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Commentary

Microbiological Cytosine Hydrolase that Facilitates Gene-Directed Enzyme and Antibody Prodrugs

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DESCRIPTION

An amid hydrolase called cytosine deaminize catalysis the deamination of cytosine into uracil and ammonia. Microorganisms that have the ability to transform the non-toxic 5-fluorocytosine into the toxic 5-fluorouracil have been found to contain Congenital Dyserythropoietic Anemia (CDA). The most effective chemotherapeutic regimens in cancer therapy are 5-fluorouracil and its oral product capecitabine, which are used to treat a variety of neoplasms, including head and neck squamous cell carcinoma, gastrointestinal adenocarcinoma, and uterine cervix. Inhibitors of vascular endothelial growth factor and 5-FU have recently been recognized as an effective cancer treatment strategy.

The activity of 5-FU is basically attributed to its affinity to block the activity of cellular thymidylate synthase, thus preventing DNA replication. Nevertheless, the main obstacles preventing this enzyme from being used in clinical settings are its brief half-life, relative lack of selectivity, and drug resistance to 5-FU. Thus, one of the most sophisticated anticancer strategies involves modifying the toxicity and target ability of 5-FU through the prodrug 5-FC-mediated CDA. In comparison to more conventional anticancer treatments like chemotherapy and radiotherapy, the CDA-5-FC has been recognized as a targeted/directed therapy with few side effects, higher effectiveness, and lower proliferative activity. One of the most effective cutting-edge technologies for cancer therapy is the CDA-5-FC prodrugs enzyme-mediated therapy. In order to avoid the chemotherapeutic side effects of conventional approaches, the strategy of gene-directed enzyme prodrug therapy, or "suicide gene therapy," using CDA, has recently been developed.

This drug-mediated system's enhanced proliferative activity results from the overactive uracil pathway in tumour cells when compared to normal cells. Recently, a number of strategies have been concentrated on the analysis of CDA with high turnover and catalytic efficiency, less antigenicity from different microorganisms, and the activation of the prodrug 5-FC into active 5-FU for targeting the tumour cells only while having no effect on normal cells. Although yeast enzymes such as CDA have received much less attention than bacterial CDA, it has been found that yeast CDA has a higher catalytic efficiency for delaminating 5-FC. However, the main obstacle limiting CDA's wide range of clinical applications is their thermal and conformational/structural stability. Additionally the intrinsic CDA's ability to delaminate the non-toxic 5-FC into the toxic 5-FU was thought to be responsible for the 5-FC's potential antifungal activity.

The higher solubility in water and smaller molecular size of 5-FC, which enable its quick diffusion in the body, contribute to its superior therapeutic effectiveness. Practically speaking, 5-FU has a wide range of bioactivity against various pathogenic microorganisms, such as *Candida*, *Cryptococcus*, *Philophora*, *Cladosporium*, and *Aspergillus*, in addition to its antiprotozoal activity against *Leishmania* and *Acanthamoeba*.

An extraordinary clinically affordable non-mammalian enzyme called CDA is used to mediate the transformation of 5-FU into 5-FC after external infusion. Pyrimidine-nucleoside phosphorylates and CDA have converted cytosine into cytidine and uracil.

Cytidine and cytidine monophosphate are hydrolyzed by ribosylpyrimidine nucleosides and pyrimidine 5-nucleotide nucleosides to produce cytosine. 5-FU has been shown to have increased anti-proliferative activity when combined with a variety of antifungal azole agents, particularly fluconazole and ketoconazole for colorectal cancer. Practically speaking, CDA, a selective strategy for treating human fungal pathogens, may have contributed to 5-FC's effective antifungal activity. Cytosine and 5-FC are rival nucleotides that compete to cross the plasma membrane by cytosine permeate. After being hydrolyzed by CDA into uracil or 5-FU, respectively, these nucleotides are then transported across the membrane. Only the presence of an active CDA is necessary for the conversion of 5-FC to 5-FU; some fungi that have been labeled as 5-FU resistant fungi do not have an active CDA.

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