



Development of ploidy diagnostic technologies to achieve personalized medicine for refractory cancers

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Abstract

Humans possess a diploid genome, but polyploidization frequently occurs in cancer, promoting malignant progression and drug resistance through chromosomal instability. Tumor cell ploidy has recently emerged as a novel biomarker associated with poor prognosis. However, conventional methods for assessing ploidy, such as genome sequencing and flow cytometry, are complex, costly, and difficult to interpret, limiting their applicability in clinical settings. In our study focusing on hepatocellular carcinoma (HCC), we identified molecular markers such as UBE2C that are highly expressed in polyploid tumors, and demonstrated that tumor ploidy is a powerful prognostic indicator. We also developed a deep learning-based image analysis model that allows straightforward assessment of ploidy from HE-stained pathological images. Validation using public datasets confirmed that this model can accurately predict patient outcomes in liver cancer.

Background & Results

To predict tumor prognosis and treatment efficacy, pathological and genetic markers have been widely studied. However, reliable prognostic prediction remains challenging due to the increasing complexity and diversity of cancer therapies. Polyploidization, or genome doubling, occurs frequently across various tumor types. This phenomenon leads to chromosomal instability, which contributes to metastasis and drug resistance, and is increasingly recognized as a marker of poor prognosis. Despite its clinical relevance, ploidy assessment has been limited by the complexity and cost of conventional techniques, making routine evaluation difficult in clinical practice.

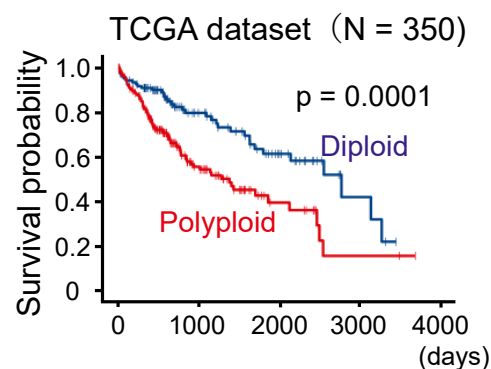
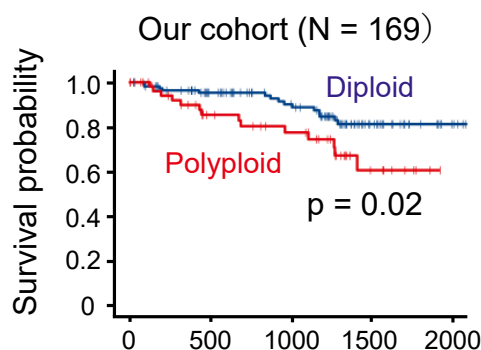
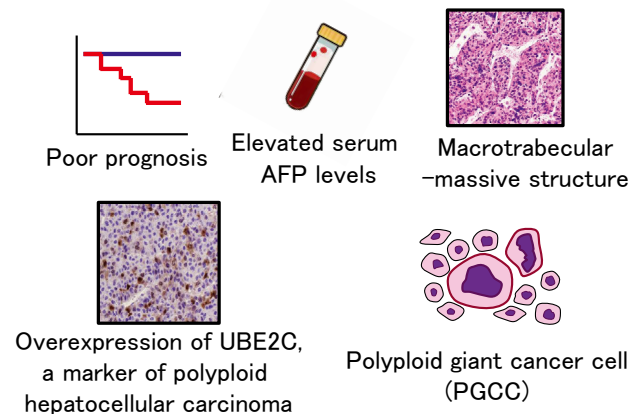
In this study, we performed chromosomal FISH to classify HCC samples into diploid and polyploid groups. We identified distinct pathological features and molecular markers, including UBE2C, that are characteristic of polyploid HCC. Furthermore, we developed a deep learning image analysis model to analyze HE-stained images and determine tumor ploidy in a rapid and practical manner. The model's utility was validated using multiple patient cohorts

and public databases, confirming its effectiveness in predicting clinical outcomes. This approach is expected to be applicable to other cancer types, enabling broader implementation of ploidy-based diagnostics.

Significance of the research and Future perspective

This technology enables rapid detection of polyploid tumors and supports prognostic prediction and treatment planning. It is expected to serve as a companion diagnostic tool for emerging therapies targeting polyploidization and chromosomal instability. In research settings, it offers a valuable platform for exploring cancer pathogenesis and drug development focused on targeting polyploidy. We are actively engaged in drug discovery targeting polyploid cancers. As precision medicine advances, genomic features such as ploidy are becoming key indicators for characterizing refractory cancers. Our method provides a novel approach to patient stratification and optimization of clinical decision-making, contributing to the development of personalized cancer therapies.

Features of polyploid hepatocellular carcinoma

**Patent** Japanese Patent Application No.2024-26830, PCT/JP2024/044155**Treatise** Abe, Masatoshi; Niioka, Hirohiko; Matsumoto, Tomonori et al. Selective identification of polyploid hepatocellular carcinomas with poor prognosis by artificial intelligence-based pathological image recognition. *Commun Med (Lond)*. 2025, 5(1), 270. doi: 10.1038/s43856-025-00967-8
Matsuura, Takanori; Harada, Yoshihide; Matsumoto, Tomonori et al. Histological diagnosis of polyploidy discriminates an aggressive subset of hepatocellular carcinomas with poor prognosis. *Br J Cancer*. 2023, 129(8), 1251-1260. doi: 10.1038/s41416-023-02408-6**U R L** <https://www.matsumoto-ploidy.com/en>**Keyword** ploidy, genome doubling, polyploidization, chromosomal instability, cancer