**Decoding the Spatial Genomic Evolution of Metastatic Colorectal Cancer Through a Novel Spatial Whole Genome Technology**

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Whole-genome sequencing (WGS) has become an important platform for precision cancer diagnosis because it provides comprehensive genomic information beyond targeted sequencing approaches. However, current single-cell and spatial WGS technologies remain limited by high cost, low scalability, and technical biases that restrict accurate detection of genome-wide somatic mutations. Current state-of-the-art WGS methods rely on DNA extraction from lysed cells followed by whole-genome amplification before sequencing library construction. Although this strategy has been adapted for single-cell WGS, it has not yet been extended to spatial assays.

To address this limitation, this project aims to develop a scalable method that combines unbiased in situ whole-genome amplification with in situ DNA tagmentation for spatial whole-genome sequencing directly in patient-derived colorectal cancer tissues with measurable genomic signal. Specifically, in situ multiple displacement amplification (MDA) will amplify genomic DNA directly within intact tissue sections, with systematic optimization of reaction timing, primer length, and debranching conditions to maximize coverage uniformity. The amplified DNA will be tagmented in situ using Tn5 transposase, and fragments will be captured on the commercially available 10x Visium High-Definition platform for spatial barcoding via engineered bridge oligonucleotide architectures. While full end-to-end spatial WGS and comprehensive biological interpretation are beyond the timeframe of this project, this work will lay the technical foundation for future development of scalable spatial genomics approaches capable of resolving intratumoral heterogeneity and lineage relationships at genome-wide scale.