

**Supplementary Table 1. Interaction between the p53 Arg72Pro polymorphism and MC1R variants on hair color and childhood sunburn reaction among controls**

| p53   | MC1R             | WT/WT            | WT/NRHC or NRHC/NRHC | WT/RHC            | RHC/RHC or NRHC/RHC |
|---|------------------|------------------|----------------------|-------------------|---------------------|
| <b>Hair color</b>                             |                  |                  |                      |                   |                     |
| <b>Arg/Arg</b>                                |                  |                  |                      |                   |                     |
| Blonde or red/<br>Black or brown <sup>a</sup> | 16/116           | 17/176           | 14/63                | 16/34             |                     |
| Crude OR                                      | 1.00             | 0.70 (0.34-1.44) | 1.61 (0.74-3.52)     | 3.41 (1.55-7.53)  |                     |
| Multivariate OR <sup>b</sup>                  | 1.00             | 0.68 (0.32-1.42) | 1.40 (0.63-3.11)     | 2.29 (1.01-5.19)  |                     |
| <b>Arg/Pro or Pro/Pro</b>                     |                  |                  |                      |                   |                     |
| Blonde or red/<br>Black or brown <sup>a</sup> | 11/96            | 13/105           | 15/49                | 15/22             |                     |
| Crude OR                                      | 0.83 (0.37-1.88) | 0.90 (0.41-1.95) | 2.22 (1.02-4.84)     | 4.94 (2.14-11.44) |                     |
| Multivariate OR <sup>b</sup>                  | 1.03 (0.45-2.39) | 0.84 (0.38-1.87) | 2.31 (1.03-5.18)     | 3.42 (1.44-8.14)  |                     |
| p53   | MC1R             | WT/WT            | WT/NRHC or NRHC/NRHC | WT/RHC            | RHC/RHC or NRHC/RHC |
| <b>Sunburn reaction</b>                       |                  |                  |                      |                   |                     |
| <b>Arg/Arg</b>                                |                  |                  |                      |                   |                     |
| Burn/Non-burn <sup>a</sup>                    | 37/95            | 77/116           | 40/37                | 28/22             |                     |
| Crude OR                                      | 1.00             | 1.70 (1.06-2.75) | 2.78 (1.54-4.99)     | 3.27 (1.66-6.42)  |                     |
| Multivariate OR <sup>c</sup>                  | 1.00             | 1.87 (1.12-3.11) | 2.63 (1.39-4.96)     | 1.88 (0.90-3.93)  |                     |
| <b>Arg/Pro or Pro/Pro</b>                     |                  |                  |                      |                   |                     |
| Burn/Non-burn <sup>a</sup>                    | 27/80            | 42/76            | 30/34                | 28/9              |                     |
| Crude OR                                      | 0.87 (0.49-1.55) | 1.42 (0.83-2.42) | 2.27 (1.22-4.21)     | 7.99 (3.44-18.53) |                     |
| Multivariate OR <sup>c</sup>                  | 1.09 (0.59-2.02) | 1.47 (0.83-2.60) | 2.54 (1.29-5.01)     | 5.04 (2.01-12.65) |                     |

WT stands for consensus allele. NRHC stands for non-red hair color allele. RHC stands for red hair color allele.

Four categories of the responses to the question of childhood sunburn reaction were grouped into burn (burn, painful burn, and painful burn with blisters) and non-burn (practically none and some redness only).

<sup>a</sup>The number of participants does not add up to the total women because of missing genotypes.

<sup>b</sup>Unconditional logistic regression adjusted for natural skin color (*p*, interaction, 0.46).

<sup>c</sup>Unconditional logistic regression adjusted for natural skin color and natural hair color (*p*, interaction, 0.24).

