The Crystal Structure of Human CA II Bound to a Strong Benzenesulfonamide Inhibitor

Anna Di Fiore[a], Giuseppina De Simone[a], Valeria Menchise[a], Carlo Pedone[a], Angela Casini[b], Andrea Scozzafava[b], Claudiu T. Supuran[b], [a]*IBB-CNR, Naples, Italy.* [b]*University of Florence, Florence, Italy.* E-mail: difiore@chemistry.unina.it

Carbonic anhydrases (CAs) are ubiquitous metalloenzymes present in prokaryotes and eukaryotes, which catalyze the reversible hydration of CO_2. In previous studies we have investigated by means of X-ray crystallography the rational design of sulfonamide/sulfamate/sulfamide inhibitors of this enzyme, which is involved in a multitude of physiological and pathological processes [1]. At least fourteen different CA isozymes are presently known in humans, and many of them are targets for the design of inhibitors with potential use as antiglaucoma, anti-obesity, or anticancer drugs among others. A class of CA inhibitors which showed very promising applications are the thioureas obtained from isothiocyanato sulfonamides and amines, hydrazines or amino acids. Such compounds generally showed potent inhibitory activity against the human cytosolic isozyme CA II as well as the transmembrane, tumor-associated isozyme CA IX, being thus interesting candidates for developing antiglaucoma/antitumor therapies based on them.

Here we report the first X-ray crystal structure of a thioureido-benzensulfonamide derivative in complex with human CA II as well as its inhibitory properties against isozymes I, II and IX [2].

[1] Supuran C.T., Scozzafava A., Casini A., *Med. Res. Rev*., 2003, **23**, 146. [2] Di Fiore A., De Simone G., Menchise V., Pedone C., Casini A., Scozzafava A., Supuran C.T., *Bioorg. Med. Chem. Lett*., 2005, *in press.*

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