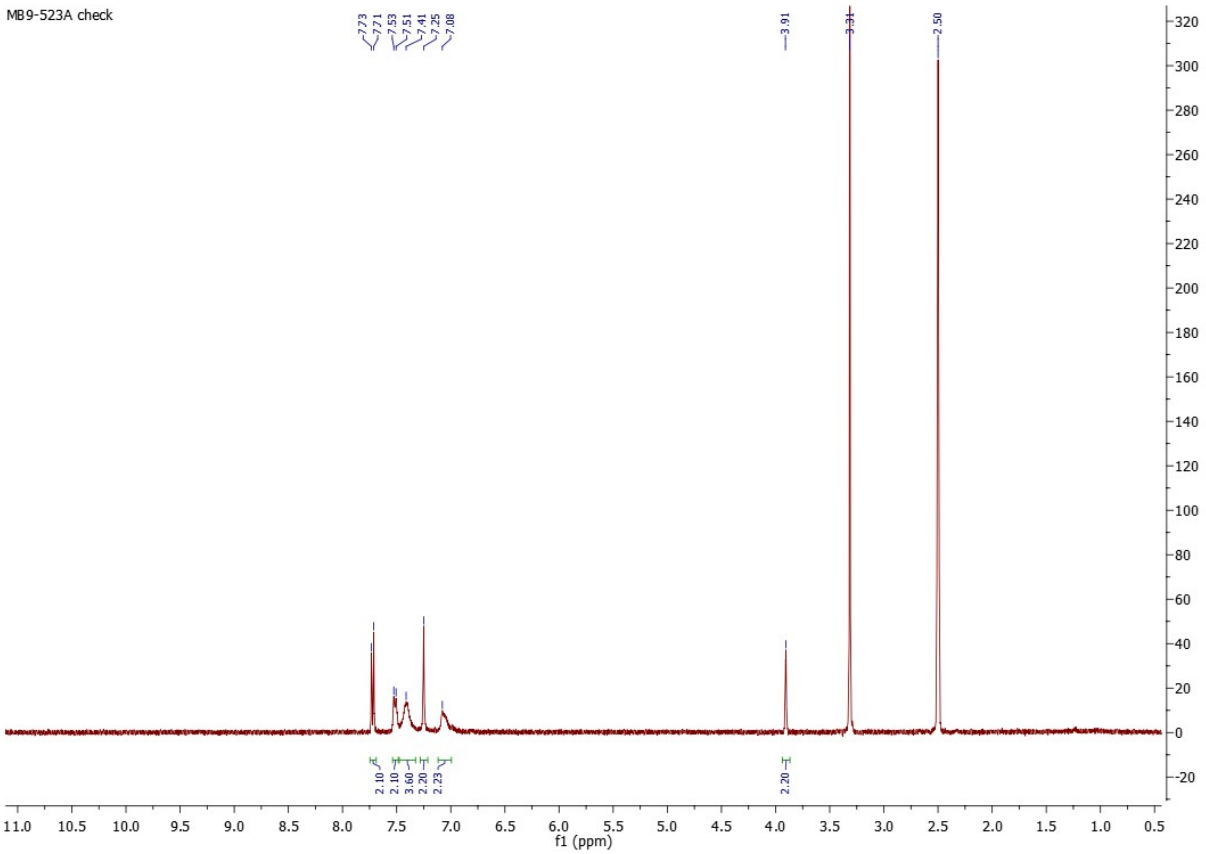
[1]H NMR spectrum of compound **5a** (400 MHz, DMSO-*d6*)



