**Tables**

|  |
| --- |
| **Supplemental Table 1:** Detailed characteristics of studies included in the ASSET meta-analysis of DNA damage repair and signaling genes |
| **Cancer Site** | **Study Name** | **Locations** | **Cases (N)** | **Controls (N)** | **Genotyping Platforms** | **Covariates** |
| **CORECT: Colorectal** |  | **5,100** | **4,831** | Affymetrix: Axiom | Age, sex, PCs |
|  | ACS CPS | US | 548 | 538 |
|  | Australia | Australia | 539 | 469 |
|  | Colon CFR | US | 1,660 | 1,393 |
|  | KY | US | 1,038 | 1,134 |
|  | MECC | US | 1,120 | 820 |
|  | NF | Canada | 195 | 477 |
| **DRIVE: Breast** |  | **15,748** | **18,084** | Affymetrix: 5.0, 6.0; Illumina: 240K, 317K, 370K, 550K, 610K, 610K + Cyto 12, 660K, 670K, 1.2M | Age, PCs  |
|  | ABCFS | Australia | 282 | 285 |
|  | BBCS | UK | 1,609 | 1,224 |
|  | DFBBS | The Netherlands | 464 | 3,255 |
|  | GCHBOC | Germany | 634 | 477 |
|  | HEBCS | Finland | 726 | 1,012 |
|  | MARIE | Germany | 652 | 470 |
|  | SASBAC | Sweden | 790 | 756 |
|  | UK2 | UK | 3,628 | 2,663 |
|  | BPC3 | Europe, US | 1,998 | 2,305 |
|  | BCFR | Australia, US | 3,486 | 2,457 |
|  | TN-GWAS | Australia, Europe, US | 1,479 | 3,180 |
| **DRIVE: ER Negative Breast** |  | **4,939** | **13,128** | Affymetrix: 5.0, 6.0; Illumina: 240K, 317K, 370K, 550K, 610K, 610K + Cyto 12, 660K, 670K, 1.2M | Age, PCs  |
|  | ABCFS | Australia | 72 | 285 |
|  | HEBCS | Finland | 145 | 1,012 |
|  | MARIE | Germany | 76 | 470 |
|  | SASBAC | Sweden | 109 | 756 |
|  | UK2 | UK | 160 | 2,663 |
|  | BPC3 | Europe, US | 1,998 | 2,305 |
|  | BCFR | Australia, US | 900 | 2,457 |
|  | TN-GWAS | Australia, Europe, US | 1,479 | 3,180 |
| **ELLIPSE: Prostate** |  | **14,160** | **12,724** | Affymetrix: GeneChip 500K, GeneChip 5.0K; Illumina: Infinium HumanHap 550 Array, iSELECT, Human610, 610K, Human Omni 2.5  | Age, study, PCs |
|  | BPC3 | US | 2,068 | 3,011 |
|  | CAPS1 | Sweden | 474 | 482 |
|  | CAPS2 | Sweden | 1,458 | 512 |
|  | CRUK1 | UK | 1,854 | 1,894 |
|  | CRUK2 | UK | 3,706 | 3,884 |
|  | Pegasus | US | 4,600 | 2,941 |
| **ELLIPSE: Aggressive Prostate** |  | **4,450** | **12,724** | Affymetrix: GeneChip 500K, GeneChip 5.0K; Illumina: Infinium HumanHap 550 Array, iSELECT, Human610, 610K, Human Omni 2.5  | Age, study, PCs |
|  | BPC3 | US | 1,069 | 3,011 |
|  | CAPS1 | Sweden | 443 | 482 |
|  | CAPS2 | Sweden | 648 | 512 |
|  | CRUK1 | UK | 625 | 1,894 |
|  | CRUK2 | UK | 1,110 | 3,884 |
|  | Pegasus | US | 555 | 2,941 |
| **FOCI: Ovarian** |  | **4,369** | **9,123** | Illumina: 317K, 370K, 550K, 610K, 670K, 2.5M | Site, PCs |
|  | U19 GWAS | US | 441 | 441 |
|  | UK GWAS | UK | 1,763 | 6,118 |
|  | US GWAS | Canada, Poland, US | 2,165 | 2,564 |
| **FOCI: Invasive Serous Ovary** |  | **2,556** | **9,123** | Illumina: 317K, 370K, 550K, 610K, 670K, 2.5M | Site, PCs |
|  | U19 GWAS | US | 357 | 441 |
|  | UK GWAS | UK | 869 | 6,118 |
|  | US GWAS | Canada, Poland, US | 1,330 | 2,564 |
| **FOCI: Invasive Mucinous Ovary** |  | **306** | **9,123** | Illumina: 317K, 370K, 550K, 610K, 670K, 2.5M | Site, PCs |
|  | U19 GWAS | US | 10 | 441 |
|  | UK GWAS | UK | 182 | 6,118 |
|  | US GWAS | Canada, Poland, US | 114 | 2,564 |
| **TRICL: Lung**  |  | **12,160** | **16,838** | Illumina: 317K, 370Duo, 550K, 610Quad, 1.2M | Age, sex, PCs |
|  | HGF Germany | Germany | 481 | 478 |
|  | IARC | Europe | 2,533 | 3,791 |
|  | MDACC | US | 1,150 | 1,134 |
|  | NCI | Europe, US | 5,713 | 5,736 |
|  | SLRI/Toronto  | Canada | 331 | 499 |
|  | ICR UK | UK | 1,952 | 5,200 |
| **TRICL: Adenocarcinoma of the Lung**  |  | **3,718** | **15,871** | Illumina: 317K, 370Duo, 550K, 610Quad, 1.2M | Age, sex, PCs |
|  | HGF Germany | Germany | 186 | 478 |
|  | IARC | Europe | 517 | 2,824 |
|  | MDACC | US | 619 | 1,134 |
|  | NCI | Europe, US | 1,841 | 5,736 |
|  | SLRI/Toronto  | Canada | 90 | 499 |
|  | ICR UK | UK | 465 | 5,200 |

