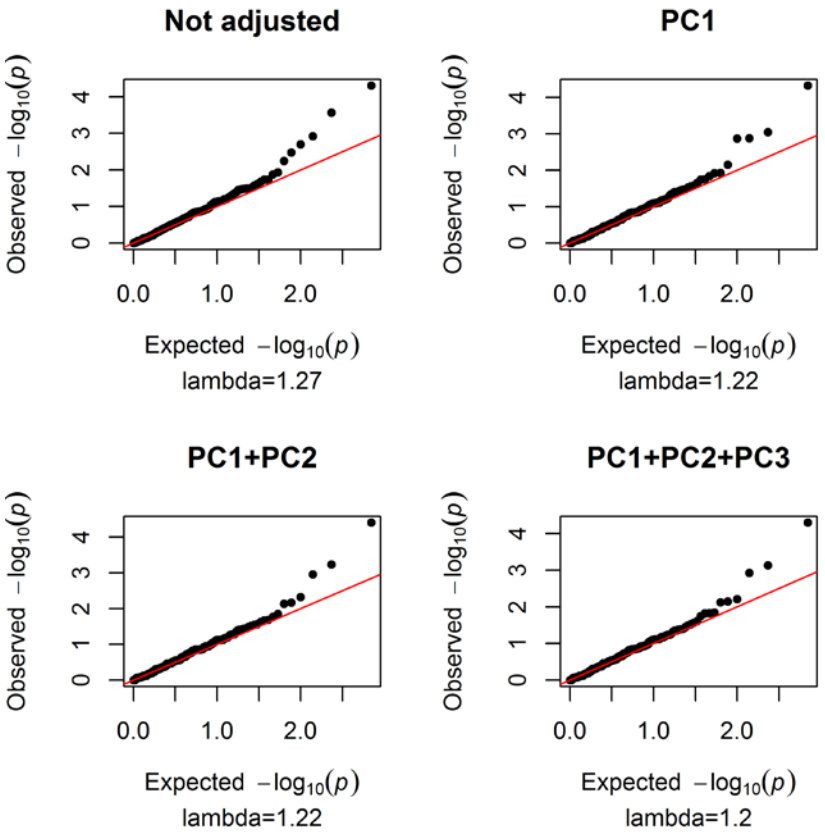
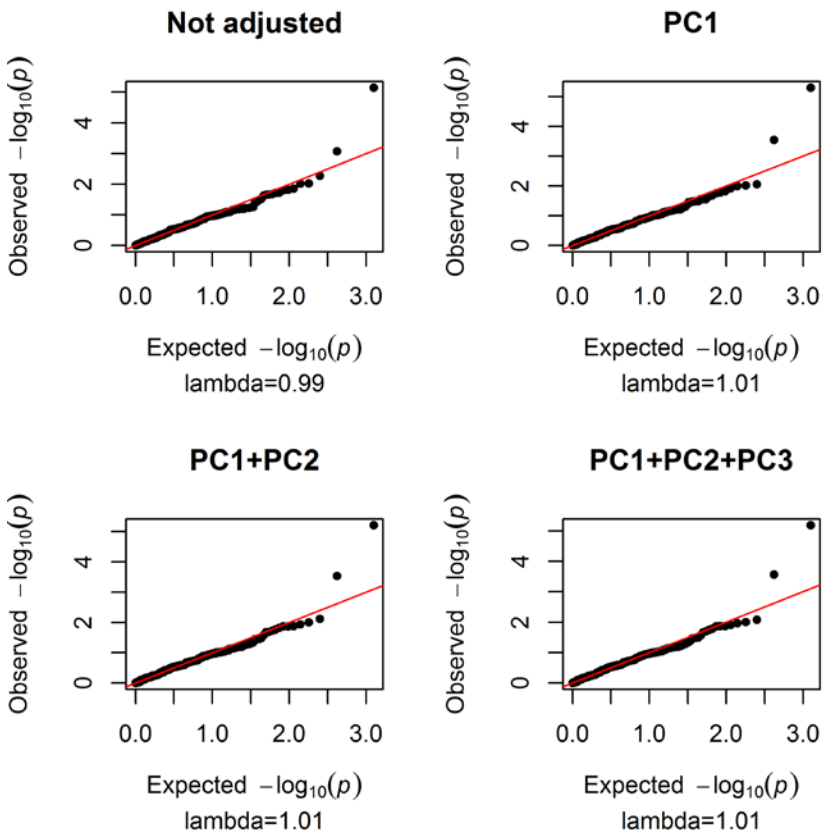
**Supplemental Figure 1. Quantile-Quantile plots for GWAS of common CNV for two array datasets**
Principal component analysis was conducted on the matrix of copy number status (0,1) of all deletion and duplication CNVR regions. Logistic regression was performed to estimate the association of all common CNVR with EOC risk using unadjusted and principal component adjusted models. The inflation factor (lambda) was calculated to assess the correction of population stratification by PC covariates.