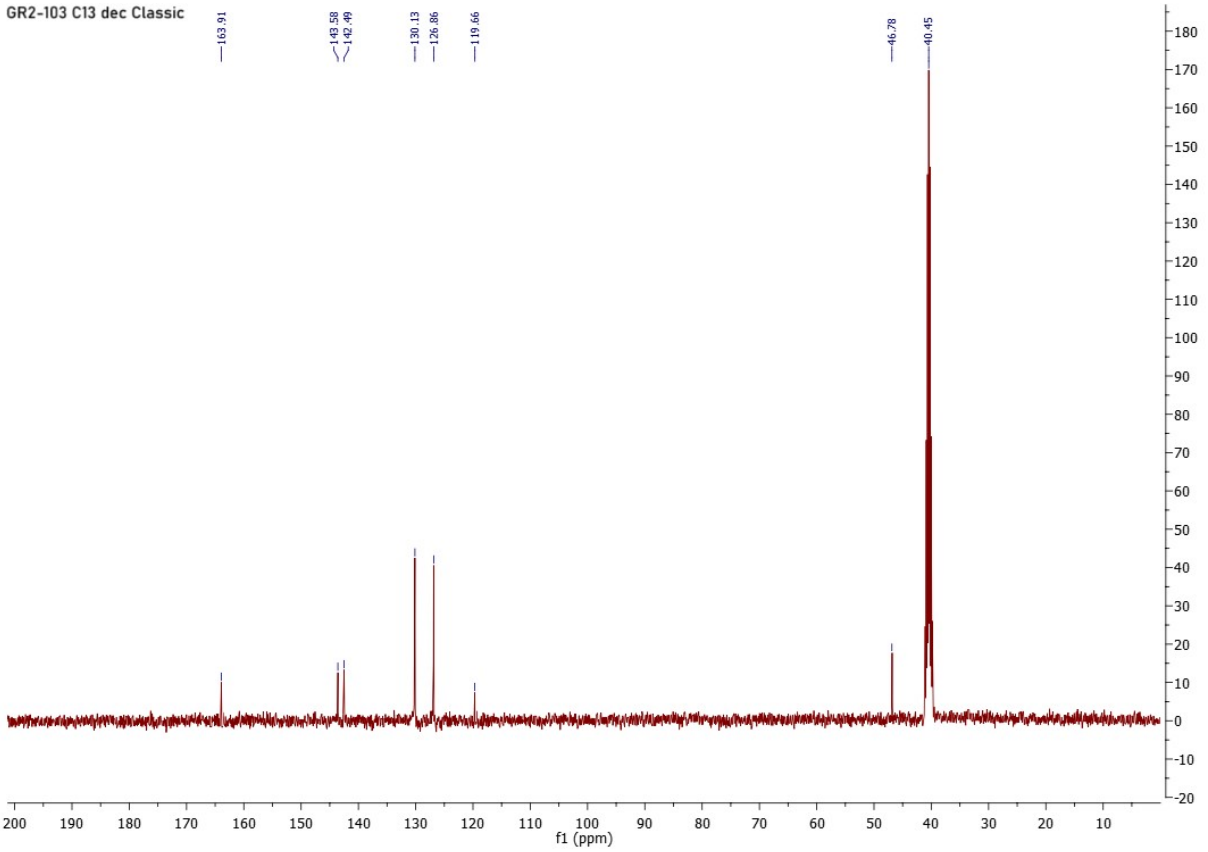
[13]C NMR spectrum of compound **5a** (100 MHz, DMSO-*d6*)



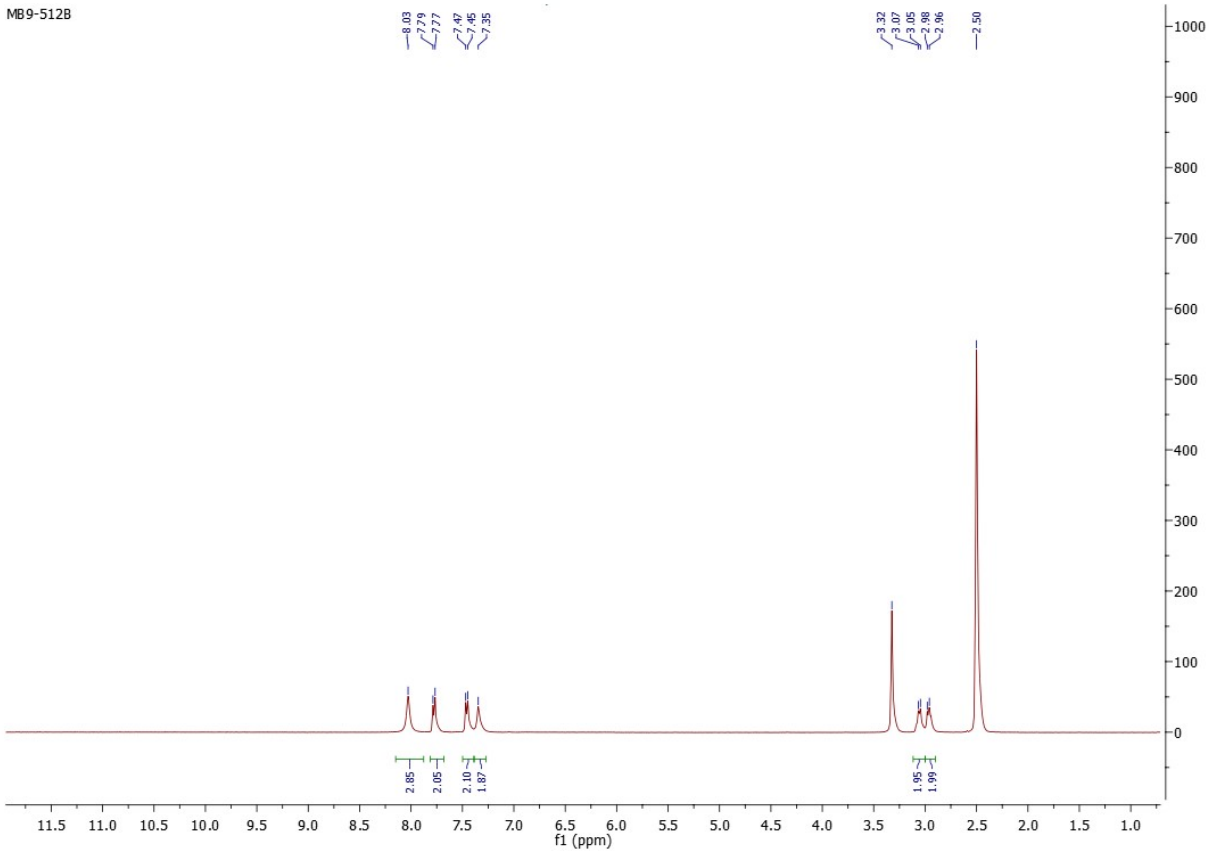
^{1}H NMR spectrum of compound **5b** (400 MHz, DMSO-*d6*)