Abbreviations: N, number; PCA, principal components; UK, United Kingdom; US, United States.

**Supplemental Table 2:** DNA repair gene, region, and final SNP selection data, using human reference genome assembly, GRCh38.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **NCBI GeneID** | **Symbol** | **Chr** | **Gene Start - 50 kB** | **Gene End + 50 kB** | **Strand** | **SNPs** |
| 8863 | PER3 | 1 | 7734340 | 7895181 | plus | 334 |
| 378708 | APITD1 | 1 | 10380102 | 10492815 | plus | 147 |
| 6924 | TCEB3 | 1 | 23693366 | 23812059 | plus | 75 |
| 6118 | RPA2 | 1 | 27841524 | 27964797 | minus | 213 |
| 64789 | EXO5 | 1 | 40458719 | 40566556 | plus | 307 |
| 4595 | MUTYH | 1 | 45279242 | 45390470 | minus | 115 |
| 8438 | RAD54L | 1 | 46197695 | 46328473 | plus | 109 |
| 7398 | USP1 | 1 | 62386304 | 62501804 | plus | 135 |
| 4438 | MSH4 | 1 | 75746871 | 75963238 | plus | 477 |
| 164045 | HFM1 | 1 | 91210766 | 91454869 | minus | 355 |
| 64858 | DCLRE1B | 1 | 113855293 | 113964086 | plus | 96 |
| 10286 | BCAS2 | 1 | 114517557 | 114631644 | minus | 186 |
| 29089 | UBE2T | 1 | 202281657 | 202391966 | minus | 82 |
| 142 | PARP1 | 1 | 226310691 | 226458100 | minus | 298 |
| 9156 | EXO1 | 1 | 241798189 | 241939939 | plus | 350 |
| 6241 | RRM2 | 2 | 10072568 | 10181419 | plus | 283 |
| 348654 | GEN1 | 2 | 17703885 | 17835365 | plus | 239 |
| 4436 | MSH2 | 2 | 47353067 | 47562577 | plus | 448 |
| 2956 | MSH6 | 2 | 47733082 | 47856953 | plus | 249 |
| 57223 | SMEK2 | 2 | 55497292 | 55667725 | minus | 398 |
| 55120 | FANCL | 2 | 58109243 | 58291381 | minus | 287 |
| 200558 | APLF | 2 | 68417559 | 68630162 | plus | 502 |
| 56655 | POLE4 | 2 | 74908648 | 75019732 | plus | 178 |
| 51455 | REV1 | 2 | 99350475 | 99540030 | minus | 233 |
| 2071 | ERCC3 | 2 | 127207290 | 127344176 | minus | 226 |
| 5433 | POLR2D | 2 | 127796266 | 127908155 | minus | 242 |
| 5378 | PMS1 | 2 | 189734085 | 189927629 | plus | 216 |
| 91526 | ANKRD44 | 2 | 196917017 | 197360797 | minus | 824 |
| 7520 | XRCC5 | 2 | 216057658 | 216256293 | plus | 250 |
| 79840 | NHEJ1 | 2 | 219025324 | 219210865 | minus | 256 |
| 8452 | CUL3 | 2 | 224420150 | 224635397 | minus | 495 |
| 8864 | PER2 | 2 | 238194038 | 238340102 | minus | 388 |
| 56852 | RAD18 | 3 | 8827196 | 9013475 | minus | 380 |
| 4968 | OGG1 | 3 | 9699944 | 9837790 | plus | 191 |
| 2177 | FANCD2 | 3 | 9976384 | 10151930 | plus | 390 |
| 7508 | XPC | 3 | 14095147 | 14228672 | minus | 246 |
| 23243 | ANKRD28 | 3 | 15617236 | 15909546 | minus | 462 |
| 4292 | MLH1 | 3 | 36943350 | 37100846 | plus | 191 |
| 57599 | WDR48 | 3 | 39001986 | 39146664 | plus | 291 |
| 84126 | ATRIP | 3 | 48396710 | 48515655 | plus | 85 |
| 23132 | RAD54L2 | 3 | 51488910 | 51718660 | plus | 143 |
| 10039 | PARP3 | 3 | 51892286 | 51998867 | plus | 71 |
| 151987 | PPP4R2 | 3 | 72946968 | 73115860 | plus | 389 |
| 10721 | POLQ | 3 | 121381420 | 121596006 | minus | 352 |
| 8930 | MBD4 | 3 | 129380944 | 129490179 | minus | 207 |
| 545 | ATR | 3 | 142399235 | 142628826 | minus | 408 |
| 6596 | HLTF | 3 | 148980117 | 149136554 | minus | 278 |
| 5437 | POLR2H | 3 | 184311714 | 184418595 | plus | 216 |
| 5984 | RFC4 | 3 | 186739892 | 186856695 | minus | 213 |
| 3280 | HES1 | 3 | 194086142 | 194188612 | plus | 253 |
| 353497 | POLN | 4 | 2021918 | 2279231 | minus | 382 |
| 5981 | RFC1 | 4 | 39237449 | 39416381 | minus | 236 |
