**TITLE:** Induction of Telomere Dysfunction to Prolong Disease Control in Chemo-Resistant or Treatment-Refractory Melanoma  
**INVENTORS:** Jerry Shay, Gao Zhang  
**TECHNOLOGY:** Small Molecule  
**UTSD:** 3243  

**SUMMARY:**

This technology describes the use of a small molecule inhibitor of telomere extension for melanoma therapy, including those melanomas that are refractory and/or resistant to immune checkpoint and/or mitogen-activated protein kinase (MAPK) inhibitor therapy. Telomeres are protective structures found at the end of linear eukaryotic chromosomes. Telomeres in all normal somatic cells undergo progressive shortening with each cell division eventually resulting in cellular senescence. Replication-dependent telomeric shortening is counteracted by telomerase. While most normal somatic human cells do not have telomerase activity, it is detected, almost universally, in primary human cancer cells (~85-90%), and it is an almost universal biomarker in advanced human cancers including melanoma.

Melanoma is the third most common cancer among women ages 20-39 and the second most common cancer in men ages 20-39. In the US, melanoma is currently the fifth most common cancer in men and the sixth most common in women of all age groups. Immune checkpoint blockade inhibitors and MAPK inhibitors have emerged as first-line therapies for patients with advanced melanomas. However, many patients do not respond and even those that do initially respond ultimately relapse. There is an unmet and urgent need to prolong disease control for patients who fail multiple therapies.

The present invention demonstrates the efficacy of a small molecule inhibitor of telomere extension (disclosed in technology utsd-3242) in various models of therapy-resistant cells, including primary melanoma tumor biopsy cultures derived from patients who had disease progression on multiple therapies including anti-CTLA-4 or anti-PD1. Moreover, the inventors showed efficacy in therapy-resistant mouse pancreatic cancer and human ovarian cancer cells indicating that it may be a viable salvage therapy approach to prolong disease control of therapy-resistant tumors. The results are highly supportive of using this inhibitor singly or in combination as a first- or second-line therapeutic approach in a variety of human tumors that express telomerase activity.

Please contact the Office for Technology Development for more details:

Phone: 214-648-1888  
Email: TechnologyDevelopment@utsouthwestern.edu  
Please reference UT Southwestern Case Number: 3243