Extrachromosomal DNA in Cancer

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Extrachromosomal DNA amplifications is a phenomenon first described in the 1960's but surprisingly little was known until recently. The studies from our lab and collaborators have suggested that oncogene carrying extrachromosomal DNA elements ('ecDNA') can be detected in cancer models using sequencing and have tumor-driving roles. We also built upon those works to analyze more than 1 petabyte of sequencing and imaging data (including nearly 5,000 tumor-normal whole-genome sequencing pairs) across 29 cancer types. Our analysis demonstrated that ecDNAs were found in 25 cancer types analyzed, including at high frequency in aggressive histological cancers such as glioblastoma, sarcoma and esophageal carcinoma, but not non-neoplastic samples, result in higher levels of transcription compared to copy number matched linear amplifications, and associate with worse clinical outcomes compared to those with other types of amplification. Through the studies from our lab and collaborators, focal DNA copy number gains through extrachromosomal elements (ecDNA) have emerged as a critical driver of proto-oncogene transcription, also representing an important vehicle for oncogene amplification in cancer with distinct molecular features, most of which are currently not fully understood.

We anticipate that those findings will have profound impact on the way we interpret tumor biology, but will also prove important for drug response, as ecDNA has been selected as one of the important topics in the cancer research society.