| 5431 | POLR2B | 4 | 56928943 | 57081168 | plus | 386 |
| 5356 | PLRG1 | 4 | 154484997 | 154600433 | minus | 265 |
| 55247 | NEIL3 | 4 | 177259837 | 177412938 | plus | 380 |
| 5810 | RAD1 | 5 | 34855260 | 34965675 | minus | 166 |
| 10309 | CCNO | 5 | 55181152 | 55283680 | minus | 167 |
| 1161 | ERCC8 | 5 | 60823832 | 60995078 | minus | 268 |
| 1022 | CDK7 | 5 | 69184795 | 69327430 | plus | 240 |
| 5884 | RAD17 | 5 | 69319297 | 69464801 | plus | 133 |
| 51426 | POLK | 5 | 75461832 | 75651144 | plus | 231 |
| 4437 | MSH3 | 5 | 80604648 | 80926815 | plus | 617 |
| 7518 | XRCC4 | 5 | 83027498 | 83403760 | plus | 542 |
| 902 | CCNH | 5 | 87326254 | 87463033 | minus | 95 |
| 10111 | RAD50 | 5 | 132506924 | 132694621 | plus | 165 |
| 7320 | UBE2B | 5 | 134321179 | 134442108 | plus | 110 |
| 135458 | HUS1B | 6 | 605939 | 706964 | minus | 294 |
| 2968 | GTF2H4 | 6 | 30858200 | 30964103 | plus | 30 |
| 4439 | MSH5 | 6 | 31689948 | 31812678 | plus | 48 |
| 2178 | FANCE | 6 | 35402339 | 35517141 | plus | 274 |
| 5429 | POLH | 6 | 43526141 | 43670523 | plus | 202 |
| 988 | CDC5L | 6 | 44337514 | 44500424 | plus | 303 |
| 10973 | ASCC3 | 6 | 100458194 | 100931372 | minus | 846 |
| 5980 | REV3L | 6 | 111249031 | 111533715 | minus | 398 |
| 404672 | GTF2H5 | 6 | 158118347 | 158249344 | plus | 322 |
| 4521 | NUDT1 | 7 | 2192222 | 2301145 | plus | 302 |
| 5395 | PMS2 | 7 | 5923239 | 6059106 | minus | 245 |
| 6119 | RPA3 | 7 | 7586944 | 7768607 | minus | 626 |
| 27434 | POLM | 7 | 44022062 | 44132540 | minus | 84 |
| 5425 | POLD2 | 7 | 44064680 | 44173570 | minus | 200 |
| 3364 | HUS1 | 7 | 47913285 | 48029625 | minus | 202 |
| 5982 | RFC2 | 7 | 74181502 | 74304458 | minus | 84 |
| 7979 | SHFM1 | 7 | 96638767 | 96759891 | minus | 246 |
| 5439 | POLR2J | 7 | 102423100 | 102528999 | minus | 131 |
| 246721 | POLR2J2 | 7 | 102586748 | 102721729 | minus | 6 |
| 7516 | XRCC2 | 7 | 152596498 | 152726165 | minus | 391 |
| 252969 | NEIL2 | 8 | 11719663 | 11837345 | plus | 491 |
| 79873 | NUDT18 | 8 | 22056872 | 22159419 | minus | 198 |
| 7486 | WRN | 8 | 30983262 | 31223761 | plus | 374 |
| 5423 | POLB | 8 | 42288455 | 42421813 | plus | 178 |
| 5591 | PRKDC | 8 | 47723108 | 48010183 | minus | 106 |
| 7336 | UBE2V2 | 8 | 47958435 | 48114708 | plus | 53 |
| 6921 | TCEB1 | 8 | 73895138 | 74022287 | minus | 273 |
| 4683 | NBN | 8 | 89883336 | 90034724 | minus | 271 |
| 25788 | RAD54B | 8 | 94321960 | 94525115 | minus | 584 |
| 5440 | POLR2K | 8 | 100100611 | 100204002 | plus | 133 |
| 50484 | RRM2B | 8 | 102154501 | 102289118 | minus | 291 |
| 9401 | RECQL4 | 8 | 144461284 | 144567826 | minus | 96 |
| 54840 | APTX | 9 | 32922606 | 33051641 | minus | 395 |
| 2189 | FANCG | 9 | 35023838 | 35130016 | minus | 141 |
| 80010 | RMI1 | 9 | 83930720 | 84054074 | plus | 153 |
| 2176 | FANCC | 9 | 95049054 | 95367709 | minus | 227 |
| 7507 | XPA | 9 | 97584451 | 97747409 | minus | 220 |
| 5887 | RAD23B | 9 | 107233236 | 107382194 | plus | 350 |
| 54107 | POLE3 | 9 | 113357235 | 113460749 | minus | 257 |
| 5537 | PPP6C | 9 | 125096573 | 125239939 | minus | 181 |
| 64421 | DCLRE1C | 10 | 14854611 | 15004432 | minus | 360 |
| 2074 | ERCC6 | 10 | 49404480 | 49589123 | minus | 353 |
| 1791 | DNTT | 10 | 96254328 | 96388564 | plus | 280 |
| 64210 | MMS19 | 10 | 97408324 | 97548794 | minus | 177 |
| 27343 | POLL | 10 | 101528882 | 101638270 | minus | 153 |
| 9937 | DCLRE1A | 10 | 113784724 | 113904404 | minus | 147 |
