

Loss of function of the gene encoding the histone methyltransferase KMT2D leads to deregulation of mitochondrial respiration

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Supplemental data

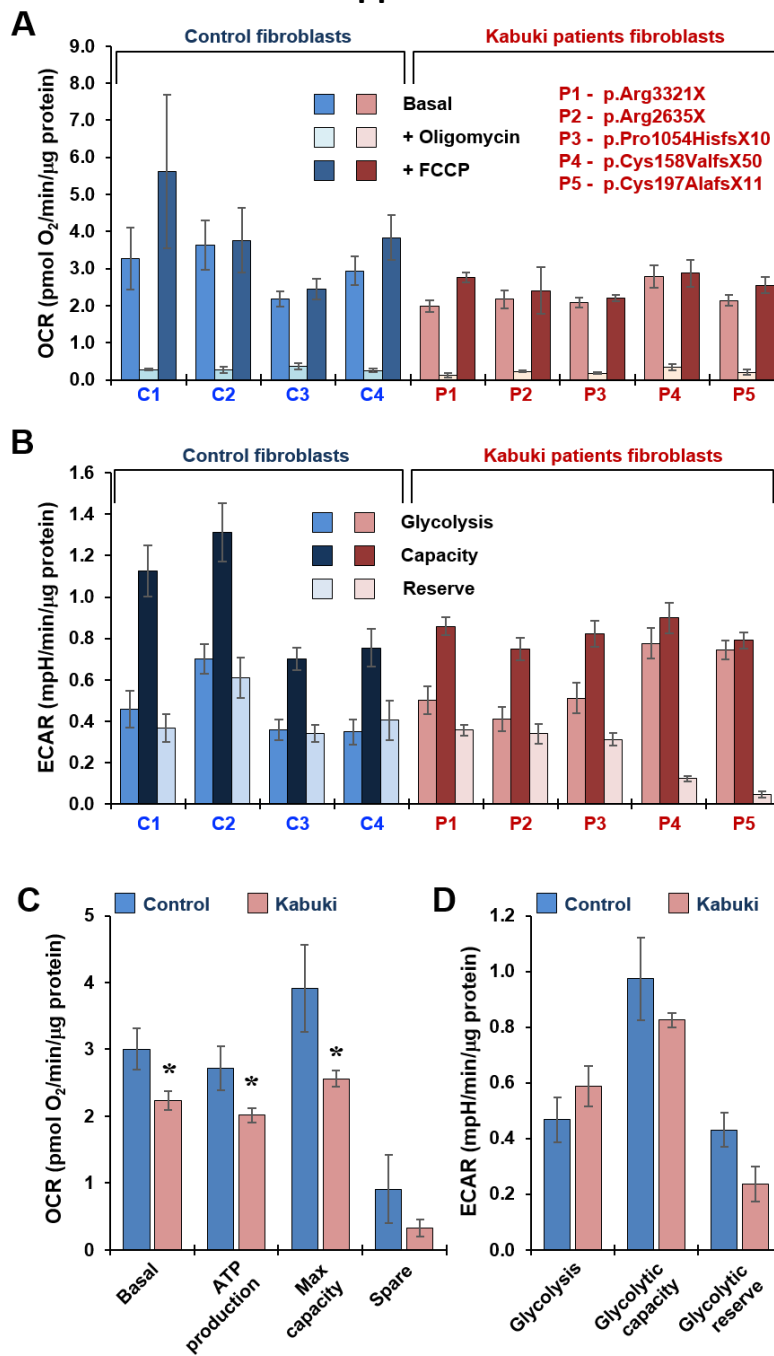


Figure S1. Metabolic fluxes analysis in normal and Kabuki syndrome-affected patients' fibroblasts, as described in the legend of Figure 1. The mutations in *KMT2D* carried on by each Kabuki patient are indicated in (A). (A) and (B) are metabolic parameters inferred from the OCR and ECAR assays, respectively. The bars are means $\pm$ SEM of three independent experiments carried out in triplicate under each condition. (C) and (D) are OCR- and ECAR-related parameters resulting from the averaging of the four Control and five Kabuki fibroblasts; *, $P < 0.05$ vs control fibroblasts. In the table below further features of the patients' fibroblasts are indicated.