**Supplementary Table 2. SCC and BCC risks by p53 Arg72Pro polymorphism and hair color**

| SCC                        |                  |                  |                   |          |
|----------------------------|------------------|------------------|-------------------|----------|
| Hair color                 | Arg/Arg          | Arg/Pro          | Pro/Pro           | P, trend |
| Black or dark brown        |                  |                  |                   |          |
| Case/Controls <sup>a</sup> | 60/237           | 50/118           | 6/19              |          |
| OR <sup>b</sup>            | 1.00             | 1.68 (1.08-2.59) | 1.24 (0.47-3.23)  | 0.06     |
| Light brown                |                  |                  |                   |          |
| Case/Controls <sup>a</sup> | 58/181           | 34/136           | 4/22              |          |
| OR <sup>b</sup>            | 1.26 (0.84-1.90) | 0.98 (0.61-1.57) | 0.70 (0.23-2.12)  | 0.12     |
| Blonde or red              |                  |                  |                   |          |
| Case/Controls <sup>a</sup> | 33/68            | 23/53            | 7/5               |          |
| OR <sup>b</sup>            | 1.91 (1.15-3.16) | 1.69 (0.96-2.98) | 5.54 (1.70-18.09) | 0.24     |
| BCC                        |                  |                  |                   |          |
| Hair color                 | Arg/Arg          | Arg/Pro          | Pro/Pro           | P, trend |
| Black or dark brown        |                  |                  |                   |          |
| Case/Controls <sup>a</sup> | 46/237           | 39/118           | 6/19              |          |
| OR <sup>b</sup>            | 1.00             | 1.72 (1.06-2.78) | 1.65 (0.62-4.37)  | 0.04     |
| Light brown                |                  |                  |                   |          |
| Case/Controls <sup>a</sup> | 75/181           | 49/136           | 12/22             |          |
| OR <sup>b</sup>            | 2.16 (1.42-3.27) | 1.86 (1.18-2.93) | 2.94 (1.35-6.39)  | 0.93     |
| Blonde or red              |                  |                  |                   |          |
| Case/Controls <sup>a</sup> | 40/68            | 24/53            | 4/5               |          |
| OR <sup>b</sup>            | 3.07 (1.86-5.08) | 2.36 (1.33-4.22) | 4.47 (1.15-17.39) | 0.94     |

p-value for trend was calculated across the three p53 genotypes.

<sup>a</sup>The number of participants does not add up to the total women because of missing genotypes.

<sup>b</sup>Unconditional logistic regression adjusted for the matching variables: age and race

(Caucasian/missing) (interaction p-values for SCC and BCC were 0.46 and 0.11, respectively).

**Supplementary Table 3. SCC and BCC risks by p53 Arg72Pro polymorphism and MC1R variants**

|                              |                  | SCC              |                   |         |
|------------------------------|------------------|------------------|-------------------|---------|
|                              |                  | Arg/Arg          | Arg/Pro           | Pro/Pro |
| MC1R \ P53                   |                  |                  |                   |         |
| WT/WT                        |                  |                  |                   |         |
| Case/Controls <sup>a</sup>   | 27/135           | 20/92            | 2/15              |         |
| Multivariate OR <sup>b</sup> | 1.00             | 1.08 (0.57-2.05) | 0.66 (0.14-3.05)  |         |
| Multivariate OR <sup>c</sup> | 1.00             | 1.18 (0.62-2.26) | 0.79 (0.17-3.71)  |         |
| WT/NRHC or NRHC/NRHC         |                  |                  |                   |         |
| Case/Controls <sup>a</sup>   | 54/196           | 36/102           | 7/18              |         |
| Multivariate OR <sup>b</sup> | 1.38 (0.83-2.31) | 1.76 (1.01-3.10) | 1.89 (0.72-4.97)  |         |
| Multivariate OR <sup>c</sup> | 1.40 (0.83-2.35) | 1.80 (1.02-3.19) | 1.97 (0.74-5.23)  |         |
| WT/RHC                       |                  |                  |                   |         |
| Case/Controls <sup>a</sup>   | 38/78            | 21/55            | 2/9               |         |
| Multivariate OR <sup>b</sup> | 2.49 (1.41-4.39) | 1.93 (1.00-3.70) | 1.05 (0.21-5.16)  |         |
| Multivariate OR <sup>c</sup> | 2.40 (1.35-4.30) | 1.94 (1.00-3.77) | 1.02 (0.21-5.08)  |         |
| RHC/RHC or NRHC/RHC          |                  |                  |                   |         |
| Case/Controls <sup>a</sup>   | 27/50            | 24/35            | 4/3               |         |
| Multivariate OR <sup>b</sup> | 2.73 (1.45-5.11) | 3.44 (1.77-6.70) | 7.31 (1.53-35.00) |         |
| Multivariate OR <sup>c</sup> | 2.38 (1.24-4.58) | 2.88 (1.45-5.73) | 6.74 (1.37-33.21) |         |
| BCC                          |                  |                  |                   |         |
| MC1R \ P53                   |                  | Arg/Arg          | Arg/Pro           | Pro/Pro |
| WT/WT                        |                  |                  |                   |         |
| Case/Controls <sup>a</sup>   | 27/135           | 26/92            | 3/15              |         |
| Multivariate OR <sup>b</sup> | 1.00             | 1.42 (0.78-2.60) | 0.99 (0.27-3.65)  |         |
| Multivariate OR <sup>c</sup> | 1.00             | 1.54 (0.83-2.83) | 0.97 (0.26-3.67)  |         |
| WT/NRHC or NRHC/NRHC         |                  |                  |                   |         |
| Case/Controls <sup>a</sup>   | 64/196           | 32/102           | 9/18              |         |
| Multivariate OR <sup>b</sup> | 1.64 (0.99-2.70) | 1.57 (0.88-2.78) | 2.56 (1.04-6.34)  |         |
| Multivariate OR <sup>c</sup> | 1.63 (0.98-2.72) | 1.53 (0.85-2.74) | 2.83 (1.13-7.09)  |         |
| WT/RHC                       |                  |                  |                   |         |
| Case/Controls <sup>a</sup>   | 31/78            | 29/55            | 5/9               |         |
| Multivariate OR <sup>b</sup> | 2.01 (1.12-3.63) | 2.60 (1.41-4.79) | 2.89 (0.90-9.33)  |         |
| Multivariate OR <sup>c</sup> | 1.87 (1.03-3.40) | 2.28 (1.22-4.25) | 2.44 (0.75-8.02)  |         |
| RHC/RHC or NRHC/RHC          |                  |                  |                   |         |
| Case/Controls <sup>a</sup>   | 23/50            | 15/35            | 3/3               |         |
| Multivariate OR <sup>b</sup> | 2.36 (1.24-4.51) | 2.13 (1.02-4.43) | 5.08 (0.97-26.61) |         |
| Multivariate OR <sup>c</sup> | 1.86 (0.95-3.65) | 1.64 (0.76-3.53) | 3.75 (0.70-20.05) |         |

