A Novel in Vivo Role for CXCR4 Inhibition in Neuroblastoma

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Abstract:
High-risk cases of neuroblastoma have extremely poor long-term survival rates, and novel therapies are needed. The chemokine receptor CXCR4 is over-expressed in many cancers where it has been shown to affect metastasis, angiogenesis, and microenvironment-mediated chemoresistance. The role of CXCR4 and its ligand SDF1 alpha in neuroblastoma are not clear. We hypothesized that CXCR4 would be important for neuroblastoma tumor growth and that inhibition of CXCR4 would be effective against neuroblastoma tumors. We explored the effects of SDF1 alpha and its competitive inhibitor AMD3100 in vitro and in vivo.

Established neuroblastoma cell lines all expressed significant levels of CXCR4 protein by immunoblot analysis. Neuroblastoma cell lines were treated with varying concentrations of SDF1 alpha or AMD3100 and assays for proliferation, survival, migration, and invasion were performed. SDF1 alpha and CXCR4 did not affect neuroblastoma tumor cell migration, invasion or survival, and inhibition of CXCR4 with AMD3100 had no effect on neuroblastoma tumor cell viability in vitro. In a mouse xenograft model, however, AMD3100 significantly inhibited tumor growth and resulted in a reduction in pericytes.

These results show that, although inhibition of CXCR4 with AMD3100 has minimal effects in vitro, treatment of mouse xenograft neuroblastoma tumors results in significant growth inhibition. Although the mechanisms of this tumor growth suppression remain to be elucidated, these results suggest that inhibition of CXCR4 may be effective for the treatment of children with neuroblastoma.

References:
