CANONICAL DE NOVO SYNTHESIS OF ASPARTATE IS DISPENSABLE FOR TUMOR GROWTH

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Mitochondrial oxidative phosphorylation (OXPHOS) system is important for tumorigenesis, and OXPHOS-deficient cancer cells cannot form tumors in mice. One of the major consequences of OXPHOS deficiency is the failure to synthesize aspartate, an amino acid essential for proliferation, in the absence of NADH/NAD+ recycling at complex I. However, whether complex I deficiency is equivalent to the deficiency of aspartate biosynthesis with respect to in vivo tumor growth remains unclear. Two transaminases called GOT1 and 2 are known to produce aspartate de novo in mammals. Hence, we directly compared tumor-forming capacity of aspartate synthesis deficient (GOT1-2 dKO) B16 mouse melanoma cancer cells to their complex I deficient (NDUFV1 KO) counterparts. While NDUFV1 KO cells exhibit a large defect in tumor formation, GOT1/2 KO cells produce tumors with kinetics similar to the parental cells. This suggests that GOT1-2 dKO tumors must be able to obtain aspartate in some other way. Currently we are establishing molecular details underlying this observation. To summarize, we demonstrate that, contrary to current believes, complex I deficiency is not equivalent to aspartate synthesis deficiency regarding tumorigenesis in mice.