*p*-value for trend was calculated across the three p53 genotypes.

WT stands for consensus allele. NRHC stands for non-red hair color allele. RHC stands for red hair color allele.

<sup>a</sup>The number of participants does not add up to the total women because of missing genotypes.

<sup>b</sup>Unconditional logistic regression adjusted for the matching variables: age and race

(Caucasian/missing) (interaction *p*-values for SCC and BCC were 0.75 and 0.96, respectively).

<sup>c</sup>Unconditional logistic regression adjusted for the matching variables, natural skin color, natural hair color (interaction *p*-values for SCC and BCC were 0.94 and 0.88, respectively).

**Supplementary Table 4. SCC and BCC risks by p53 Arg72Pro polymorphism and constitutional susceptibility score**

| Constitutional susceptibility score | SCC              |                  |                    | <i>P</i> , trend |
|-------------------------------------|------------------|------------------|--------------------|------------------|
|                                     | Arg/Arg          | Arg/Pro          | Pro/Pro            |                  |
| <b>Low</b>                          |                  |                  |                    |                  |
| Case/Controls <sup>a</sup>          | 22/160           | 16/93            | 4/20               |                  |
| Multivariate OR <sup>b</sup>        | 1.00             | 1.25 (0.63-2.51) | 1.43 (0.45-4.59)   | 0.33             |
| <b>Medium</b>                       |                  |                  |                    |                  |
| Case/Controls <sup>a</sup>          | 51/156           | 28/110           | 4/14               |                  |
| Multivariate OR <sup>b</sup>        | 2.41 (1.40-4.18) | 1.90 (1.03-3.50) | 2.04 (0.62-6.78)   | 0.39             |
| <b>High</b>                         |                  |                  |                    |                  |
| Case/Controls <sup>a</sup>          | 80/178           | 67/106           | 9/13               |                  |
| Multivariate OR <sup>b</sup>        | 3.42 (2.03-5.77) | 4.79 (2.78-8.25) | 5.25 (2.00-13.75)  | 0.07             |
| <b>BCC</b>                          |                  |                  |                    |                  |
| Constitutional susceptibility score | Arg/Arg          | Arg/Pro          | Pro/Pro            | <i>P</i> , trend |
| <b>Low</b>                          |                  |                  |                    |                  |
| Case/Controls <sup>a</sup>          | 25/167           | 21/95            | 4/24               |                  |
| Multivariate OR <sup>b</sup>        | 1.00             | 1.50 (0.79-2.82) | 1.12 (0.36-3.50)   | 0.46             |
| <b>Medium</b>                       |                  |                  |                    |                  |
| Case/Controls <sup>a</sup>          | 55/153           | 37/111           | 7/14               |                  |
| Multivariate OR <sup>b</sup>        | 2.42 (1.43-4.09) | 2.21 (1.26-3.87) | 3.37 (1.23-9.19)   | 0.83             |
| <b>High</b>                         |                  |                  |                    |                  |
| Case/Controls <sup>a</sup>          | 83/174           | 55/103           | 12/9               |                  |
| Multivariate OR <sup>b</sup>        | 3.20 (1.95-5.26) | 3.62 (2.12-6.20) | 10.01 (3.78-26.52) | 0.05             |

*p*-value for trend was calculated across the three p53 genotypes.

<sup>a</sup>The number of participants does not add up to the total women because of missing genotypes.

<sup>b</sup>Unconditional logistic regression adjusted for the matching variables: age and race

(Caucasian/missing) (interaction *p*-values for SCC and BCC were 0.50 and 0.51, respectively).