Inhibition of carbonic anhydrase IX: a new strategy against cancer.


Abstract

Of the thirteen active carbonic anhydrase (CA) isozyms, the transmembrane isoform CA IX has been shown to be linked with carcinogenesis. CA IX presents an ectopic expression in a multitude of carcinomas derived from cervix, uteri, kidney, lung, oesophagus, breast, colon, etc., contrasting with its restricted expression in normal tissues, namely in the epithelia of the gastrointestinal tract. It has been demonstrated that this membrane-bound CA is strongly overexpressed in hypoxic tumors, participating in tumor cell environment acidosis and contributing to malignant progression and poor treatment outcome. Targeting CA IX could thus be an important means of controlling cancer disease. Modulation of extracellular tumor pH via inhibition of CA IX activity represents a promising approach to novel anticancer therapies. Much attention has recently been paid to the CA IX inhibitors drug design, and efforts have been made to obtain isozyme IX inhibitors, with putative applications as antitumor drugs/diagnostic agents. This review will focus on the different CA IX inhibitors described in the literature which could represent excellent potential as candidate therapeutic agents in cancer chemotherapy.

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