

Figure S1 Characterization of HEMn cells. Genetic ancestry of HEMn-LP and HEMn-DP estimated by STRUCTURE using 24 autosomal ancestry-sensitive markers (ASMs) shows a European origin for HEMn-LP and an African origin for HEMn-DP, confirming a light skin colour and dark skin colour of the donors.

Figure S2: rs6497271 does not influence the activity of the rs12913832 enhancer region.

(A) Sequence alignment of the cloned rs12913832 enhancer region from HEMn-LP (top) and HEMn-DP cells (bottom). Positions of rs12913832 and rs6497271 are indicated in bold type and grey shading. The positions of putative binding sites for HLTF, MITF and LEF1 are indicated by boxes (Sturm et al., 2008). The position of the XmnI restriction site used to produce the chimerical luciferase constructs is indicated by a dotted line. (B) Luciferase reporter assay demonstrates that rs6497271 doesn't influence the enhancer activity of the rs12913832 region. Chimerical luciferase reporter plasmids containing the C or T allele of rs12913832 region in combination with the C or T allele of rs6497271 were transfected into G361 melanoma cells and luciferase activity was determined. Luciferase expression is normalised to renilla luciferase expression. Data are represented as mean +/- SEM (* = $p < 0.05$).

Figure S3 No chromatin loop is present between the *OCA2* promoter and the *HERC2* rs12913832 enhancer region in MCF7 control cells. (A-B) Locus wide cross-linking frequencies observed in MCF7 control cells. The analyzed region of the human *OCA2*-*HERC2* locus is depicted on top of each graph. X-axis shows the approximate position on chromosome 15 (UCSC browser NCBI36/hg18 assembly; NCBI36/hg18 assembly; <http://genome.ucsc.edu/cgi-bin/hgGateway?db=hg18>). Black shading shows the position and size of the 'fixed' restriction fragment. Grey shading indicates position and size of other

restriction fragments analyzed. Black vertical bars in the locus graph indicate EcoRI sites, red vertical bars ApoI sites. Cross-linking frequencies are normalized to the highest interaction within an experiment. (A) Cross-linking frequencies for an ApoI restriction fragment containing *HERC2* rs12913832 in MCF7 cells. Relatively low cross-linking frequencies with restriction fragments containing the *OCA2* promoter are observed in MCF7 control cells. (B) Cross-linking frequencies for an ApoI restriction fragment containing the *OCA2* promoter in MCF7 cells. Relatively low cross-linking frequencies with restriction fragments containing rs12913832 are observed in MCF7 control cells. (C) Comparison of cross-linking frequencies between an ApoI restriction fragment containing rs12913832 and an ApoI restriction fragment containing the *OCA2* promoter in MCF7 and HEMn cells. Highest interaction is set to 1. Data are represented as mean \pm SEM (* = $p < 0.05$; *** = $p < 0.005$).

Figure S4 A potential additional regulatory site is present just downstream of the *HERC2* gene. (A) Comparison of crosslinking frequencies between an ApoI restriction fragment containing rs12913832 and an ApoI restriction fragment containing the region just downstream of *HERC2* in MCF7 and HEMn cells indicates a comparable interaction frequency in all cell lines. Highest interaction is set to 1. (B) Tracks from the UCSC browser (NCBI36/hg18 assembly; <http://genome.ucsc.edu/cgi-bin/hgGateway?db=hg18>) displaying several chromatin marks associated with regulatory elements (Top panel) and DNase sensitivity (bottom panel) in the human *OCA2-HERC2* intergenic region as determined by the ENCODE consortium are shown. A region of “enhancer” chromatin marks (boxed) is detected in the region between *HERC2* and *OCA2*. (C) ChIP-qPCR of Acetylated histone H3 and histone H3 mono methylated on lysine 4 demonstrates active chromatin marks in the *OCA2-HERC2* intergenic region in MCF7 and HEMn-DP cells. A schematic overview of the locus is depicted on top of the figure.

Approximate position on chromosome 15 of the PCR amplicons is indicated with letters A = 26.0392Mb; B = 26.0287Mb; C = 26.0267Mb; D = 26.0210Mb. ChIP enrichments displayed are relative to *NDN*. Data are represented as mean \pm SEM.