Deep Sequencing of Circulating Tumor DNA for Personalized Cancer Detection and Monitoring

Awardee: Maximilian Diehn
Award: New Innovator Award
Awardee Institution: Stanford University

Circulating tumor DNA (ctDNA) represents a promising biomarker for non-invasively detecting disease burden in cancer patients while simultaneously providing access to tumor genomes. However, several technical shortcomings of existing methods for ctDNA detection, including lacking the necessary analytic sensitivity, limited breadth of patient coverage, and the need for patient-specific optimization, have prevented routine clinical application. We therefore developed a novel deep sequencing-based approach for quantifying ctDNA that is extremely sensitive and specific and can be broadly applied to nearly every cancer type. Our approach, called Cancer Personalized Profiling by Deep Sequencing (CAPP-Seq), incorporates technical and bioinformatic innovations to ultrasensitively and specifically detect ctDNA. We have successfully applied this method to plasma samples from patients with a wide variety of cancer types, including malignancies such as non-small cell lung cancer, esophageal carcinoma, and lymphoma. CAPP-Seq achieves extremely high analytic sensitivity (<0.01%), and simultaneously detects single nucleotide variants, indels, rearrangements, and copy number alterations. We will provide evidence for the potential application of our approach in a variety of clinical settings, including the detection minimal residual disease, analysis of tumor heterogeneity and subclonal resistance mutations, and distinguishing between post-treatment normal tissue changes and recurrent cancer. Finally, we will describe our work on applying CAPP-Seq for biopsy-free tumor genotyping and early detection of cancer. Our method represents a novel approach to blood-based cancer detection since it provides a personalized biomarker without the need for patient-specific optimization. Future studies will focus on further improving CAPP-Seq's technical performance and documenting clinical utility of ctDNA detection, which promises to facilitate the personalized detection, monitoring, and treatment of cancer.