Overcoming Bioinformatic Challenges in the Genomic Characterization of Metastatic and Recurrent Cancers

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Treatment-naive primary tumour samples are readily available from surgical resection for many solid cancer subtypes, and primary tumours have thus been extensively characterized by genomic technologies. However, cancer treatments often failure due to recurrent and metastatic disease, which are less well studied. We will describe our efforts in studying the genomics of metastatic and recurrent tumours, as well as bioinformatic tools that we have developed to overcome technical challenges that arise in the analysis of metastatic and recurrent tumours. These challenges include limited sample size, low tumour purity, and poor-quality tumour samples from remnant FFPE material. Additionally, due to technical variability, intratumour heterogeneity, and sampling noise, the observed genomic differences between primary tumours vs. metastatic tumours can be difficult to interpret. For each of these challenges, we propose approaches and methods to facilitate data analysis and interpretation. Indeed, overcoming the bioinformatic challenges in analyzing difficult tumour samples opens new avenues to the application of cancer genomics to address clinically important questions regarding cancer evolution post frontline treatment.