GMNC-MCIDAS Multiciologenesis and Choroid Plexus Carcinoma

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Background

Choroid plexus carcinoma (CPC) is a rare and aggressive brain cancer that primarily affects children. CP Papilloma (CPP) is a benign type of Choroid Plexus Tumor that can be easily removed through surgery. CP Carcinoma (CPC) is a highly lethal tumor that has a unique phenotype. This phenotype includes solitary cilia instead of multiciliated cells (MCCs), persistent TP53 mutations, and disruptions to the multi-ciliogenesis program that is led by GMNC-MCIDAS transcription factors.

In order to study these phenotypes, mice models were created to mimic the multi-ciliogenesis of CPC to better understand the development of CPC's in humans.

Hypothesis

We hypothesize that complications between the GMNC-MCIDAS transcription factors and amplification of NOTCH signaling pathway leads to the defected multiciliated phenotype in CPC.

Results

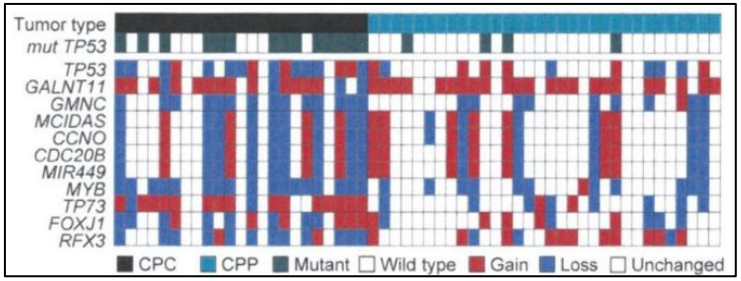

Figure 1: Analysis of Human CPC & CPP

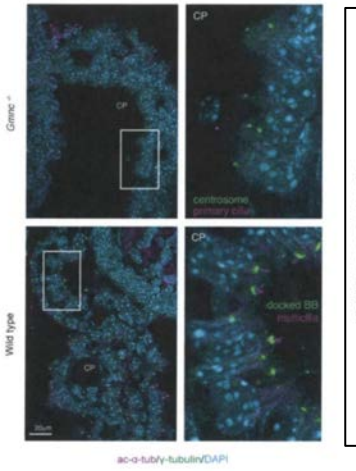

Figure 2: Immunofluorescence Comparison of GMC-/- vs Wild Type

Magnified image of box on right

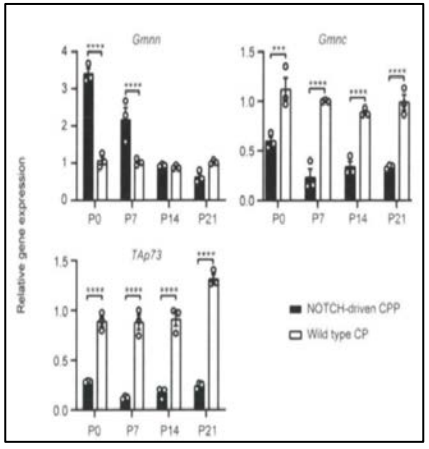

Figure 4: qt-PCR analysis of NOTCH-driven CPP

A.

B.

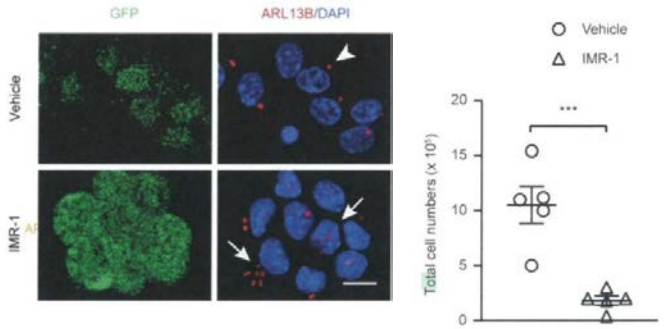

Figure 3A: Immunofluorescence of NOTCH inhibition driving multicilation
3B: Total Number of Cells

Summary & Conclusions

When analyzing human CPC and CPP samples, they displayed a reduced or complete loss of GMNC and MCIDAS expression, and solitary cilia. When GMNC-/- mice were used, both the ependymal cells and CP epithelium showed monocilaition as well. As researchers learned of the Gmnc role in the multiciliated pathway, they also found that activation of the NOTCH pathways led to increased proliferation, loss of differentiated epithelial CP cells and the development of malignant tumors in murine models similar to those of human CPC. However, faulty NOTCH signaling can be remedied by NOTCH inhibition which leads to the restoration of multiciliated cells and decreased tumor growth.