| 4255 | MGMT | 10 | 129417190 | 129817519 | plus | 1195 |
| 5441 | POLR2L | 11 | 789721 | 892529 | minus | 168 |
| 6240 | RRM1 | 11 | 4044694 | 4188876 | plus | 380 |
| 2965 | GTF2H1 | 11 | 18272269 | 18417043 | plus | 295 |
| 2188 | FANCF | 11 | 22572533 | 22675841 | minus | 111 |
| 221120 | ALKBH3 | 11 | 43830807 | 43970275 | plus | 407 |
| 1408 | CRY2 | 11 | 45797118 | 45933248 | plus | 232 |
| 1643 | DDB2 | 11 | 47164465 | 47289218 | plus | 208 |
| 27339 | PRPF19 | 11 | 60840547 | 60956589 | minus | 201 |
| 1642 | DDB1 | 11 | 61249447 | 61383212 | minus | 39 |
| 2237 | FEN1 | 11 | 61742637 | 61847244 | plus | 66 |
| 5436 | POLR2G | 11 | 62711539 | 62816715 | plus | 80 |
| 80198 | MUS81 | 11 | 65810401 | 65916443 | plus | 125 |
| 57804 | POLD4 | 11 | 67300765 | 67403596 | minus | 94 |
| 5883 | RAD9A | 11 | 67341952 | 67448412 | plus | 49 |
| 55291 | PPP6R3 | 11 | 68410718 | 68665334 | plus | 418 |
| 10714 | POLD3 | 11 | 74542530 | 74719341 | plus | 367 |
| 4361 | MRE11A | 11 | 94367300 | 94543874 | minus | 364 |
| 8065 | CUL5 | 11 | 107958682 | 108157768 | plus | 287 |
| 472 | ATM | 11 | 108172832 | 108419102 | plus | 114 |
| 1111 | CHEK1 | 11 | 125575136 | 125726255 | plus | 330 |
| 5893 | RAD52 | 12 | 862089 | 1040868 | minus | 345 |
| 5965 | RECQL | 12 | 21418910 | 21551669 | minus | 444 |
| 23583 | SMUG1 | 12 | 54130358 | 54238994 | minus | 140 |
| 283373 | ANKRD52 | 12 | 56187807 | 56308359 | minus | 74 |
| 8914 | TIMELESS | 12 | 56366373 | 56499416 | minus | 74 |
| 7334 | UBE2N | 12 | 93358312 | 93492250 | minus | 233 |
| 6996 | TDG | 12 | 103915815 | 104038878 | plus | 358 |
| 1407 | CRY1 | 12 | 106941364 | 107143857 | minus | 343 |
| 121642 | ALKBH2 | 12 | 109038188 | 109143631 | minus | 5 |
| 7374 | UNG | 12 | 109047594 | 109160993 | plus | 203 |
| 144715 | RAD9B | 12 | 110451724 | 110582086 | plus | 139 |
| 5985 | RFC5 | 12 | 117966701 | 118082239 | plus | 216 |
| 2967 | GTF2H3 | 12 | 123583739 | 123712604 | plus | 267 |
| 5426 | POLE | 12 | 132573762 | 132737524 | minus | 326 |
| 143 | PARP4 | 13 | 24370931 | 24562810 | minus | 435 |
| 3146 | HMGB1 | 13 | 30408740 | 30515944 | minus | 112 |
| 675 | BRCA2 | 13 | 32265480 | 32449672 | plus | 168 |
| 5983 | RFC3 | 13 | 33768069 | 34016558 | plus | 538 |
| 55270 | NUDT15 | 13 | 47987567 | 48097146 | plus | 307 |
| 100533467 | BIVM-ERCC5 | 13 | 102757146 | 102926001 | plus | 336 |
| 3981 | LIG4 | 13 | 108157442 | 108268368 | minus | 249 |
| 8451 | CUL4A | 13 | 113158193 | 113315078 | plus | 143 |
| 10038 | PARP2 | 14 | 20293614 | 20407904 | plus | 278 |
| 328 | APEX1 | 14 | 20405131 | 20507772 | plus | 226 |
| 57697 | FANCM | 14 | 45085933 | 45250890 | plus | 176 |
| 5427 | POLE2 | 14 | 49593552 | 49738380 | minus | 201 |
| 4331 | MNAT1 | 14 | 60684741 | 61018680 | plus | 161 |
| 5890 | RAD51B | 14 | 67769779 | 68733172 | plus | 1650 |
| 27030 | MLH3 | 14 | 74963764 | 75101532 | minus | 61 |
| 55775 | TDP1 | 14 | 89905600 | 90094764 | plus | 414 |
| 55671 | SMEK1 | 14 | 91407481 | 91560554 | minus | 246 |
| 57718 | PPP4R4 | 14 | 94124312 | 94329755 | plus | 381 |
| 7517 | XRCC3 | 14 | 103647608 | 103765486 | minus | 167 |
| 22909 | FAN1 | 15 | 30782893 | 30993108 | plus | 306 |
| 5888 | RAD51 | 15 | 40645129 | 40782158 | plus | 203 |
| 1854 | DUT | 15 | 48281167 | 48393373 | plus | 171 |
| 54962 | TIPIN | 15 | 66286670 | 66436736 | minus | 352 |
