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Novel Telomerase Inhibitors Synthesized from BIBR 1532 Derivatives

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As of 2011, cancer was the leading cause of death in the United States, second only to heart disease. Cancer is often referred to as being "immortal" because of its ability to divide a seemingly infinite amount of times. Normal cells are limited in the number of times they can divide by the caps on the ends of their chromosomes, called telomeres. These caps are supposed to become degraded over time, signaling the cell to die when they become too short. As cancer continues to become an ever-increasing threat to human health, the race is on to find an effective telomerase inhibitor. If telomerase is inhibited, the telomeres of cancer cells can no longer be elongated. Stripped of their immortality, cancer cells will eventually undergo apoptosis, or controlled cell death. This inhibitor has to be able to destroy cancer cells while leaving healthy cells unharmed. Research has uncovered that the molecular structure of a compound known as BIBR 1532 has proven to be an effective telomerase inhibitor. Current research has shown that BIBR 1532 inhibits telomerase by preventing it from extending the copied strand any further than the length of the original strand of DNA.

Research has not yet discovered what portion of BIBR 1532 causes it to be such a good telomerase inhibitor, though several theories do exist. The most popular theory, supported by past research, is that three structures present in the BIBR molecule contribute to its efficacy: an aromatic ring containing a carboxylic acid and a conjugated amine group. This is the theory on which my current research is based upon and served as the basis for the synthesized compounds. Three compounds were made via the synthesis of cinnamic acid and contained the aforementioned substructures found in BIBR 1532. The basic skeleton of the chemical structure was created from cinnamic acid, due to its natural ability to inhibit telomerase. Using the reactive properties of cinnamic acid, several different substituents were added while maintaining the three key structures. The Schotten-Baumann protocol was utilized to synthesize the final product, the purity of which was tested using HNMR and CNMR techniques. The results of this experiment were three novel chemical compounds that each contains an aromatic ring, a carboxylic acid, and a conjugated amine group. These compounds also possess the natural anticancer properties of cinnamic acid.

These three compounds are currently undergoing testing for telomerase inhibition using the Telomerase Repeat Amplification Protocol assay. The compounds will be tested on prostate cancer cell lines, in order to determine whether my compounds are active against telomerase. Their efficacy will be compared against BIBR 1532 itself, as well as other known telomerase inhibitors. The compounds will also be tested to determine if it has the ability to destroy cancer cells, while leaving healthy cells untouched. If one of these compounds is found to be more effective at fighting cancer than BIBR 1532, it would open doors to a newer and safer drug treatment program.