

**Weiwei Zhai**

Chinese Academy of Sciences

## **Dissecting and targeting a dynamic landscape of tumor evolution in Hepatocellular Carcinoma**

Hepatocellular carcinoma (HCC) has high intratumor heterogeneity (ITH). However, how multi-omic ITH evolves and affects treatment is under-explored. In this work, we found that:

- 1) Multi-omic ITH fluctuates through time and transcriptomic heterogeneity peaks at intermediate stages with multiple molecular subtypes co-existing within a single tumor.
- 2) Tumor heterogeneity segregates into variegated blocks with large genotypic and phenotypic differences. Interestingly, 30% of patients had a “spatially competing distribution” (SCD) where different spatial blocks have distinct transcriptomic subtypes co-existing within a tumor.
- 3) Using evolutionary analysis, we found that natural selection is driving rapid clonal replacement for patients in SCD distribution, capturing critical stage of disease progression.
- 4) We designed a phase II clinical trial combining radiation together with ICB, significantly increasing patient response rate from 15-20% to around 30%. Taken together, we uncovered a unique landscape of multi-omic ITH in HCC and pinpointed a novel combination therapy battling immune heterogeneity.

**Monday, 28 April 2025, 14:00 CEST**

Zoom only

[Click here to Join](#)

Hosted by Axel Hillmer