**Supplementary Table S1.** List of 88 selected genes in the peroxisome pathway

| Gene | Location | Type | P | FDR (0.1) | BFDP (Prior probability) |
|------|----------|------|---|-----------|--------------------------|
| Supplementary Table S2. | Multiple testing corrections of the two independent SNPs in MDACC study |
| Supplementary Table S3. | Stratified analysis of the risk genotypes of selected SNPs in the MDACC and NHS/HPFS datasets |

*BFDP, Bayesian false-discovery probability; FDR, false discovery rate; MDACC, The University of Texas MD Anderson Cancer Center; NHS, the Nurse Health Study; HPFS, the Health Professionals Follow-up Study; NRG, number of risk genotypes; HR, hazards ratio; CI, confidence interval.*

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### Supplementary Table S4. Function prediction of independent SNPs and high linkage disequilibrium (LD) ($r^2 \geq 0.8$) associated with them in the peroxisome pathway

| SNP       | Chr | Gene | RegDB\(^a\) | Promoter histone marks | Enhancer histone marks | DNAse | Proteins bound | Motifs changed | GRASP QTL hits | Selected eQTL hits | dbSNP func annot |
|-----------|-----|------|-------------|------------------------|------------------------|-------|---------------|----------------|----------------|-----------------|--------------------|
| rs542279  | 11  | TMEM135 | Haploreg v4.1 | 0.81 | 4 tissues | 5 altered motifs | intronic |
| rs631930  | 11  | TMEM135 | 6 | 0.81 | STRM | RXS5 | 1 hit | intronic |
| rs520718  | 11  | TMEM135 | No data | 0.81 | 8 tissues | 9 tissues | in intronic |
| rs556724  | 11  | TMEM135 | 5 | 0.81 | 10 tissues | Hmx1, Nox2, Nox3 | in intronic |
| rs605658  | 11  | TMEM135 | 5 | 0.81 | 5 tissues | 4 tissues | PAX-4 | 1 hit | in intronic |
| rs518159  | 11  | TMEM135 | 5 | 0.81 | STRM | 1 hit | in intronic |
| rs518059  | 11  | TMEM135 | No data | 0.85 | 4 tissues | 4 tissues | PAX-4 | 1 hit | in intronic |
| rs578116  | 11  | TMEM135 | No data | 0.85 | SKIN, BRN | GR, Ir | in intronic |
| rs482844  | 11  | TMEM135 | 4 | 0.85 | STRM, SKIN, BRN, VAS | Bcl-6b, Irx, Sp100 | in intronic |
| rs34782550| 11  | TMEM135 | 5 | 0.85 | STRM, SKIN, PANC | 4 altered motifs | in intronic |
| rs34806361| 11  | TMEM135 | 6 | 0.85 | STRM, SKIN, PANC | 12 altered motifs | in intronic |
| rs500725  | 11  | TMEM135 | No data | 0.85 | 17 altered motifs | in intronic |
| rs493708  | 11  | TMEM135 | No data | 0.85 | GI | BLD | NF-Y, Pbx3 | 4 altered motifs | in intronic |
| rs139109823| 11 | TMEM135 | No data | 0.85 | STRM, GI | 4 altered motifs | in intronic |
| rs567403  | 11  | TMEM135 | 5 | 1 | 4 tissues | CBS, CJUN, JUND | Dobox4, Ir | 1 hit | in intronic |
| rs7139158 | 12  | PEX5  | 5 | 0.86 | GI | 4 altered motifs | 54 hits | in intronic |
| rs10743271| 12  | PEX5  | No data | 0.98 | Foxp1 | 52 hits | 504 intrinsic |
| rs10161405| 12  | PEX5  | 6 | 0.98 | GATA, Pou5f1, TAL1 | 53 hits | in intronic |
| rs10161542| 12  | PEX5  | 6 | 0.98 | 9 altered motifs | 53 hits | in intronic |
| rs3816424 | 12  | PEX5  | 6 | 0.98 | MUS | BHLHE40, Foxm1 | 3 hits | 53 hits | in intronic |
| rs10161170| 12  | PEX5  | No data | 0.99 | 58 hits | intronic |
| rs11044901| 12  | PEX5  | No data | 0.99 | Pax-5, SP1 | 52 hits | in intronic |
| rs10161103| 12  | PEX5  | 6 | 0.99 | 4 altered motifs | 51 hits | in intronic |
| rs7869508 | 12  | PEX5  | 6 | 0.99 | 6 hits | 53 hits | in intronic |
| rs7869635 | 12  | PEX5  | 5 | 1 | 52 hits | intronic |
| rs7869751 | 12  | PEX5  | 6 | 1 | 8 altered motifs | 54 hits | in intronic |

\(^a\)RegulomeDB (http://www.regulomedb.org); \(^b\)HaploReg v4.1 (http://archive.broadinstitute.org/mammals/haploreg/). Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; dbSNP funcannot, dbSNP function annotation.
Supplementary Figure S1. Manhattan plot. (a) Manhattan plot for 8,397 SNPs in the MDACC study. There were 332 SNPs with P < 0.05 and 277 SNPs with BFDP < 0.8. (b) Manhattan plot for 277 SNPs in the NHS/HPFS study. The red horizontal line indicates P-value equal to 0.05 and the blue horizontal line represents a BFDP value equal to 0.8. Abbreviations: BFDP, Bayesian false-discovery probability; MDACC, The University of Texas MD Anderson Cancer Center; SNP, single nucleotide polymorphism; NHS, the Nurse Health Study; HPFS, the Health Professionals Follow-up Study; PEX5, peroxisomal biogenesis factor 5; TMEM135, transmembrane protein 135.

Supplementary Figure S2. Regional association plots showing 50 kb upstream and downstream of the gene regions in (a) TMEM135 and (b) PEX5. Abbreviations: PEX5, peroxisomal biogenesis factor 5; TMEM135, transmembrane protein 135.

Supplementary Figure S3. The 5-year CMSS predicted by ROC curves in the (a) MDACC dataset, (c) NHS/HPFS dataset, and (e) the combined dataset. Time-dependent AUC estimation based on clinical variables in the (b) MDACC dataset, (d) NHS/HPFS dataset, and (f) the combined dataset. Abbreviations: CMSS, cutaneous melanoma-specific survival; ROC, receiver operating characteristic; MDACC, The University of Texas MD Anderson Cancer Center; NHS, the Nurse Health Study; HPFS, the Health Professionals Follow-up Study; AUC, area under ROC curve.
Supplementary Figure S4. Functional prediction of SNPs in the ENCODE project. (a) Location and functional prediction of SNP rs567403. (b) Location and functional prediction of SNP rs7969508. Abbreviations: SNP, single nucleotide polymorphism; PEX5, peroxisomal biogenesis factor 5; TMEM135, transmembrane protein 135.

Supplementary Figure S5. The expression quantitative trait loci (eQTL) analysis for TMEM135 rs567403 in GTEx in (a) unexposed skin, (b) sun-exposed skin (lower leg), and (c) whole blood cells. Abbreviations: GTEx, Genotype-Tissue Expression Project; TMEM135, transmembrane protein 135.