| 79661 | NEIL1 | 15 | 75296990 | 75405251 | plus | 83 |
| 64782 | AEN | 15 | 88570927 | 88682281 | plus | 320 |
| 55215 | FANCI | 15 | 89193963 | 89367131 | plus | 233 |
| 641 | BLM | 15 | 90667327 | 90865462 | plus | 406 |
| 4350 | MPG | 16 | 27019 | 135851 | plus | 147 |
| 9894 | TELO2 | 16 | 1443351 | 1560459 | plus | 491 |
| 197342 | EME2 | 16 | 1723222 | 1826627 | plus | 384 |
| 4913 | NTHL1 | 16 | 1989815 | 2097866 | minus | 187 |
| 6923 | TCEB2 | 16 | 2721414 | 2827296 | minus | 62 |
| 84464 | SLX4 | 16 | 3531181 | 3661584 | minus | 281 |
| 116028 | RMI2 | 16 | 11295454 | 11401760 | plus | 477 |
| 2072 | ERCC4 | 16 | 13870157 | 14002348 | plus | 301 |
| 79728 | PALB2 | 16 | 23553162 | 23691357 | minus | 275 |
| 5531 | PPP4C | 16 | 30025976 | 30135377 | plus | 82 |
| 548593 | SLX1A | 16 | 30143843 | 30247566 | plus | 49 |
| 5432 | POLR2C | 16 | 57412639 | 57522009 | plus | 208 |
| 2175 | FANCA | 16 | 89687551 | 89866658 | minus | 612 |
| 6117 | RPA1 | 17 | 1779979 | 1949554 | plus | 445 |
| 10514 | MYBBP1A | 17 | 4488896 | 4605626 | minus | 302 |
| 5430 | POLR2A | 17 | 7434379 | 7564618 | plus | 359 |
| 7157 | TP53 | 17 | 7618402 | 7737550 | minus | 297 |
| 5187 | PER1 | 17 | 8090470 | 8206405 | minus | 200 |
| 7156 | TOP3A | 17 | 18223921 | 18365007 | minus | 273 |
| 3980 | LIG3 | 17 | 34930498 | 35055069 | plus | 86 |
| 5892 | RAD51D | 17 | 35049792 | 35169869 | minus | 114 |
| 201299 | RDM1 | 17 | 35868080 | 35980776 | minus | 300 |
| 672 | BRCA1 | 17 | 42994295 | 43175483 | minus | 224 |
| 146956 | EME1 | 17 | 50323220 | 50431459 | plus | 333 |
| 5889 | RAD51C | 17 | 58642573 | 58784342 | plus | 204 |
| 83990 | BRIP1 | 17 | 61629186 | 61913559 | minus | 356 |
| 9400 | RECQL5 | 17 | 75576845 | 75717190 | minus | 310 |
| 80233 | C17orf70 | 17 | 81489885 | 81602403 | minus | 315 |
| 201254 | STRA13 | 17 | 81968703 | 82072910 | minus | 136 |
| 9989 | PPP4R1 | 18 | 9496791 | 9664607 | minus | 462 |
| 728929 | TCEB3CL | 18 | 46918695 | 47019912 | minus | 90 |
| 51224 | TCEB3B | 18 | 46982572 | 47085617 | minus | 111 |
| 11201 | POLI | 18 | 54219479 | 54370843 | plus | 303 |
| 5434 | POLR2E | 19 | 1036579 | 1145392 | minus | 358 |
| 5886 | RAD23A | 19 | 12895814 | 13003643 | plus | 137 |
| 91442 | C19orf40 | 19 | 32922234 | 33027495 | plus | 362 |
| 5438 | POLR2I | 19 | 36063709 | 36165304 | minus | 230 |
| 7515 | XRCC1 | 19 | 43493312 | 43625578 | minus | 251 |
| 2068 | ERCC2 | 19 | 45301391 | 45420587 | minus | 227 |
| 2067 | ERCC1 | 19 | 45357333 | 45528837 | minus | 239 |
| 3978 | LIG1 | 19 | 48065445 | 48220603 | minus | 434 |
| 11284 | PNKP | 19 | 49811203 | 49917565 | minus | 167 |
| 5424 | POLD1 | 19 | 50334278 | 50468018 | plus | 233 |
| 22870 | PPP6R1 | 19 | 55179779 | 55309030 | minus | 244 |
| 5111 | PCNA | 20 | 5064953 | 5176622 | minus | 167 |
| 7335 | UBE2V1 | 20 | 50031124 | 50165959 | minus | 158 |
| 387521 | TMEM189 | 20 | 50073737 | 50203798 | minus | 55 |
| 23626 | SPO11 | 20 | 57279775 | 57393993 | plus | 194 |
| 8940 | TOP3B | 22 | 21905493 | 22032843 | minus | 17 |
| 11200 | CHEK2 | 22 | 28637743 | 28791834 | minus | 258 |
| 5435 | POLR2F | 22 | 37903667 | 38038153 | plus | 74 |
| 11144 | DMC1 | 22 | 38468928 | 38620286 | minus | 116 |
| 9978 | RBX1 | 22 | 40901347 | 41023015 | plus | 94 |
| 2547 | XRCC6 | 22 | 41571163 | 41714048 | plus | 170 |
| 9701 | PPP6R2 | 22 | 50293317 | 50495090 | plus | 498 |

