Advancing a clinically relevant perspective of the clonal nature of cancer

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Cancers frequently arise as a result of an acquired genomic instability and the subsequent clonal evolution of neoplastic cells with variable patterns of genetic aberrations. Thus, the presence and behaviors of distinct clonal populations in each patient's tumor may underlie multiple clinical phenotypes in cancers. We applied DNA content-based flow sorting to identify and isolate the nuclei of clonal populations from tumor biopsies, which was coupled with array CGH and targeted resequencing. The results produced high-definition genomic profiles of clonal populations from 40 pancreatic adenocarcinomas and a set of prostate adenocarcinomas, including serial biopsies from a patient who progressed to androgen-independent metastatic disease. The genomes of clonal populations were found to have patient-specific aberrations of clinical relevance. Furthermore, we identified genomic aberrations specific to therapeutically responsive and resistant clones arising during the evolution of androgen-independent metastatic prostate adenocarcinoma. We also distinguished divergent clonal populations within single biopsies and mapped aberrations in multiple aneuploid populations arising in primary and metastatic pancreatic adenocarcinoma. We propose that our high-definition analyses of the genomes of distinct clonal populations of cancer cells in patients in vivo can help guide diagnoses and tailor approaches to personalized treatment.
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