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Abstract: Past, present and future structure-function studies of carbonic anhydrase

The carbonic anhydrases (CA) comprise of a group of well-studied and distinct gene families (α,β and γ) of mostly zinc-metalloenzymes that catalyze the hydration of carbon dioxide. These ubiquitous enzymes, present throughout virtually all living organisms, including animals, plants, algae, bacteria, and archaebacteria, are involved in a vast number of physiological processes and therefore are a uniquely broad and interesting family of enzymes, since the reaction they catalyze is linked to respiration, acid-base homeostasis, photosynthesis, and other biosynthetic pathways. The mammalian α-class of CA is comprised of 14 expressed isozymes (CA I – XIV) with varying tissue distributions and catalytic activity. Human CA II is the most extensively studied of these isozymes, as it has widespread tissue distribution and because it is the most efficient of the HCAs with a catalytic turnover rate of 10^6 s^{-1}.

From a basic science stand-point, HCA II is an excellent model system for the study of proton transfer, the rate limiting step in CA catalyzes. Recent studies, combining high-resolution x-ray and medium resolution neutron crystallography, with molecular dynamics and kinetic studies have yielded a new level of understanding of the proton transfer mechanism.

In addition, from an applied science application, the broad involvement of CA in physiological processes makes it an attractive drug target in the treatment of human diseases such as glaucoma and cancer, and the possible control of mosquito populations and the human pathogens they carry.

Both current basic science and application studies of CA will be discussed and the possible future directions of CA studies will be considered.

Bio-sketch: Robert McKenna received a Ph.D. (1989) in crystallography at the University of London under the direction of Professor Stephen Neidle and did his postdoctoral work with Professor Michael G. Rossmann at Purdue University. Since 1999 he has work at the University of Florida where he is currently an Associate Professor. His research interests are broadly based on the elucidation of structural information of biological molecules, and correlating this knowledge to functional and/or interaction data, to explain the role of structure on function.