

Combined Inhibition of Polo-Like Kinase 1 and BRD4 Overcome Resistance to Prostate Cancer Therapy

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Polo-like kinase 1 (Plk1), a critical regulator of many cell cycle-related events, is overexpressed in Prostate Cancer (PCa) and high levels of Plk1 correlate with

unfavorable patient outcomes. Therefore, Plk1 serves as a prognostic indicator for PCa patients and as a strong candidate target for the development of novel approaches to manage PCa. Several potent and selective ATP competitive inhibitors of Plk1, including GSK461364, are in clinical trials to treat PCa patients. However, emerging data has shown that many types of PCa are resistant to Plk1 inhibitors. Members of the BET family of proteins (BRD2, BRD3, BRD4, and BRDT) facilitate the recruitment of transcriptional proteins to chromatin. Pharmacological inhibition of BET proteins has been shown to lower the expression of a variety of genes that are crucial for cell lineage and viability in several types of malignancy. In this study, we set out to investigate whether inhibition of SK461364 in human PCa cells. This was done by testing for the presence of cleaved-PARP, an apoptotic cell marker. Toward that purpose, 3 different prostate cancer cell lines (22RV1, C4-2 and LNCaP) were treated with Plk1 inhibitor or BRD4 inhibitor of both inhibitors. The preliminary data shows that BRD 4 inhibitor enhances the efficacy of Plk1 inhibitor and causes more cancer cell death in LNCaP and 22RV1 cell lines.

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Albert was born in Maryland, but shortly after being born, he went to live in Cameroon. After living in Cameroon for 5 years, he came back to the United States and attended school from kindergarten to twelfth grade. He is a rising senior at The University of Maryland, College Park (UMD) and he is studying Biochemistry. During the 2015-2016 school year, Albert was involved in the University of Maryland Hip-Hop Festival where he served as a committee member. In his role as a committee member, he helped brainstorm ways to display appreciation for Hip-Hop on the UMD campus. The ideas culminated into constructing a UMD Hip-Hop week, a week in which different events were held showcasing aspects of Hip-Hop. These events included graffiti, a music panel, and a modified lip-synching event to name a few. Albert has also been involved in two different scholars programs at UMD: The College Park Scholars (CPS) and College Success Scholars (CSS) program. The CPS program was a 2 year program (2013-2015) designed to make students think critically about the world, in specific relation to climate change. The critical thinking skills we acquired were meant to be interdisciplinary in application; regardless of our major, the skills would still prove useful. The program helped advance my way of thinking and kept me mentally engaged. The CSS program (2013-2017) is a scholars program that was designed to academically empower minorities. The program provides brotherhood among members, tutoring in multiple courses and professional development opportunities. Albert knows that all of his experiences have given him different possibilities; there are many opportunities to impact the world. After receiving his bachelors in biochemistry, Albert hopes to either pursue dermatology as a Medical Student or pursue a graduate degree in relation to cancer research. Albert is positioning himself to make the best decision available by continuing to gain experience and learning new things.