

MYCN---induced Calcium Signaling Promotes the Malignant Progression of Neuroblastoma

Background:

- Neuroblastoma is an extra---cranial pediatric cancer that is difficult to treat because most patients are diagnosed at an advanced stage of aggressive tumor progression.
- The long---term goal of the project is to elucidate the mechanisms that promote the malignant progression of neuroblastoma, and identify novel targets for the development of more effective chemotherapeutic agents and treatment strategies.
- MYCN gene amplification is an indicator of poor outcome.
- How MycN contributes to neuroblastoma cell migration (metastatic potential) was the focus on this study.

Advance:

- MycN expression in neuroblastoma was shown to upregulate expression and activity of TRPM7 channels, resulting in significantly increased intracellular calcium, which, in turn, strongly promoted neuroblastoma cell migration.
- Inhibition of ornithine decarboxylase, the key enzyme in the polyamine synthesis pathway, sharply inhibited TRPM7 expression.
- The findings indicate 1) that polyamines regulate TRPM7 expression by MycN and 2) that inhibition of the polyamine pathway in neuroblastoma, along with TRPM7 inhibition, could provide an avenue for therapy against neuroblastoma metastatic potential.

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MycN promotes TRPM7 expression and cell migration in neuroblastoma through a process that involves polyamines



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