

# **A Novel Topoisomerase 1 Binding Protein for Use in Cancer Diagnostics and Cancer Therapeutics**

## **Background**

Topoisomerase 1 is a DNA binding protein that regulates DNA topology. This enzyme is the target of antineoplastic agents such as camptothecins. Several other proteins are presumed to be necessary for top1 functions and in the cytotoxic mechanisms of camptothecins. Previous studies at UMDNJ have identified a novel topoisomerase 1 and p53 binding protein called topors. This protein was characterized to be a RING protein rich in serine and arginine domains. The RING domain was shown to be similar to SUMO and E3 ubiquitin ligases. Recent studies in other labs have revealed the relevance of postranslational modification of proteins via covalent attachment of SUMO in cell cycle progression, stress response and signal transduction.

**The present invention relates to further characterization of this novel protein and its uses in cancer diagnostics and therapeutics.**

## **Description of the Technology**

Topors protein was detected in normal human tissue samples but not in matched human tumor tissue specimens from kidney, colon, endometrium and lung. Consistent with the protein data, endometrium and colon tumor tissue samples lacking topors protein did not reveal measurable mRNA levels. Furthermore, overexpression of Topors in cervical cancer cell lines leads to cell death. Thus, it is proposed that lack of topors in cancer cells contributes to the selection and persistence of mutant phenotype and progression to tumorigenesis. Additionally, it was shown that topors functions as an E3-type ubiquitin ligase and E3-type SUMO ligase for topoisomerase and p53. Thus, topors is a dual function ubiquitin and SUMO ligase. Collectively these data indicate that topors is a candidate tumor suppressor gene similar to p53 and the loss of topors SUMO ligase activity could lead to cancer. Furthermore, it is possible that modulation of topors ubiquitin and/or SUMO ligase activities may be useful in diseases associated with alterations in ubiquitin or SUMO pathways, including cancer.

## **Applications**

### **I. Diagnostic and Screening**

- . • The topors antibody and gene sequence will be useful for research involving the cellular role of topors
- . • The topors antibody and gene sequence will be useful in screening for the absence or presence of topors in cancer tissues
- . • Genetic screening to identify individuals susceptible to developing cancer

### **II. Therapeutics**

- . • In gene therapy to re-introduce topors gene into cells lacking the gene
- . • In vaccination strategies to treat diseases associated unchecked cell proliferation
- . • Both the antibody to topors and topors protein can be used to modulate DNA repair process
- . • The topors gene sequence and protein will be useful in efforts to develop small

molecule inhibitors for topors ubiquitin and SUMO ligase activities.

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### **Deliverables**

- . •Polyclonal antibody
- . •Bacterial, yeast, and mammalian expression vectors
- . •Purified protein (a limited amount is available)

### **Patent Status**

- . •United States patent application filed.
- . •Application published on 09/18/2003 (Publication No.: US-2003-0176343-A1)

### **Licensing Opportunity**

- This technology is available for non-exclusive or exclusive license.

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