A Novel Specific Inhibitor of the Cyclin Kinase Inhibitor p21 for Breast Cancer Therapy

(VA Reference No. 03-080)

Use of antisense p21 oligodeoxynucleotide for therapeutic applications in breast cancer

Technology
Antisense p21 oligodeoxynucleotide for treatment of breast cancer

Inventor
Robert Weiss, M.D.
Sacramento VA Medical Center

Key Features
- Inhibits the cyclin kinase inhibitor p21Waf1/Cip1
- Causes inhibition of p21 protein levels and decrease in angiogenesis
- Could be used with radiation therapy and chemotherapy

Stage of Development
Reduced to practice with successful demonstration in both in-vitro and animal models

Keywords
Therapeutic
- Oncology
- Breast cancer

Patent Status
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Contact
Lee Sylvers, Ph.D.
Technology Transfer Program
Department of Veterans Affairs
Office of Research & Development (12TT)
810 Vermont Avenue, NW
Washington, DC 20420
Phone: 202-461-1714
Fax: 202-254-0460
E-mail: lee.sylvers@va.gov

Technology
The Department of Veterans Affairs has developed an antisense p21 oligodeoxynucleotide (ODN) technology that specifically inhibits the cyclin kinase inhibitor p21Waf1/Cip1. The antisense p21 ODN has potential therapeutic application for the treatment of breast cancer.

Description
The VA has developed novel targets for breast cancer therapy. P21Waf1/Cip1 is a potent inhibitor of cyclin-dependent kinase that has been shown to be a critical downstream effector of p53, a tumor suppressor protein. P21 has been clearly demonstrated to have an anti-apoptotic, pro-survival function in cells which have had their DNA damaged (as in conventional chemotherapy), and antisense p21 administered to cancer cells in-vitro and in animal models results in a pro-apoptotic effect and decreased tumor growth, respectively. Thus the use of antisense p21 ODN has potentially important therapeutic applications as combination chemotherapy with conventional cancer chemotherapeutic agents.

Competitive Advantage
The therapeutic potential of the technology has been demonstrated in both in-vitro and animal models. Research results demonstrate that the technology causes inhibition of p21 protein levels in-vitro, inhibition of breast cancer growth in mouse model, a decrease of angiogenesis, and attenuation of p21 resulting in apoptosis in human breast cancer cell lines.

This invention:

- Provides a narrow therapeutic approach to breast cancer resulting in a reduction or elimination of side effects compared to established radiation and chemotherapy methods.
- Could be used in conjunction with radiation therapy and chemotherapy.

Status
The Department of Veterans Affairs is looking for a partner for further development and commercialization of this technology through a license, and the VA inventors are available to collaborate with interested companies through a Cooperative Research and Development Agreement (CRADA).