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MAIN FIELDS OF RESEARCH; ABSTRACT

Neuroblastoma is the primary cause of death from pediatric cancer and accounts for ~13% of all pediatric cancer mortality. However, death results not from primary tumor but rather from metastasis or recurrence in most cases. The International Neuroblastoma Risk Group (INRG) classification defines approximately half of all new neuroblastoma cases each year as high risk. Patients with high risk neuroblastoma require intensive treatment including surgery, chemotherapy, radiation therapy, and immunotherapy. However, clinical outcome of high-risk patients still remains poor with long-term survival less than 50%. The majority of primary tumors arise in adrenal medulla, and metastasize to regional lymph nodes, bone marrow and live. Although more than 50% of neuroblastoma patients present with metastatic disease, little is known of the process and the mechanism. Investigating the molecular basis of neuroblastoma metastasis is crucial to develop more effective therapies.

The similarities between neural crest development and neuroblastoma progression have been recognized. Neuroblastoma originates from the precursor cells of the sympathoadrenal lineage that are derived from the neural crest. The neural crest cells consist of multipotent and migratory cell populations that give rise to diverse cell lineages during embryonic development. Neural crest cells serve as multipotent stem cells that differentiate into mature peripheral neural tissues. It is now assumed that the multipotent neural crest cells with genetic mutations may contribute to neuroblastoma tumorigenesis. Recent studies have revealed the presence of several genomic alterations in neuroblastoma. These include amplification of MYCN, mutations of ALK, and copy number aberrations of chromosomes. Aggressive NB often harbors MYCN amplification (in ~20% of tumors), deletion of chromosome 1p, gain of chromosome 17q, and loss of chromosome 11q.

SOX9 is a transcription factor involved in neural crest cells delaminating from the neural tube and migrating into periphery during development. SOX9 has been implicated in formation and progression of tumors in prostate, skin, pancreas, ovary, and esophagus. However, the role of SOX9 in neuroblastoma remains unclear. Considering SOX9 is required for migration of neural crest cells, we hypothesized that SOX9 is functionally involved in neuroblastoma metastasis. The goal of study is to investigate the function of SOX9 and to find out its downstream targets, which can further provides therapeutic targets in metastasis prevention.

SPECIAL TECHNIQUES AND EQUIPMENT

Cell culture, Transfection, Lentivirus production, RT-PCR and qPCR, Immunoblotting, Immunohistochemistry and Immunocytochemistry, Proliferation assay, Migration and Invasion assay, Colony formation assay, Tumor sphere assay, Xenograft model