**Supplemental Table 3:** List of all DNA repair genes and DNA repair pathways included in this study.

**Total Genes (n = 229)**

AEN ALKBH2 ALKBH3 ANKRD28 ANKRD44 ANKRD52 APEX1 APITD1 APLF APTX ASCC3 ATM ATR ATRIP BCAS2 BIVM-ERCC5 BLM BRCA1 BRCA2 BRIP1 C17orf70 C19orf40 CCNH CCNO CDC5L CDK7 CHEK1 CHEK2 CRY1 CRY2 CUL3 CUL4A CUL5 DCLRE1A DCLRE1B DCLRE1C DDB1 DDB2 DMC1 DNTT DUT EME1 EME2 ERCC1 ERCC2 ERCC3 ERCC4 ERCC6 ERCC8 EXO1 EXO5 FAN1 FANCA FANCC FANCD2 FANCE FANCF FANCG FANCI FANCL FANCM FEN1 GEN1 GTF2H1 GTF2H3 GTF2H4 GTF2H5 HES1 HFM1 HLTF HMGB1 HUS1 HUS1B LIG1 LIG3 LIG4 MBD4 MGMT MLH1 MLH3 MMS19 MNAT1 MPG MRE11A MSH2 MSH3 MSH4 MSH5 MSH6 MUS81 MUTYH MYBBP1A NBN NEIL1 NEIL2 NEIL3 NHEJ1 NTHL1 NUDT1 NUDT15 NUDT18 OGG1 PALB2 PARP1 PARP2 PARP3 PARP4 PCNA PER1 PER2 PER3 PLRG1 PMS1 PMS2 PNKP POLB POLD1 POLD2 POLD3 POLD4 POLE POLE2 POLE3 POLE4 POLH POLI POLK POLL POLM POLN POLQ POLR2A POLR2B POLR2C POLR2D POLR2E POLR2F POLR2G POLR2H POLR2I POLR2J POLR2J2 POLR2K POLR2L PPP4C PPP4R1 PPP4R2 PPP4R4 PPP6C PPP6R1 PPP6R2 PPP6R3 PRKDC PRPF19 RAD1 RAD17 RAD18 RAD23A RAD23B RAD50 RAD51 RAD51B RAD51C RAD51D RAD52 RAD54B RAD54L RAD54L2 RAD9A RAD9B RBX1 RDM1 RECQL RECQL4 RECQL5 REV1 REV3L RFC1 RFC2 RFC3 RFC4 RFC5 RMI1 RMI2 RPA1 RPA2 RPA3 RRM1 RRM2 RRM2B SHFM1 SLX1A SLX4 SMEK1 SMEK2 SMUG1 SPO11 STRA13 TCEB1 TCEB2 TCEB3 TCEB3B TCEB3CL TDG TDP1 TELO2 TIMELESS TIPIN TMEM189 TOP3A TOP3B TP53 UBE2B UBE2N UBE2T UBE2V1 UBE2V2 UNG USP1 WDR48 WRN XPA XPC XRCC1 XRCC2 XRCC3 XRCC4 XRCC5 XRCC6

