Department of Biostatistics and Medical Informatics Seminar

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Friday, October 10, 2025
12:00-1:00 pm
Morgridge Hall Seminar Room 7560 or
Zoom:
https://uwmadison.zoom.us/j/99879638765?pwd=wbtqxoucEFIlPVCVc9SFbvKB1Av7Xk.1
Passcode: 343271

Deciphering tumor heterogeneity for benefits from immunotherapy in cancer

Abstract: Intra-tumor heterogeneity is characterized by a diverse population of tumor clones and subclones which are important drivers of tumor evolution and therapeutic response. However, accurate subclonal reconstruction at scale remains challenging. We developed a machine learning based method, CliPP, and surveyed 10,409 tumors from 32 cancer types. We found that high subclonal mutation fraction (sMF), the fraction of subclonal single nucleotide variants (SNVs) to all SNVs in the coding region, was prognostic of survival (progression free survival or overall survival) in 18 cancer types. In 14 cancers with low to moderate tumor mutation burden (TMB), high sMF was associated with better prognosis. In four cancers with high TMB, the opposite association was observed. In immunotherapy trials for advanced prostate cancer, a low-TMB cancer, high sMF was predictive of favorable response to ipilimumab and associated with increased CD8+ T-cell infiltration. The biphasic property of sMF that is distinct between cancers with low-moderate TMB and high TMB is further replicated within the SU2C-MARK (n=227) lung cancer cohort, where both directions of associations were observed in patients treated with immune checkpoint blockade (ICB). Our study highlights sMF as a key feature of cancer evolution, with its accurate measurement from DNA sequencing data being supported by CliPP. Our findings with response to ICB therapy advocates using sMF and TMB jointly as a marker of interplay between evolutionary dynamics and immune environments.

Bio: Dr. Wenyi Wang is a Professor of Bioinformatics and Computational Biology and Biostatistics at the University of Texas MD Anderson Cancer Center. She received her PhD from Johns Hopkins University and performed postdoctoral training in statistical genomics at UC Berkeley with Terry Speed and genome technology at Stanford with Ron Davis. Wenyi's research includes significant contributions to statistical bioinformatics in cancer, including MuSE for subclonal mutation calling, DeMixT for transcriptomic deconvolution. She led a pan-cancer characterization of genetic intra-tumor heterogeneity in subclonal selection, and a pan-cancer biomarker identification through integrative deconvolution of transcriptomic/genomic data. Her current research directions are 1) multi-omic deconvolution to study DNA–RNA dynamics in cancer, and 2) cancer risk modeling using machine learning and Bayesian models.

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