34th Euro-Global Summit on Cancer Therapy & Radiation Oncology
&
6th International Conference on Big Data Analysis and Data Mining
&
13th International Conference on Orthopedics, Arthroplasty and Rheumatology
July 25-27, 2019 London, UK

Combination strategy of drug repositioning for neuroendocrine cervical carcinoma treatment

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Precision cancer medicine is an evolving treatment approach that aims to associate the tumor's unique genomic characters and histological changes to first determine the cancer subtype, and use the information to select targeted therapy for enhanced efficacy. In this study, we focus on neuroendocrine cervical carcinoma (NECC), which is a rare and aggressive subtype of cervical cancer. A NECC specimen obtained from a consented 44-year-old female patient was first analyzed by RNA sequencing. Interestingly, we found the transcription profile of the tumor case highly correlated with metabolic disease. Meanwhile, we processed and established a novel NECC cell line (annotated as Hsinchu Mackay-4, HM-4) from the patient's ex vivo biopsy, and used it to explore novel drug combination for enhanced cytotoxic response. Drug screening revealed that, when etoposide (a known genotoxic drug for NECC) was used in combination with agent X (an FDA-approved metabolic disease drug), the proliferation of HM-4 cells was significantly inhibited as compared to etoposide or agent X treatment alone. Immunoblot assay revealed the expression level of pAKT was remarkably reduced, while p21 was upregulated when HM-4 cells were treated with a combination of etoposide and agent X. These results suggested that the drug combination of etoposide and agent X might become a novel synergistic treatment option for NECC.

Recent Publications

1. Shing-Jyh Chang, et al., (2018) Proteomic investigating the cooperative lethal effect of EGFR and MDM2 inhibitors on ovarian carcinoma. Archives of Biochemistry and Biophysics, 647:10-32.
2. Zih-Yin Lai, et al., (2017) PI3K inhibitor enhances the cytotoxic response to etoposide and cisplatin in a newly established neuroendocrine cervical carcinoma cell line. Oncotarget, 8(28):45323-45334.
3. Lawrence Yu-Min Liu, et al., (2016) Motor neuron-derived Thsd7a is essential for zebrafish vascular development via the Notch-dll4 signaling pathway. Journal of Biomedical Science, 23(1):59.
4. Li-Hsun Lin, et al., (2014) Biomarker discovery for neuroendocrine cervical cancer. Electrophoresis, 35(14):2039-2045.
5. Chieh-Huei Wang, et al., (2011) Zebrafish Thsd7a is a neural protein required for angiogenic patterning during development. Developmental Dynamics 240(6):1412-1421

Biography

Zih-Yin Lai is a Postdoctoral Fellow of the Institute of Bioinformatics and Structural Biology at National Tsing Hua University in Taiwan. She is the manager of Dr. Yung-Jen Chuang's lab with excellent ability to guide other lab members. Her work focuses specifically on precision cancer medicine and drug combination strategy. She has established a special primary neuroendocrine tumor cultured model from the patient's ex vivo biopsy after years of experience. Moreover, she is also responsible for two projects: boron neutron capture therapy for melanoma and EGFR/MDM2 combined inhibition therapy for ovarian cancer. Her recent publication can be found in Archives of Biochemistry and Biophysics, Oncotarget and Journal of Biomedical Science.

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