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GPC3: A Novel Mutated Gene in Pleuropulmonary Blastoma

Pleuropulmonary blastoma (PPB), a rare pediatric sarcoma linked to DICER1 mutations, exhibits clinical heterogeneity suggesting additional genetic drivers. Here, we identify a novel GPC3 missense mutation and evaluate its prognostic role in PPB. Whole-genome sequencing of a three-generation PPB family prioritized 17 candidate genes, including GPC3, through autosomal recessive inheritance analysis. Immunohistochemical profiling revealed significantly elevated GPC3 expression in PPB tumors compared to adjacent non-tumor tissues and congenital pulmonary airway malformations (CPAM). Survival analysis demonstrated a striking correlation between GPC3 expression levels and clinical outcomes: patients with high GPC3 expression (GPC3+++) had a two-year survival rate of 30%, versus 75% (moderate, GPC3++) and 90.9% (Low, GPC3+) (p=0.0035). These findings establish GPC3 not only as a novel susceptibility gene in PPB pathogenesis but also as a robust prognostic biomarker, where overexpression predicts aggressive disease progression. Our study further proposes GPC3 as a potential therapeutic target, offering critical insights for risk stratification and personalized management strategies in this lethal childhood cancer.

Keywords

Pleuropulmonary blastoma, GPC3 mutation, Prognostic biomarker, Whole-genome sequencing, Immunohistochemistry, Pediatric sarcoma

Biography

Dr. Zefeng Lin is an Associate Professor at Guangzhou Women and Children's Medical Center, specializing in pediatric thoracic oncology. As Principal Investigator of an NSFC Youth Program and 3 municipal grants, he leads research on congenital pulmonary malformations (lung organoids), pleuropulmonary blastoma, and malignant rhabdoid tumors, while collaborating on 20+ national/provincial projects on structural birth defects. He published 8 first/co-first-author SCI papers, including a landmark study in CELL revealing biliary atresia pathogenesis. Holder of 8 patents and recipient of Guangzhou Medical Association Awards (2017-2019), his work bridges translational medicine and rare pediatric disease management.

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