Kabuki Patient	Sex	Age of biopsy (years)	Culture passage
#1	F	3	5
#2	F	3	5
#3	M	4	6
#4	M	5	5
#5	M	5	5

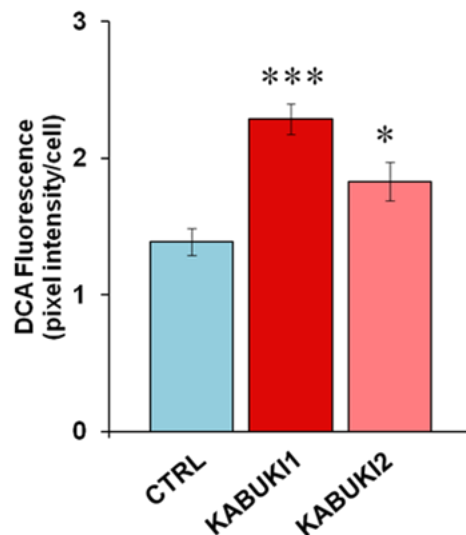


Figure S2. Measurement of the intracellular ROS in normal and Kabuki syndrome-affected patients' fibroblasts. DCF-loaded fibroblasts were analysed by confocal microscopy as in Figure 5A and the mean fluorescence intensity/cell of the probe was estimated as described in Materials and Methods. The bars are mean $\pm$ SEM of three independent experiments for each sample; *, $P < 0.05$ and ***, $P < 0.0005$ vs normal (CTRL) fibroblasts.

Table S1. OFF Target prediction for gRNA used for *KMT2D* KO of human patient's cell lines. (<http://www.rgenome.net/cas-offinder/>).

crRNA-gRNA_A	DNA TARGET SEQUENCES	Chromosome	Position	Mismatches
GTGCGGCGTTGTGCTCTCTGNNG	GTGCTGCGcTGTGtTCTCTGAGG	chr1	94025031	3
GTGCGGCGTTGTGCTCTCTGNNG	aTGCGGCGcTGTGtTCTCTGAGG	chr6	7840822	3
GTGCGGCGTTGTGCTCTCTGNNG	GTGCGGatTTGTGCTCTCcGGGG	chr14	100726557	3
GTGCGGCGTTGTGCTCTCTGNNG	GTGaGGCGTTGgGCTCTCTtAGG	chrX	11084607	3
GTGCGGCGTTGTGCTCTCTGNNG	GTGCTGgGTTGTtCTCTCTGTGG	chr18	48142412	3
crRNA-gRNA_B	DNA TARGET SEQUENCES	Chromosome	Position	Mismatches
CTCACCATTGGTGTGCTGCANGG	CTCACCATTGaTaaGCTGCAGGG	chr3	101257523	3
CTCACCATTGGTGTGCTGCANGG	CTCACCATTGGgaTGCTcCAGGG	chr1	103708618	3
CTCACCATTGGTGTGCTGCANGG	CTCACCATTGGgaTGCTcCAGGG	chr1	103643330	3
CTCACCATTGGTGTGCTGCANGG	CTCACCATTGGgaTGCTcCAGGG	chr1	103737468	3

