



Office of Technology Management

UIC2 - Therapeutic and Diagnostic Antibody

Technology Reference

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Inventor

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Field

Antibodies

Oncology

Key Words

Chemotherapy

MDRI gene

PGP

Neoplastic Cells

License Status

Seeking Licensing Partner

- Exclusive-therapeutic
- Nonexclusive-diagnostic

Patent Status

US patent 6,479,439

Overview

The major determinant of the multidrug resistance phenomenon is the expression of P-glycoprotein (Pgp, the product of the MDR1 gene) on the surface of tumor cells. Pgp is a large protein that forms a pore-like structure in the membrane and extrudes chemotherapy drugs from tumor cells. The vast majority of medicines used in treatment of cancer possess the ability to induce Pgp expression in tumors, resulting in their increased resistance to chemotherapy. Thus, inhibition of the Pgp efflux activity in cancer cells represents a major challenge in cancer treatment. Introduction of efficient Pgp inhibitors in clinical practices would result in increased survival and better quality of life for cancer patients.

UIC investigators have developed a therapeutic monoclonal antibody, UIC2, which causes significant inhibition of Pgp-mediated efflux of chemotherapy drugs. In tumor cells exposed to common chemotherapy agents such as taxol, doxorubicin, and gleevec, the Pgp efflux pump is inactivated by the presence of the UIC2 antibody. That, in turn, leads to tumor cell death at relatively low concentrations of anti-cancer drugs. This strategy, therefore, may result not only in efficient eradication of tumors but also in decreased drug toxicity and fewer side effects.

Another application of the technology is the use of the UIC2 monoclonal antibody to inhibit Pgp-mediated efflux function of the blood-brain barrier. This method allows physicians to use anti-cancer and anti-stroke drugs that would otherwise be extruded from the brain and never reach their target sites. It was also demonstrated that UIC2 could be utilized to detect, isolate and modulate human hematopoietic stem cells.

Technical Summary

UIC2 is a monoclonal antibody that specifically blocks the multidrug transporter p-glycoprotein (PGP) – an ATP-driven efflux pump – by trapping the PGP in a conformation that prohibits efflux. Multidrug resistance, a hallmark of failed chemotherapy, has been linked to the MDR1 gene that encodes PGP. Blocking PGP's efflux function would allow chemotherapeutic agents to reside in the neoplastic cells for longer periods of time. Although antibodies to PGP have existed for many years, the UIC2 antibody is the only one that results in complete PGP inhibition upon binding.

Benefits

- UIC2 monoclonal antibody specifically the multidrug transporter p-glycoprotein and be used with one or more chemotherapeutic agents to enhance their efficacy and combat multidrug resistance.
- Enhance the efficacy of a variety of drugs.
- Co-administered therapy to enhance the efficacy of CNS acting drugs, NSAIDS, and HIV therapeutics.

Areas of Application

- Cancer
- HIV/AIDS
- Inflammation
- CNS
- Stem Cells

Stage of Development

- *In vitro* studies done

