

## Supplementary Information

**Table I1: List of all used patient derived melanoma cell lines in this study.** ATCC: American Type Culture Collection

Name	Tissue	Morphology	Source	BRAF mutation
A375	skin	epithelial	ATCC (CRL-1619)	BRAF V600E
Mel1617	skin	epithelial	M. Herlyn <sup>1</sup>	BRAF V600E
451lu	skin	epithelial	M. Herlyn <sup>1</sup>	BRAF V600E
SKMel28	skin	polygonal	ATCC (HTB-72)	BRAF V600E
SKMel19	skin	epithelial	C. Garbe <sup>2</sup>	BRAF V600E

- 1 Herlyn, D. *et al.* Properties of Human Melanoma Cells Metastatic in Nude Mice. *Cancer Research* **50**, 2296-2302 (1990).
- 2 Sinnberg, T. *et al.* A Nexus Consisting of Beta-Catenin and Stat3 Attenuates BRAF Inhibitor Efficacy and Mediates Acquired Resistance to Vemurafenib. *EBioMedicine* **8**, 132-149, doi:10.1016/j.ebiom.2016.04.037 (2016).

**Table I2: Top five down-and up-regulated proteins of vemurafenib-resistant and -sensitive A375 proteome.**

Uniprot ID	Gene name	Protein name	SILAC ratio (log <sub>2</sub> )	Intensity (log <sub>10</sub> )
P02751	FN1	Fibronectin	-2.81	10.22
P48681	NES	Nestin	-2.71	10.20
P35625	TIMP3	Metalloproteinase inhibitor 3	-1.92	9.44
Q13938	CAPS	Calcyphosin	-1.79	9.58
P04233	CD74	HLA class II histocompatibility antigen gamma chain	-1.38	9.96
A0A0G2JJ56	SPANXB1	Sperm protein associated with nucleus on X chromosome B/F	2.10	8.29
Q9GZP8	IMUP	Immortalization up-regulated protein	2.01	7.69
P80723	BASP1	Brain acid soluble protein 1	2.00	8.21
P00533	EGFR	Epidermal growth factor receptor	1.65	7.83
Q52LW3	ARHGAP29	Rho GTPase-activating protein 29	1.34	7.61

**Table I3: List of FFPE specimens used in this study.**

Patient	Surgery date	Localisation	Treatment	Remarks
#1	09.11.2011	Abdomen		Immunohistochemistry
	05.06.2014	Buttocks (gluteal, left)	Vemurafenib (12 months)/Ipilimumab (3 months)	Immunohistochemistry
#2	23.11. 2011	Tight (left)		Immunohistochemistry and proteomics
	25.02.2013	Lower leg (right)	Vemurafenib (3 months)	Immunohistochemistry and proteomics

**Table I4: Predicted off-target effects of crRNA guide CCTCGACGGCGCGCCGGTTG using cas-offinder. Chr: chromosome.**

crRNA	DNA	Chr	Position	Direction	mismatch
CCTCGACGGCGCG CCGGTTGNGG	CCTCGACGGCGCG CCGGTTGCGG	chr1	1570000	+	0
CCTCGACGGCGCG CCGGTTGNGG	CCcCGACGGCGCG gCGGTTcCGG	chr17	7478944	+	3
CCTCGACGGCGCG CCGGTTGNGG	CCcCaACGGCGCGC CGGcTGTGG	chr20	62861781	-	3