**A) 610K Array**




**B) 2.5M Arra**



**Supplemental Table 1. Distribution of copy number variation (CNV) by EOC histotype and stage in the 610k array set**

| | DELETIONS | | | | | | | DUPLICATIONS | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Model 1 [a] (Histology) | | Model 2 [c] (Histology + Histology*Stage) N=778 | | | | | Model 1 [a] (Histology) | | Model 2 [c] (Histology + Histology*Stage) N=778 | | | | |
| | All, mean | $P_{hist}$ [b] | All, mean | $P_{hist}$ [d] | Stage 1/2, mean | Stage 3, mean | $P_{int}$ [e] | All, mean | $P_{hist}$ [b] | All, mean | $P_{hist}$ [d] | Stage 1/2, mean | Stage 3, mean | $P_{int}$ [e] |
| HGS, *n* | *410* | | *410* | | *99* | *311* | | *410* | | *410* | | *99* | *311* | |
| NSEG | 16.7 | ref | 16.7 | ref | 20.8 | 15.4 | ref | 5.8 | ref | 5.8 | ref | 4.1 | 6.4 | ref |
| KB | 1005.0 | ref | 1005.0 | ref | 1498.9 | 847.7 | ref | 836.8 | ref | 836.8 | ref | 553.1 | 927.1 | ref |
| LGS, *n* | *121* | | *119* | | *24* | *95* | | *121* | | *119* | | *24* | *95* | |
| NSEG | 18.0 | 0.06 | 17.9 | 0.68 | 18.7 | 17.7 | 0.50 | 5.7 | 0.48 | 5.7 | 0.16 | 6.1 | 5.6 | 0.07 |
| KB | 879.6 | 0.07 | 874.0 | 0.25 | 990.7 | 844.6 | 0.84 | 703.1 | 0.42 | 709.0 | 0.75 | 633.1 | 728.2 | 1.00 |
| Endometrioid, *n* | *241* | | *137* | | *87* | *50* | | *241* | | *137* | | *87* | *50* | |
| NSEG | 17.9 | 0.20 | 16.8 | **0.0003** | 16.8 | 23.8 | **0.0008** | 5.3 | 0.44 | 5.7 | 0.41 | 4.9 | 7.0 | 0.13 |
| KB | 1095.4 | 0.73 | 980.2 | **0.02** | 943.1 | 1044.7 | **0.01** | 692.8 | 0.05 | 674.0 | 0.24 | 590.6 | 819.1 | 0.79 |
| Clearcell, *n* | *112* | | *78* | | *56* | *22* | | *112* | | *78* | | *56* | *22* | |
| NSEG | 17.8 | 0.42 | 17.6 | 0.75 | 18.8 | 14.6 | 0.06 | 5.3 | 0.88 | 5.3 | 0.79 | 5.3 | 5.5 | 0.84 |
| KB | 943.7 | 0.23 | 896.8 | 0.13 | 964.1 | 725.3 | 0.78 | 728.0 | 0.36 | 739.6 | 0.89 | 759.0 | 690.3 | 0.46 |
| Mucinous, *n* | *63* | | *34* | | *31* | *3* | | *63* | | *34* | | *31* | *3* | |
| NSEG | 19.6 | 0.43 | 18.6 | 0.13 | 18.8 | 16.7 | 0.60 | 5.3 | 0.66 | 5.9 | 0.13 | 5.5 | 9.7 | 0.63 |
| KB | 1364.7 | 0.14 | 1262.3 | 0.39 | 1277.4 | 1106.3 | 0.94 | 701.5 | 0.63 | 779.1 | 0.96 | 624.5 | 2377.3 | **0.007** |
| Overall Pvalue [f] | Histology | | Histology | | | Histology*Stage | | Histology | | Histology | | | Histology*Stage | |
| NSEG | 0.17 | | **2.6E-05** | | | **0.0003** | | 0.83 | | 0.12 | | | 0.07 | |
| KB | 0.09 | | 0.04 | | | 0.14 | | 0.42 | | 0.69 | | | 0.08 | |

HGS=high-grade serous; LGS=low-grade serous; NSEG=number of CNV segments; KB=total length in KB of CNV segments.

[a] Model 1 reports regression models with NSEG or KB as the dependent variable and histology as the independent variable, including covariates for age and batch. NSEG was modeled using poisson regression with log-link function. KB was modeled using linear regression.

