3D QSAR Selectivity Analyses of Carbonic Anhydrase Inhibitors: Insights for the Design of Isozyme Selective Inhibitors

(Supporting Information)

Alexander Weber[1,4], Markus Böhm[3], Claudiu T. Supuran[2]*, Andrea Scozzafava[2], Christoph A. Sotriffer[1], and Gerhard Klebe[1]*

[1] Department of Pharmaceutical Chemistry, University of Marburg, Marbacher Weg 6, D-35032 Marburg, Germany.

[2] Università degli Studi di Firenze, Dipartimento di Chimica, Laboratorio di Chimica Bioinorganica, Via della Lastruccia, 3, Rm. 188, I-50019 Sesto Fiorentino (Florence), Italy.

[3] Pfizer Global R&D, Eastern Point Road, Groton, Connecticut 06340

[4] Discovery IT, ALTANA Pharma AG, Konstanz, Germany.

---

* Corresponding Authors, Phone: +49 6421 28 21313, Fax: +49 6421 28 28994, E-mail: klebe@mailer.uni-marburg.de (GK) and Phone: +39-055-4573005, Fax: +39-055-4573385, E-mail: claudiu.supuran@unifi.it (CTS).

Tab. S01) Parameters of the grid boxes used for CoMFA and CoMSIA analyses.

	1 Å Grid			2 Å Grid		
	x	y	z	x	y	z
Lower corner	-15.8	-23.5	-11.0	-15.8	-23.5	-11.0
Higher corner	10.0	10.2	13.4	10.0	10.2	13.4
Grid Spacing	1.0	1.0	1.0	2.0	2.0	2.0
Numer of steps	26	34	25	13	17	13
Grid points		22100			2873	

Tab. S02) Distances between atoms that are involved in a hydrogen bond network in CA I and CA II. For each isozyme, one complex structure (CA I: *1azm*, 2.0 Å resolution, **A_18**; CA II: *1cil*, 1.6 Å, **B_05**) and one apo structure (CA I: 2cab, 2.0 Å; CA II: 2cba, 1.54 Å) were selected to determine the distances.

CA I	**Atomtyp**	**Distance (2cab)**	**Distance (1azm)**
His94 – Gln92	ND1 – OE1	2.7 Å	2.8 Å
Gln92 – Asn69	NE1 – OD1	3.1 Å	3.2 Å
Asn69 – Glu58	ND2 – OE1	3.5 Å	3.6 Å
CA II	**Atomtyp**	**Distance (2cba)**	**Distance (1cil)**
His94 – Gln92	ND1 – OE1	2.7 Å	2.8 Å
Glu69 – Arg58	OE2 – NH2	3.1 Å	3.0 Å
Glu69 – Arg58	OE1 – NE	2.7 Å	2.7 Å
Glu69 – Arg58	OE1 – NH2	3.1 Å	3.2 Å