CTCACCATTGGTGTGCTGCANGG	CTCACCATcaGTtTGCTGCATGG	chr2	87517362	3
CTCACCATTGGTGTGCTGCANGG	CTCACCATcaGTtTGCTGCATGG	chr2	111433440	3
CTCACCATTGGTGTGCTGCANGG	CTCACCCtGGTGaGCTGCAGGG	chr17	18382352	3
CTCACCATTGGTGTGCTGCANGG	CTCAtCATTGGTcTGtTGCAAGG	chrX	38275793	3
crRNA-gRNA_C	DNA TARGET SEQUENCES	Chromosome	Position	Mismatches
CATGTGGGAGAGGTCTCTGTNGG	CATGTGGGAGAGtTtTCTGTTGG	chr15	57808715	2
CATGTGGGAGAGGTCTCTGTNGG	CATGTtGGAcAGGTCTCTGTTGG	chr9	117255859	2
CATGTGGGAGAGGTCTCTGTNGG	CATGTGGGAGAtGTagCTGTGGG	chr8	83559819	3
CATGTGGGAGAGGTCTCTGTNGG	aAaGTGGGAGAGaTCTCTGTGGG	chr8	130198977	3
CATGTGGGAGAGGTCTCTGTNGG	CcTGTGGGAGAGGTCcCgTAGG	chr7	64293094	3
CATGTGGGAGAGGTCTCTGTNGG	gcTGTGGaAGAGGTCTCTGTGGG	chr5	179642176	3
CATGTGGGAGAGGTCTCTGTNGG	gcTGTGGaAGAGGTCTCTGTGGG	chr5	179652583	3
CATGTGGGAGAGGTCTCTGTNGG	CAGTGGGAcAGGTCaCTGTGGG	chr16	29978546	3
CATGTGGGAGAGGTCTCTGTNGG	CATGTGGGgGgGcTCTCTGTGGG	chr1	1042876	3
CATGTGGGAGAGGTCTCTGTNGG	CcTGTGGGAGAGaTaTCTGTAGG	chr1	117031559	3
CATGTGGGAGAGGTCTCTGTNGG	CATGTGGGAGAGGcagCTGTGGG	chr1	155235916	3
CATGTGGGAGAGGTCTCTGTNGG	CATtTtGcAGAGGTCTCTGTCCG	chr1	208447791	3
CATGTGGGAGAGGTCTCTGTNGG	CAaGTGtGAGAGGTCTgTGTAGG	chr2	96164938	3
CATGTGGGAGAGGTCTCTGTNGG	CAGTGGcAGAGGgCTCTGTTGG	chr19	28145548	3
CATGTGGGAGAGGTCTCTGTNGG	CAaGaGGGAGAGGTCaCTGTAGG	chr19	37345061	3
CATGTGGGAGAGGTCTCTGTNGG	CATGTGGcAGAGGTgTCTtTAGG	chr21	38603168	3
CATGTGGGAGAGGTCTCTGTNGG	CATGTGGGtGAGGTCTCaGgGGG	chr21	42186755	3
CATGTGGGAGAGGTCTCTGTNGG	CAGTtGGAGgGGTCTCTGTGGG	chr17	74516601	3
CATGTGGGAGAGGTCTCTGTNGG	CATGTGtGAGAGGTgTtTGTGGG	chr10	12534865	3
CATGTGGGAGAGGTCTCTGTNGG	CATGTGGGAGAGGctTCTGcTGG	chr6	146676669	3
CATGTGGGAGAGGTCTCTGTNGG	CATtTGcGgGAGGTCTCTGTGGG	chr9	39364626	3
CATGTGGGAGAGGTCTCTGTNGG	CATtTGcGgGAGGTCTCTGTGGG	chr9	60923316	3
CATGTGGGAGAGGTCTCTGTNGG	CATtTGcGgGAGGTCTCTGTGGG	chr9	61198945	3
CATGTGGGAGAGGTCTCTGTNGG	CATtTGcGgGAGGTCTCTGTGGG	chr9	66983615	3
CATGTGGGAGAGGTCTCTGTNGG	CATaTGGGAGAGGTtTCTGcAGG	chr18	78098590	3
CATGTGGGAGAGGTCTCTGTNGG	CAGGaGGGAGgGGTCTCTGTAGG	chr11	67435476	3