**BER (base exicision repair) (n = 37)**

APEX1 APLF APTX CCNO FEN1 HMGB1 LIG1 LIG3 MBD4 MPG MUTYH NEIL1 NEIL2 NEIL3 NTHL1 OGG1 PARP1 PARP2 PARP3 PARP4 PCNA PNKP POLB POLD1 POLD2 POLD3 POLD4 POLE POLE2 POLE3 POLE4 POLL SMUG1 TDG TDP1 UNG XRCC1

**Check point factors (n = 22)**

AEN ATM ATR ATRIP CHEK1 CHEK2 HUS1 HUS1B PER1 PER2 PER3 RAD1 RAD17 RAD9A RAD9B RFC2 RFC3 RFC4 RFC5 TIMELESS TIPIN TP53

**FA (Fanconi anemia) pathway (n = 30)**

APITD1 BLM BRCA1 BRCA2 BRIP1 C17orf70 C19orf40 FAN1 FANCA FANCC FANCD2 FANCE FANCF FANCG FANCI FANCL FANCM HES1 PALB2 RAD51 RAD51C RMI1 RMI2 STRA13 TELO2 TOP3A TOP3B UBE2T USP1 WDR48

**HR (homologous recombination) (n = 44)**

BLM BRCA1 BRCA2 DMC1 EME1 EME2 GEN1 HFM1 MRE11A MUS81 NBN PPP4C PPP4R1 PPP4R2 PPP4R4 RAD50 RAD51 RAD51B RAD51C RAD51D RAD52 RAD54B RAD54L RAD54L2 RDM1 RECQL RECQL4 RECQL5 RMI1 RMI2 RPA1 RPA2 RPA3 SHFM1 SLX1A SLX4 SMEK1 SMEK2 SPO11 TOP3A TOP3B WRN XRCC2 XRCC3

**MMR (mismatch exicision repair) (n = 25)**

EXO1 HMGB1 LIG1 MLH1 MLH3 MSH2 MSH3 MSH4 MSH5 MSH6 PCNA PMS1 PMS2 POLD1 POLD2 POLD3 POLD4 RFC1 RFC2 RFC3 RFC4 RFC5 RPA1 RPA2 RPA3

**NER (nucleotide excision repair) (n = 47)**

BIVM-ERCC5 CCNH CDK7 CUL3 CUL4A CUL5 DDB1 DDB2 ERCC1 ERCC2 ERCC3 ERCC4 ERCC6 ERCC8 GTF2H1 GTF2H3 GTF2H4 GTF2H5 LIG1 MMS19 MNAT1 POLR2A POLR2B POLR2C POLR2D POLR2E POLR2F POLR2G POLR2H POLR2I POLR2J POLR2J2 POLR2K POLR2L RAD23A RAD23B RBX1 RPA1 RPA2 RPA3 TCEB1 TCEB2 TCEB3 TCEB3B TCEB3CL XPA XPC

