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JARID1B expression plays a critical role in chemoresistance and stem cell-like phenotype of neuroblastoma cells

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Neuroblastoma (NB) is a common neural crest-derived extracranial solid cancer in children. Among all childhood cancers, NB causes devastating loss of young lives as it accounts for 15% of childhood cancer mortality. Neuroblastoma, especially high-risk stage 4 NB with MYCN amplification has limited treatment options and associated with poor prognosis. This necessitates the need for novel effective therapeutic strategy. JARID1B, also known as KDM5B, is a histone lysine demethylase, identified as an oncogene in many cancer types. Clinical data obtained from freely-accessible databases show a negative correlation between JARID1B expression and survival rates. Here, we demonstrated for the first time the role of JARID1B in the enhancement of stem cell-like activities and drug resistance in NB cells. We showed that JARID1B may be overexpressed in either MYCN amplification (SK-N-BE(2)) or MYCN-non-amplified (SK-N-SH and SK-N-FI) cell lines. JARID1B expression was found enriched in tumor spheres of SK-N-BE(2) and SK-N-DZ. Moreover, SK-N-BE(2) spheroids were more resistant to chemotherapeutics as compared to parental cells. In addition, we demonstrated that JARID1B-silenced cells acquired a decreased propensity for tumor invasion and tumorsphere formation but increased sensitivity to cisplatin treatment. Mechanistically, reduced JARID1B expression led to the down-regulation of Notch/Jagged signaling. Collectively, we provided evidence that JARID1B via modulation of stemness-related signaling is a putative novel therapeutic target for treating malignant NB.

Biography

Chi-Tai Yeh has received his PhD in Food Science and Biotechnology from National Chung Hsing University. He is currently the Research Fellow and Executive Secretary of Department of Research of Taipei Medical University-Shuang Ho Hospital. He has contributed 2 book chapters, published 35 articles in the field of cancer & nutritional chemistry journal and got 2 patents in the medical compound of cancer therapy. His major research interests include cancer cell biology, cancer stem cell research, nutrigenomics and cancer chemoprevention with dietary phytochemicals.

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