Uncovering Molecular Features Associated with DNA Copy Amplifications

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Genome instability and drug resistance are hallmark features of cancer. We have recently uncovered the first enzyme KDM4A capable of generating transient site-specific copy gains of regions linked to drug resistance and hard to treat cancer, which provides a novel tool to carefully interrogate the molecular features affiliated with copy gains. In this application, we are developing methods to characterize the genomic features associated with copy amplification. We will develop microscopy-based strategies to characterize factors that promote these events as well as the impact that copy gains have on gene expression. We are also developing microfluidic devices to isolate the copy gained DNA for sequencing analyses. Our proposed studies will shed light on basic regulatory mechanisms influencing genome organization and expression, while identifying novel biomarkers associated with amplification. Ultimately, we hope that the combination of the molecular insights gained from this pilot study combined with the microfluidic DNA sorting technology will enable the broad dissemination of these assays such that site-specific copy gains can be used to inform clinical designs and help improve patient outcomes.