A new role for the von Hippel-Lindau tumor suppressor protein: stimulation of mitochondrial oxidative phosphorylation complex biogenesis.

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Abstract

Although mitochondrial deficiency in cancer has been described by Warburg, many years ago, the mechanisms underlying this impairment remain essentially unknown. Many types of cancer cells are concerned and, in particular, clear cell renal carcinoma (CCRC). In this cancer, the tumor suppressor gene, VHL (von Hippel-Lindau factor) is invalidated. Previous studies have shown that the transfection of the VHL gene in VHL-deficient cells originating from CCRCs could suppress their ability to form tumors when they were injected into nude mice. However, various additional genetic alterations are observed in such cancer cells. In order to investigate whether VHL invalidation was related to the mitochondrial impairment, we have studied the effects of wild-type VHL transfection into VHL-deficient 786-0 or RCC10 cells on their oxidative phosphorylation (OXPHOS) subunit contents and functions. We show that the presence of wild-type VHL protein (pVHL) increased mitochondrial DNA and respiratory chain protein contents and permitted the cells to rely on their mitochondrial ATP production to grow in the absence of glucose. In parallel to mtDNA increase, the presence of pVHL upregulated the mitochondrial transcription factor A, as shown by western blot analysis. In conclusion, in CCRCs, pVHL deficiency is one of the factors responsible for down-regulation of the biogenesis of OXPHOS complexes.

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