Testing Novel BIBR 1532 Derived Telomerase Inhibitor

Bikash Mishra
mishrabi@mail.gvsu.edu

Follow this and additional works at: http://scholarworks.gvsu.edu/mcnair

Recommended Citation

Copyright © 2015 by the authors. McNair Scholars Journal is reproduced electronically by ScholarWorks@GVSU. http://scholarworks.gvsu.edu/mcnair?utm_source=scholarworks.gvsu.edu%2Fmcnair%2Fvol19%2Fiss1%2F16&utm_medium=PDF&utm_campaign=PDFCoverPages
Cancer is one of the leading causes of death among Americans. It is estimated that approximately one-third of all Americans will be diagnosed with some form of cancer in the next 20 years (World Health Organization [WHO]). There are numerous types of cancer but the most common types are lung cancer, breast cancer (women) and prostate cancer (men), which also happens to have the highest mortality rate (WHO). Because these three forms of cancer are very dangerous, it is important to learn more about cancer to find a cure.

Unlike normal cells, cancer cells have the enzyme telomerase which prevents telomeres from degenerating so that the cell continues to divide (El-Daly et al., 2005). One of the drugs often used to treat cancer patients are telomerase inhibitors, but cancer cells are becoming increasingly resistant to the drug. BIBR 1532 is a known telomerase inhibitor and is currently in clinical trials for treating cancers. For a drug to be a good telomerase inhibitor like BIBR 1532, it must have a carboxylic acid structure bonded to an aromatic ring and a conjugated amine.

There were 18 drugs synthesized in the Department of Chemistry in the labs of Dr. Robert Smart and Dr. William Schroeder based on the structure of BIBR 1532. These drugs have been tested in our lab to see whether they show any antiproliferative effect. Out of the 18 drugs screened, about 4-5 drugs (4-43A, WS 1248, WS 76, WS 648, WS 1214) have shown an antiproliferative effect when tested against metastatic prostate cell lines that have known high telomerase activity. The drugs identified with anti-telomerase activity will be tested first at different concentrations to find the optimal concentration that inhibits proliferative activity. After the optimal concentration is identified, all the cells will be treated at this concentration and the treated cells will be frozen until further use for telomerase assay. Those drugs with antiproliferative effects will be further tested to see if they are good telomerase inhibitors by subjecting them to telomerase assays. The cell will be lysed and analyzed using TRAP assay to test whether the telomerase present in the cancer cell is inhibited by the drug or through a different mechanism.

This research is important because if the drugs tested are proven to be good telomerase inhibitors then they could be used to effectively treat prostate, breast and lung cancer, which are known to have high telomerase activity and are known to be fatal.