Cancer cell line profiling of an indirect Myc modulator

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Cancer biology research, over the years, has revealed cancer to be a disease involving dynamic changes in the genome. One of the most common oncogenic events in human malignancies is the dysregulation of a transcriptional factor, c-Myc. c-Myc activation, which can occur through several mechanisms, may result in uncontrolled cell proliferation, alterations in the apoptotic pathway, genomic instability, escape from immune surveillance, growth factor independence, and immortalization.

The focus of my summer research was to ascertain the mode of action of BRD4132- a compound that indirectly modulates Myc as established in a high throughput screen involving a dual reporter assay system aimed at monitoring Myc-mediated transcription and several secondary assays, including a kinase activity profile involving 299 kinases. The secondary studies demonstrated that the compound inhibits Myc-mediated transcription by lowering Myc transcript and protein levels and the kinase profiling suggests an indirect novel mechanism involving GSG2. A study to gain insights into the impact of the compound on cell viability across a diverse set of cell lines was also initiated. Inactivation of c-Myc driven transcription in cells, using a small molecule that either directly targets the protein, protein partners or upstream signaling enzymes may result in an effective approach to developing candidates for cancer therapeutics.

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