The Effect of Small Molecule Activators of PP2A (SMAPs) on N-Myc Driven Neuroblastomas

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Neuroblastoma is the most common extra-cranial solid cancer in children and there is about one case in 7000 live births, resulting in approximately 700 cases in the US alone. About 25% of neuroblastomas have MYCN (gene) amplification, which is associated with high risk neuroblastoma and is “the best characterized genetic-risk factor of the high-risk chemotherapy refractory diseases” (Gustafson, 2010, pg.1250). N-Myc (protein) is a part of the Myc protein family, yet not much has been discovered about it, however, it has been noticed to have a homology with another Myc protein known as C-Myc. C-Myc binds to PP2A, a well-known tumor suppressor and protein phosphatase, which then dephosphorylates C-Myc at its threonine 58 (T58) and serine 62 (S62) site resulting in the degradation of C-Myc. Yet, due to the fact that when cancer is present PP2A is inactivated, in order to reactivate the SMAPs, small molecule activators of PP2A, must be used to help reactivate the PP2As within the body to enhance the degradation process. Given that PP2A negatively regulates oncogenic C-Myc at a homologous Serine 62 site, and that N-Myc driven cancers are predicted to be responsive to small molecule activators of PP2A (SMAPs), it was hypothesized that PP2A negatively regulates oncogenic N-Myc signaling. When a series of time course experiments were done, the results showed that N-Myc was degraded at PP2A’s S62 site as well as its T58 site, allowing the conclusion to be drawn that N-Myc can be dephosphorylated on the same sites of PP2A as C-Myc in both the neuroblastoma cell lines affected by PP2A, Sknbe2 and Chp212.