A Novel Pediatric Cancer Therapy Targeting Epigenetics and Neuroblastoma Differentiation

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Neuroblastoma(NB) is a pediatric cancer present in children under the age of 16, responsible for a disproportionate 15% of all childhood cancer deaths worldwide. Traditionally cells differentiate from a stem cell into a mature cell; however, NB cells never reach full neuronal maturity and continue to proliferate in contrast to normal cells that reach maturity. Cis Retinoic Acid(CRA) is a treatment used today that induces differentiation in NB to improve patient treatment outcomes, though it causes harsh side effects and is thus not an optimal therapy for all patients. This study aimed to identify novel treatments for NB which have limited side effects for patients. Seven distinct inhibitors were investigated based on their proven ability to alter gene expression and protein regulation. Drug cytotoxicity assays were used to demonstrate anti-cancerous properties and identified Selinexor and DZNep, which are highly efficient inhibitors. To determine if differentiation was occurring, morphology and biochemical composition were examined. Microscopy identified changing morphological features of differentiation and immunofluorescence demonstrated changing protein concentrations related to neuronal differentiation. These revealed distinct differentiation properties similar to those induced by CRA. Western blot analysis further confirmed changing protein concentration related to neural differentiation patterns. In summary, this study confirmed the ability of epigenetic altering drugs to induce differentiation in NB cells in vitro and provided pre-clinical evidence of some essential, desirable properties of the drugs DZNep and Selinexor in the evaluation for new therapeutics for this disease. Both inhibitors demonstrate potential in improving treatment of NB patients.

Awards Won:
Fourth Award of $500
Drug, Chemical &amp
Associated Technologies Association (DCAT): First Award of $3,000.