^{13}C NMR spectrum of compound **5b** (100 MHz, DMSO-*d6*)



^{1}H NMR spectrum of compound **5c** (400 MHz, DMSO-*d6*)



^{13}C NMR spectrum of compound **5c** (100 MHz, DMSO-*d6*)

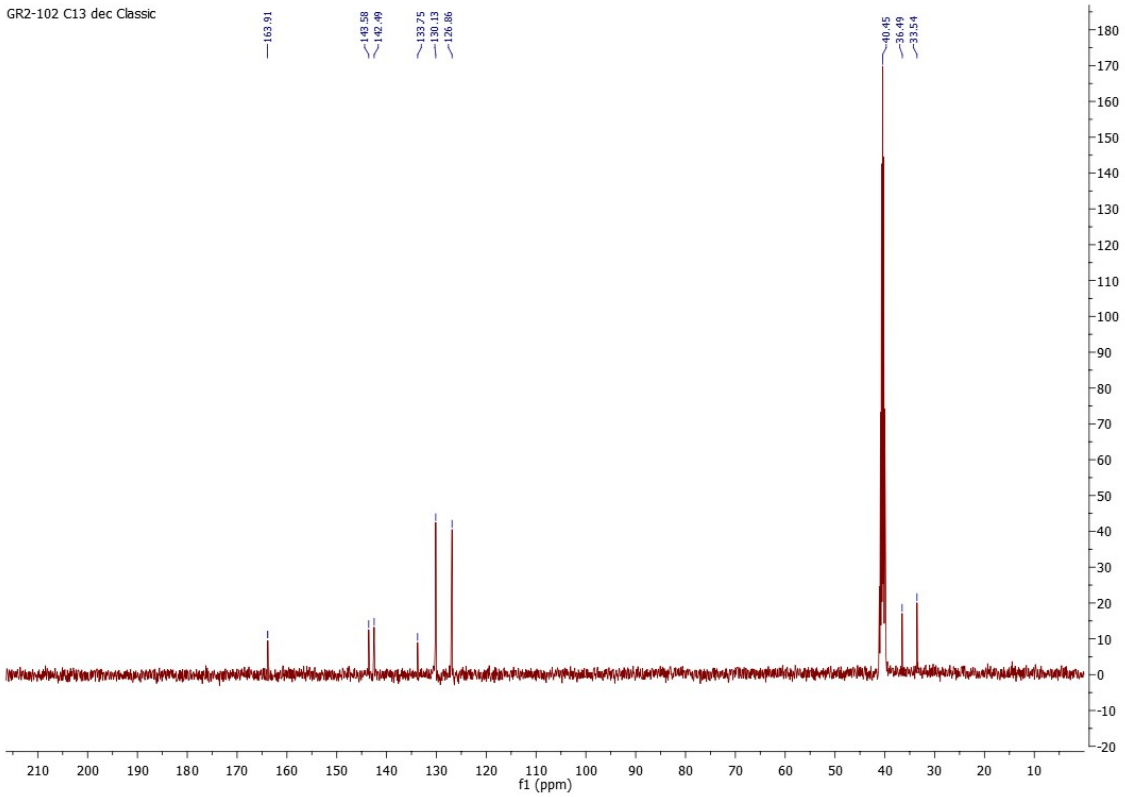


Table S1. Summary of Data Collection and Refinement Statistics Values in brackets refer to the highest resolution shell.

