We are entering the era where chemotherapies are chosen to precisely match the unique genetic alterations in each patient's tumor. New genomic technologies, such as next generation sequencing (NGS), are central to this approach. Our experience has been that NSG is currently inferior to Fluorescence in situ hybridization (FISH) with regard to assessing copy number. With the current FISH techniques being limited to analyzing one gene (or a few genes) at a time and the demands for complete genome analysis becoming clinically necessary, a highly-multiplexed FISH approach coupled with high throughput image capture and analysis platforms would be extremely attractive and could provide an optimal copy number screen in routine molecular pathology practice. The ability to assess accurately highly-multiplexed FISH probe sets requires imaging resources that the Harvard Catalyst grant mechanism can help provide.

Aim I of this proposal is to develop and test image acquisition and analysis platforms that enable the automated copy number analysis of a pilot panel of 30 genes simultaneously, each gene bar-coded with two or three fluorophores simultaneously hybridized on one slide of formalin-fixed paraffin-embedded tumor biopsy sample. Aim 2 will be to validate the clinical utility of the algorithm by exploring tumor heterogeneity in primary human brain tumors (glioblastoma multiforme cases), a tumor with known multiple copy number alterations. The ultimate goal of this proposal is to provide a comprehensive genotype assay that will guide the choice of targeted therapies and that will impact how we identify, diagnose, and alter the clinical course of cancers.