[b] $P_{hist}$ reports the pvalue for the comparison of each histology with the reference group (HGS).

[c] Model 2 builds on Model 1 by adding an interaction term for histology and stage. Stage was defined as advanced (stage 3) or not advanced (stage 1 and stage 2). Models were adjusted for age and batch, same as Model 1. Stage was included in model as covariate, but was not significant independent of histology.

[d] $P_{hist}$ from Model 2 reports the pvalue for the comparison of each histology with the reference group (HGS) after adjustment for stage and histology*stage covariates.

[e] $P_{int}$ reports the pvalue for the comparison of the difference between stages of each histology to the difference in the reference group (HGS).

[f] The overall pvalues for variables were calculated with the likelihood ratio test.

**Supplemental Table 2. Distribution of copy number variation (CNV) by EOC histotype in the 2.5M array set**

| | DELETIONS | | DUPLICATIONS | |
|---|---|---|---|---|
| | Mean | $P_{hist}$[a] | Mean | $P_{hist}$[a] |
| HGS, *n* | *303* | | *303* | |
| NSEG | 26.8 | ref | 36.8 | ref |
| KB | 672.2 | ref | 2393.0 | ref |
| LGS, *n* | *43* | | *43* | |
| NSEG | 27.2 | 0.15 | 33.7 | **0.0009** |
| KB | 659.9 | 0.83 | 2132.0 | 0.13 |
| Endometrioid, *n* | *30* | | *30* | |
| NSEG | 24.8 | 0.12 | 37.7 | 0.62 |
| KB | 632.5 | 0.83 | 2260 | 0.44 |
| Clearcell | *15* | | *15* | |
| NSEG | 26.1 | 0.97 | 40.8 | 0.17 |
| KB | 667.5 | 0.62 | 2705.0 | 0.34 |
| Mucinous, *n* | *28* | | *28* | |
| NSEG | 24.4 | **0.02** | 37.8 | 0.17 |
| KB | 700.2 | 0.88 | 2396.0 | 0.73 |
| Overall Pvalue[b], Histology | | | | |
| NSEG | | **0.02** | | **0.002** |
| KB | | 0.99 | | 0.39 |

HGS=high-grade serous; LGS=low-grade serous; NSEG=number of CNV segments; KB=total length in KB of CNV segments.

[a] $P_{hist}$ reports the pvalue for the comparison of each histology with the reference group (HGS). Regression models for deletion and duplications (separately) were modeled with NSEG or KB as the dependent variable and histology as the independent variable, including covariates for age and batch. NSEG was modeled using poisson regression with log-link function. KB was modeled using linear regression.

[b] The overall pvalues for histology were calculated with the likelihood ratio test.

**Supplemental Table 3. Comparison of rare (<1%) germline Copy Number Variation (CNV) burden between ovarian cancer cases and controls**

| | 610K array | | | | | | 2.5M array | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases N=1368 | Controls N=1450 | Unadjusted | | Adjusted [a] | | Cases N=449 | Controls N=343 | Unadjusted | | Adjusted [b] | |
| | | | OR | P-value | OR | P-value | | | OR | P-value | OR | P-value |
| All Rare CNV | | | | | | | | | | | | |
| N (%) | 1365 (99.8%) | 1447 (99.8%) | 1.00 | 0.58 | 1.02 | 0.0004 | 449 (100%) | 343 (100%) | 0.98 | 0.16 | 0.98 | 0.18 |
| Range | 1-61 | 1-57 | | | | | 4-50 | 2-36 | | | | |
| Mean | 11.5 | 11.7 | | | | | 13.7 | 13.2 | | | | |
| Deletions | | | | | | | | | | | | |
| N (%) | 1344 (98%) | 1434 (99%) | 1.00 | 0.82 | 1.02 | 0.004 | 448 (99.8%) | 340 (99%) | 0.97 | 0.08 | 0.97 | 0.08 |
| Range | 1-61 | 1-56 | | | | | 1-49 | 1-29 | | | | |
| Mean | 8.9 | 8.8 | | | | | 7.6 | 7.1 | | | | |
| Duplications | | | | | | | | | | | | |
| N (%) | 1122 (82%) | 1243 (86%) | 1.04 | 0.008 | 1.04 | 0.03 | 449 (100%) | 343 (100%) | 1.01 | 0.67 | 1.01 | 0.64 |
| Range | 1-32 | 1-17 | | | | | 1-23 | 1-15 | | | | |
| Mean | 2.6 | 2.9 | | | | | 6.1 | 6.1 | | | | |

a Adjusted for site, age (diagnosis or enrollment), and batch.

b Adjusted for age (diagnosis or enrollment). GWAS was conducted at one site and batch was not included as covariate in the model (P>0.10).