Data Collection statistics			
	CA II-5b	**CAII-5b with glycerol**	**CA XII-5b**
PDB ID	8ROU	8ROW	8RNS
Wavelength (Å)	1.0001	0.9718	1.0001
Space Group	P 2_1	$P2_1$	P 21
Unit cell (a, b, c, α, β, γ) (Å,)	42.28 41.09 72.29 90 104.20 90	42.44 41.30 72.03 90 104.29 90	41.98 41.33 71.81 90 103.87 90
Limiting resolution (Å)	70.08-1.08 (1.10-1.08)	40.02-1.05 (1.07-1.05)	40.76-1.14 (1.16-1.14)
Unique reflections	102568 (5042)	107024 (4661)	85727 (3897)
Rmerge	0.081 (1.403)	0.049 (0.706)	0.07 (1.351)
Rmeas	0.089 (1.591)	0.054 (0.801)	0.076 (1.547)
Redundancy	5.9 (4.5)	6.1 (4.5)	5.9 (4.3)
Completeness overall (%)	99.8 (99.7)	95.0 (83.7)	98.2 (90.0)
<I/σ(I)>	9.8 (1.1)	16.7 (2.2)	12.0 (1.1)
CC (1/2)	1.0 (0.3)	1.0 (0.7)	1.0 (0.4)
Refinement statistics			
Resolution range (Å)	70.08-1.08	40.02-1.05	40.76-1.14
Rfactor	0.1301	0.1160	0.1415
Rfree	0.1515	0.1386	0.1614
r.m.s.d. bonds (Å)	0.0118	0.0124	0.0113
r.m.s.d. angles ( )	1.8997	1.9011	1.7661
Ramachandran statistics (%)			
Most favored	97.3	97.3	96.9
additionally allowed	2.7	2.7	3.1
Outlier regions	0.0	0.0	0.0
Average B factor (Å^2)			
All atoms	15.1	13.9	17.9
Inhibitors	14.6	13.6 / 23.1	23.5
Solvent	17.1	15.8	20.0

Table S2. Summary of Data Collection and Refinement Statistics Values in brackets refer to the highest resolution shell.

Data Collection statistics	
	CA II-5c
PDB ID	9H0V
Wavelength (Å)	1.0002
Space Group	P 21
Unit cell (a, b, c, α, β, γ) (Å,)	42.43 41.26 72.47 90 104.72 90
Limiting resolution (Å)	35.56-1.40 (1.42-1.40)
Unique reflections	43258 (2316)
Rmerge	0.040 (0.200)
Rmeas	0.044 (0.216)
Redundancy	6.2 (6.7)
Completeness overall (%)	90.3 (97.4)
<I/σ(I)>	24.2 (8.6)
CC (1/2)	0.999 (0.981)
Refinement statistics	
Resolution range (Å)	35.56-1.40
Rfactor	0.0991
Rfree	0.1380
r.m.s.d. bonds (Å)	0.0105
r.m.s.d. angles ( )	1.9264
Ramachandran statistics (%)	
Most favored	96.1
additionally allowed	3.9
Outlier regions	0.0
Average B factor (Å²)	
All atoms	16.8
Inhibitors	22.4 / 30.9
solvent	31.6

>hCA II

MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHAFNVEFDDSQDKAVLKGGPLDGTYR
LIQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGDFGKAVQQPDGLAVLGIFLKVGSAKPGLQKVVDVLDSIKTKGKSADFTNF
DPRGLLPESLDYWTYPGSLTTPPLLECVTWIVLKEPISVSSEQVLKFRKLNFNGEGEPEELMVDNWRPAQPLKNRQIKASFK

>hCA XII mimic

MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRILNNGHSFKVNFDDSQDKAVLKGGPLDGTYR
LTQFHFHWGSLDGQGSEHTVDKKKYAAELHLVHWNTKYGDASKASQQPDGLAVLGIFLKVGSAKPGLQKVVDVLDSIKTKGKSADFTNF
DPRGLLPESLDYWTYPGSLTTPPLNETVTWIVLKEPISVSSEQVLKFRKLNFNGEGEPEELMVDNWRPAQPLKNRQIKASFK

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hCA II   MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRIL  60
hCA XII  MSHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSLRIL  60

         NNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYAAELHL  120
         NNGHSFKVNFDDSQDKAVLKGGPLDGTYRLTQFHFHWGSLDGQGSEHTVDKKKYAAELHL  120

         VHWNTKYGDFGKAVQQPDGLAVLGIFLKVGSAKPGLQKVVDVLDSIKTKGKSADFTNFDP  180
         VHWNTKYGDASKASQQPDGLAVLGIFLKVGSAKPGLQKVVDVLDSIKTKGKSADFTNFDP  180

         RGLLPESLDYWTYPGSLTTPPLLECVTWIVLKEPISVSSEQVLKFRKLNFNGEGEPEELM  240
         RGLLPESLDYWTYPGSLTTPPLNETVTWIVLKEPISVSSEQVLKFRKLNFNGEGEPEELM  240

         VDNWRPAQPLKNRQIKASFK  260
         VDNWRPAQPLKNRQIKASFK  260
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Figure S1. Amino acid sequence alignment of hCA II and hCA XII. Residues of hCA II bolded in red were replaced with the corresponding residues from hCA XII to create the mimic proteins.