Cells Expressing BRAF^{V600E} have a unique lipid profile

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Abstract

There is increasing evidence that oxidative metabolism and fatty acids play an important role in BRAF-driven tumorigenesis, yet the effect of BRAF^{V600E} expression on metabolism is poorly understood. We examined how this BRAF mutation modulates metabolite abundancy. Using NIH3T3 mouse fibroblast models, we found cells expressing BRAF^{V600E} were enriched with immunomodulatory lipids and had a unique transcriptional signature. The BRAF^{V600E} mutation promoted accumulation of long chain polyunsaturated fatty acids and rewired metabolic flux with non-Warburg behavior. This cancer-promoting mutation induced the formation of TNT-like protrusions which preferentially accumulated lipid droplets. In the plasma of melanoma patients harboring the BRAF^{V600E} mutation, levels of lysophosphatidic acid, sphingomyelin, and long chain fatty acids were significantly increased in patients who did not respond to BRAF inhibitor therapy following treatment. Our findings show BRAF^{V600} status plays an important role in regulating the immunomodulatory lipid profile and lipid trafficking which may inform future therapy across cancers.