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Clinical Research (Excluding Clinical Trials)

Abstract 488: Computer-assisted three-dimensional quantitation of programmed death-ligand 1 expression in non-small cell lung cancer using tissue clearing technology on formalin-fixed, paraffin-embedded specimen

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DOI: 10.1158/1538-7445.AM2021-488 Published July 2021

Proceedings: AACR Annual Meeting 2021; April 10-15, 2021 and May 17-21, 2021; Philadelphia, PA

Abstract

Immune checkpoint blockade therapy has revolutionized cancer treatment, achieving sustained remission even in a proportion of patients with metastatic disease. However, not all patients respond to these therapies. Currently, histological detection of PD-L1 expression in tumor specimens is the standard method for guiding checkpoint blockade therapies involving anti-PD-1/PD-L1 antibodies. Nevertheless, accumulating evidence from clinical studies indicates that the pathological assessment of PD-L1 expression is neither a consistent nor a reliable predictor of anti-PD-1/PD-L1 treatment outcome. This inconsistency can be partly attributed to tumor heterogeneity in PD-L1 expression, as well as the common practice of assessing PD-L1 expression based on a single tissue section made from limited tumor biopsy specimen. In order to overcome this obstacle, we developed a novel method that can make formalin-fixed, paraffin-embedded (FFPE) tissue translucent to light, allowing three-dimensional imaging of the specimen. Our specialized protocol can process non-small cell lung cancer tissue up to 150 micrometer in thickness, allowing fluorescence-labeled anti-PD-L1 antibody staining throughout the entire tissue, and produce high-resolution 3D images. Compared to a traditional single 4-micrometer section of the same specimen, our 3D image provides 30 times more coverage of the specimen, assessing PD-L1 expression of approximately 15 times more cells. We also developed a computer-assisted PD-L1 signal quantitation algorithm, integrating artificial intelligence (AI) models of tumor region segmentation and

PD-L1 positive cell classifier to generate PD-L1 tumor proportion score (TPS) along the specimen depth. Both AI models have greater than 90% accuracy compared to pathologist's assessment. Analysis of 3D images from seven lung adenocarcinoma specimens showed that TPS variation may reach up to 23.76% at different tissue depth levels. One of the seven cases has TPS below 1% at certain depth level but above 1% at other levels, a difference that can potentially influence clinical decision making. Importantly, our technology permits recovery of the processed tissue for subsequent analysis, including traditional histology examination, immunohistochemistry, and DNA analysis, such as EGFR mutation test. In conclusion, our novel method has the potential to increase the accuracy of tumor PD-L1 expression assessment and enable precision deployment of cancer immunotherapy.

Citation Format: Yen-Yu Lin, Lei-Chi Wang, Yu-Han Hsieh, Sih-Kai Chuang, Yung-An Chen, Yu-Chieh Lin, Yen-Yin Lin, Teh-Ying Chou. Computer-assisted three-dimensional quantitation of programmed death-ligand 1 expression in non-small cell lung cancer using tissue clearing technology on formalin-fixed, paraffin-embedded specimen [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2021; 2021 Apr 10-15 and May 17-21. Philadelphia (PA): AACR; Cancer Res 2021;81(13_Suppl):Abstract nr 488.

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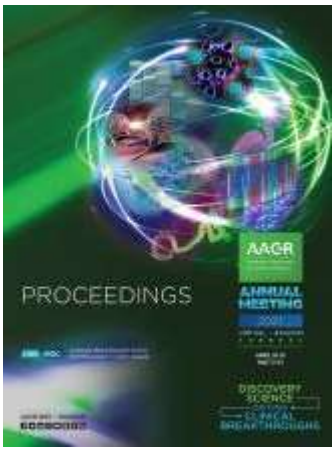

July 2021
Volume 81, Issue 13 Supplement
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