Supplemental Methods

Sequencing. Genomic DNA was extracted from peripheral blood using standard procedures and its quality was monitored using a Nanodrop spectrophotometer. DNA was amplified for CDKN2A, CDK4, MC1R, TP53 and MITF as described previously [13, S1]. PCR products were subjected to automatic sequencing by ABI PRISM 310 genetic analyzer (Applied Biosystems).

Microsatellite analysis. The primers used for microsatellite typing are reported in Table S1. In each primer pair, a 5'-FAM oligonucleotide was used. Amplification products were visualized as described for Sequencing. Analysis was conducted using Peak Scanner Software v1.0 using GeneScan-400 TAMRA size standard (Applied Biosystems).

Multiplex ligation-dependent probe amplification (MLPA). MLPA kits ME024-B1-salsa and P024-B2-salsa were used to profile the 9p21 region as detailed by the manufacturer instructions (MRC-Holland, Amsterdam, the Netherlands). Probe amplification products were run on an ABI PRISM 310 genetic analyzer using GeneScan-500 TAMRA size standard. Results were analyzed by Coffalyser v9.4 software after normalization of peaks against three samples of DNA from healthy donors.

Array-CGH. The array-CGH analysis was performed using the SurePrint G3 Human CGH Agilent 2x400K array as recommended by Agilent (protocol Version 7.2 July 2012 Agilent Technologies). A graphical visualization of the results was provided by the Agilent CytoGenomics (v 2.7.22.0) with the following parameters: aberration algorithm ADM-2, threshold 6.0 and moving average window 1Mb. Aberrant signals including 3 or more consecutive probes with the same polarity were called as deletion or duplication. Physical

mapping and gene location were obtained from the UCSC Genome Browser (hg19, NCBI Build 37).

Supplemental References

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