

dUTPase Enzyme A Marker for Cellular Proliferation

Background

dUTPase is an enzyme that hydrolyzes dUTP to dUMP and pyrophosphate, a reaction that is believed to prevent misincorporation of dUMP into DNA during replication and repair by limiting intracellular dUTP pools. In certain human tumor cell lines, increased dUTPase levels leads to an increase in resistance to the chemotherapeutic agent fluorodeoxyuridine indicating that dUTPase has a role in fluorodeoxyuridine toxicity. Since dUTPase levels increase during cell proliferation in a cell-cycle dependent manner, it is suggested that this enzyme could be used as a proliferation marker. Other human proteins such as Ki-67, C5F10 and DNA polymerase alpha, which increase during cell proliferation, have been reported to be useful as prognostic indicators of the status of a cell. For example, Ki-67 has been used as a proliferation marker for lymphoproliferative diseases, and central nervous system and breast tumors. However, this protein does not distinguish between benign and malignant forms of tumors. Given these difficulties, there is a great unmet need in the field for a proliferation marker that could be used to accurately assess the proliferation status of a cell. **The present invention describes the use of dUTPase enzyme as a marker for the determination of proliferation status of a cell in both neoplastic and normal tissues.**

Description of the Technology

Scientists at UMDNJ have isolated and completely sequenced the human dUTPase gene. In addition, the dUTPase enzyme has been isolated and purified. These studies have revealed the presence of two isoforms of the enzyme, a nuclear form and a cytoplasmic form that is targeted to the mitochondria. The invention also provides methods for determining the proliferation status of a cell and the efficacy of antineoplastic agents using dUTPase. The dUTPase enzyme of the present invention can be used as a cellular proliferation marker to diagnose tumors and to determine responses to chemotherapy.

Advantages

- Unlike ki-67, dUTPase is essential to the survival of a cell. As a result, false negatives can be eliminated.
- Unlike Ki-67, which is rapidly degraded following cell death, dUTPase is a stable enzyme and can be detected even in the necrotic centers of large tumors.
- The expression of Ki-67 is nutritionally dependent, while the expression of dUTPase does not fluctuate with nutrition.

Applications

- For the determination of the proliferation status of a cell in both neoplastic and normal tissues.
- To determine effective cancer chemotherapy
- For the development of antimicrobial and antineoplastic agents
- To determine efficacy of antineoplastic drugs such as fluorodeoxyuridine or drugs that affect thymidylate synthesis.

Deliverables

File SOM 94-12/Ladner
Antibodies dUTPase

Patent Status

- . •United States patent granted on October 5, 1999
- . •Patent Number: 5,962,246

Licensing Opportunity

This technology is available for licensing non-exclusively or exclusively.

Contact

Peter Golikov, MS, MBA
Director, Ventures and Licensing
University of Medicine and Dentistry of New Jersey
335 George Street
New Brunswick, NJ 08901
Direct Phone: (732)-235-9355
Main Office Phone: (732)-235-9350
Facsimile: (732)-235-9358
golikope@umdnj.edu

File SOM 94-12/Ladner