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BioMarker Strategies Abstract

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Functional Profiling of Melanoma Samples Using a Novel Automated Platform (SnapPath™)

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This study was designed to show that functional profiles relevant to targeted therapy can be derived from live human melanoma samples using a novel automated platform. Functional profiling was performed on a set of samples derived from metastatic melanoma procured by FNA from subcutaneous metastatic lesions (n=6) or from surgically-excised metastases (n=6). Functional profiling of these live samples involved brief ex vivo exposure to a BRAF inhibitor (PLX-4720) on an automated platform, followed by analysis of p-ERK levels by immunoassay in untreated and treated aliquots of the sample. Two samples displayed significant ex vivo PLX-4720 suppression of the MAPK pathway (69 and 71% pERK inhibition), seven showed intact MAPK pathway activity (18-56% inhibition), and three showed MAPK pathway activation (21-235% stimulation) upon ex vivo PLX-4720 exposure. Correlation of these functional profiles with known tumor BRAF genotype and clinical response to BRAF inhibitors revealed that the two patients with significant MAPK pathway suppression were the only two BRAF V600E patients who showed at least a partial response to BRAF inhibitor therapy. Of the seven samples with intact MAPK pathway activity, three were from BRAF wild type patients. The remaining four samples that showed intact activity of the MAPK pathway were BRAF V600E/K patients who were not responding to BRAF inhibitors. Of the three patients that showed MAPK pathway activation, two were wild type for BRAF and a third had the V600E mutation and was not responding to BRAF inhibitor therapy. These results indicate that functional profiles can be generated from human samples, and that functional profiles provide novel information about tumor signal transduction circuitry that may correlate with therapeutic responses.