**NHEJ (non-homologous end-joining) (n = 15)**

APLF APTX DCLRE1C DNTT LIG4 MRE11A NHEJ1 POLB POLL POLM PRKDC RAD50 XRCC4 XRCC5 XRCC6

**TLS (translesion DNA synthesis) factors (n = 13)**

HLTF POLH POLI POLK POLN RAD18 REV1 REV3L TMEM189 UBE2B UBE2N UBE2V1 UBE2V2

**Supplemental Table 4:** Statistical associations (p-values) for cancer risk versus genetic variation within DNA repair pathways. Sensitivity analysis of Table 3, with *RAD51B*, *MSH5*, and *BRCA2* gene removed from analysis. Statistically significant values are in bold (p < 0.05).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Single Strand Break Repair** |  |  **Double Strand Break Repair** |  | **Other** |
|  |  | Base Excision Repair | Nucleotide Excision Repair | Mismatch Repair | Translesion Synthesis |  | Fanconi Anemia | Homologous Recombination | Non-homologous end joining |  | Check Point Factors |
| **Cancer (Subtype)** |  |  |  |  |  |  |  |  |  |  |  |
| Colon (Overall) |  | **0.033** | 0.074 | 0.689 | 0.262 |  | 0.659 | **5.13E-05** | 0.258 |  | 0.394 |
| Breast (Overall) |  | 0.425 | **7.48E-04** | 0.806 | 0.295 |  | 0.091 | 0.207 | 0.055 |  | 0.315 |
| Breast (ER Negative) |  | 0.625 | **1.58E-03** | **0.018** | 0.893 |  | 0.219 | 0.758 | **3.64E-03** |  | 0.182 |
| Prostate (Overall) |  | 0.705 | 0.277 | **6.86E-06** | **0.031** |  | 0.688 | 0.263 | **0.035** |  | 0.102 |
| Prostate (Aggressive) |  | 0.496 | 0.906 | **1.61E-03** | 0.361 |  | 0.323 | 0.470 | **2.66E-06** |  | 0.741 |
| Ovarian (Overall) |  | **4.36E-03** | **0.014** | 0.692 | 0.524 |  | 0.477 | **5.58E-07** | 0.251 |  | 0.198 |
| Ovarian (Serous) |  | **0.028** | 0.834 | 0.596 | 0.861 |  | 0.877 | **2.21E-07** | 0.751 |  | 0.927 |
| Ovarian (Mucinous) |  | 0.089 | 0.083 | 0.636 | 0.059 |  | **2.61E-04** | **1.39E-04** | **1.60E-04** |  | **3.89E-04** |
| Lung (Overall) |  | **4.17E-03** | 0.054 | **1.26E-06** | 0.972 |  | 0.250 | 0.742 | 0.175 |  | 0.090 |
| Lung (Adenocarcinoma) |  | 0.594 | 0.889 | **2.31E-05** | **0.026** |  | 0.649 | 0.229 | **3.49E-03** |  | 0.547 |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Counts by DNA Repair Pathway** |  |  |  |  |  |  |  |  |  |  |  |
| All SNPs |  | 8758 | 10676 | 7032 | 3016 |  | 7557 | 11698 | 4054 |  | 5194 |
| SNAP Filtered SNPs |  | 1568 | 1850 | 1145 | 439 |  | 1144 | 1718 | 557 |  | 880 |
| Genes |  | 37 | 47 | 24 | 13 |  | 29 | 42 | 15 |  | 22 |

**Supplemental Table 5:** Statistical associations (p-values) for cancer risk versus genetic variation within DNA repair pathways. Sensitivity analysis of Table 3, with 6 genes removed from the analysis -- all genes containing loci with individual SNP associations of p < 1 x 10-4. Statistically significant values are in bold (p < 0.05).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Single Strand Break Repair** |  |  **Double Strand Break Repair** |  | **Other** |
|  |  | Base Excision Repair | Nucleotide Excision Repair | Mismatch Repair | Translesion Synthesis |  | Fanconi Anemia | Homologous Recombination | Non-homologous end joining |  | Check Point Factors |
| **Cancer (Subtype)** |  |  |  |  |  |  |  |  |  |  |  |
| Colon (Overall) |  | **0.043** | 0.087 | 0.700 | 0.238 |  | 0.636 | **2.35E-04** | 0.247 |  | 0.351 |
| Breast (Overall) |  | 0.478 | **1.30E-03** | 0.891 | 0.259 |  | 0.130 | 0.117 | **0.043** |  | 0.274 |
| Breast (ER Negative) |  | 0.805 | **4.20E-03** | **0.025** | 0.752 |  | 0.348 | 0.692 | **1.99E-03** |  | 0.119 |
| Prostate (Overall) |  | 0.913 | 0.440 | **1.21E-05** | **0.019** |  | 0.910 | 0.293 | **0.022** |  | 0.061 |
| Prostate (Aggressive) |  | 0.538 | 0.976 | **1.90E-03** | 0.336 |  | 0.371 | 0.429 | **2.07E-06** |  | 0.785 |
| Ovarian (Overall) |  | **3.92E-03** | **0.012** | 0.716 | 0.506 |  | 0.443 | **1.18E-06** | 0.264 |  | 0.187 |
| Ovarian (Serous) |  | **0.028** | 0.833 | 0.599 | 0.861 |  | 0.880 | **3.08E-07** | 0.750 |  | 0.926 |
| Ovarian (Mucinous) |  | 0.102 | **0.090** | 0.655 | 0.055 |  | **2.77E-04** | **4.60E-04** | **1.54E-04** |  | **4.74E-04** |
| Lung (Overall) |  | **5.60E-03** | **0.089** | **3.19E-06** | 0.949 |  | 0.388 | 0.676 | 0.131 |  | 0.072 |
| Lung (Adenocarcinoma) |  | 0.530 | 0.810 | **2.60E-05** | **0.022** |  | 0.714 | 0.263 | **2.90E-03** |  | 0.603 |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Counts by DNA Repair Pathway** |  |  |  |  |  |  |  |  |  |  |  |
| All SNPs |  | 8758 | 10676 | 7032 | 3016 |  | 7557 | 11107 | 4054 |  | 5194 |
| SNAP Filtered SNPs |  | 1568 | 1850 | 1145 | 439 |  | 1144 | 1636 | 557 |  | 880 |
| Genes |  | 37 | 47 | 24 | 13 |  | 29 | 40 | 15 |  | 22 |

**Legends to Figures**

**Supplemental Figure 1:** Manhattan plot, illustrating p-values from 60,297 SNP associations, generated from each of the 10 studies used in the meta-analysis. Statistical significance threshold is denoted by the red line (p = 5.09 x 10-6).