**Rare CNV Burden.** We estimated the influence of rare (carrier frequency <1%) copy number changes on EOC risk using a global burden test. The number of rare CNV calls in a given individual was compared between cases and controls using logistic regression performed in SAS 9.4. We analyzed the effects of site, age, and experimental batch on CNV burden as these are known sources of bias and included variables associated with CNV burden ($P < 0.10$) as covariates in the risk model. Burden comparisons were made for all rare CNV calls, rare deletions alone, and rare duplications alone.

**Supplemental Table 4. Risk-associated CNVR frequencies across both array platforms**

| Analysis Set | Locus | CNV Type | Gene | 610k | | | | 2.5M | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | CNVR (KB) | N (%) | | | CNVR (KB) | N (%) | | |
| | | | | | Controls | All Cases | HGS Cases | | Controls | All Cases | HGS Cases |
| 610k | 1p36.33 | Del | DVL1 | Chr1:943468-1706160 (763) | 84 (6) | 65 (5) | 7 (2) | Chr1: 1385211-1453373 (68) | 7 (2) | 5 (1) | 5 (2) |
| | 1p13.3 | Del | Intergenic | Chr1:111370372-111391381 (21) | 40 (3) | 49 (4) | 23 (6) | Chr1: 111380720-111387723 (7) | 1 (.3) | 3 (.7) | 0 |
| | 8p21.2 | Del | DOCK5 | Chr8:24931313-25101936 (171) | 168 (12) | 113 (8) | 27 (7) | Chr8: 24972808-24990418 (18) | 36 (10) | 52 (12) | 36 (12) |
| | 12p11.21 | Dup | RP11-428G5.5 | Chr12:31975730-32068877 (93) | 32 (2) | 32 (2) | 19 (5) | Chr12: 32001515-32061988 (60) | 11 (3) | 9 (2) | 6 (2) |
| | 19q13.2 | Del | CYP2A7 | chr19:41341589-41433931 (92) | 29 (2) | 49 (4) | 24 (6) | Chr19: 41350895-41389625 (39) | 23 (7) | 22 (5) | 13 (4) |
| | 19q13.42 | Dup | LILRA6 | chr19:54731679-54845802 (114) | 17 (1) | 39 (3) | 15 (4) | Chr19: 54722595-54847587 (125) | 98 (29) | 125 (28) | 84 (28) |
| 2.5M | 2q34 | Del | ERBB4 | Chr2: 213164837-213200920 (36) | 4 (.3) | 6 (.4) | 3 (.7) | chr2:213187034-213191389 (4) | 18 (5) | 8 (2) | 3 (1) |
| | 5p15.2 | Del | Intergenic | Chr5: 12401130-12907694 (507) | 10 (.7) | 10 (.7) | 5 (.7) | Chr5:12812336-12888815 (76) | 36 (10) | 70 (16) | 55 (18) |

**Supplemental Table 5. Risk-associated CNVR and corresponding CNVR catalogued in the Database of Genomic Variants (DGV)**

| | | | Risk-associated CNVR | | DGV[a] | | | Human CNV Map[b] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Locus** | **CNV Type** | **Gene(s)** | **CNVR (KB)** | **% Carriers[c]** | **CNVR (KB)[b]** | **Studies/ Samples Tested** | **% Carriers** | **CNVR (KB)** | **Type** | **No. Studies** | **No. Carriers** |
| 1p36.33 | Del | DVL1 | Chr1:943468-1706160 (763) | 5% | chr1:1226063-1314437 (88) | 2/12755 | 0.20% | chr1:521413-1708649 (1187) | Gain+ Loss | 17 | 821 |
| 1p13.3 | Del | Intergenic | Chr1:111370372-111391381 (21) | 3% | chr1:111374093-111395110 (11) | 14/19349 | 10.8% | chr1:111375574-111389642 (14) | Loss | 8 | 211 |
| 8p21.2 | Del | DOCK5 | Chr8:24931313-25101936 (171) | 10% | chr8:24971559-24992365 (21) | 17/19453 | 8.2% | chr8:24971559-24992365 (21) | Loss | 11 | 676 |
| 12p11.21 | Dup | RP11-428G5.5 | Chr12:31975730-32068877 (93) | 2% | chr12:31982559-32081411 (99) | 6/17251 | 1.4% | NA | NA | NA | NA |
| 19q13.2 | Del | CYP2A7 | chr19:41341589-41433931 (92) | 3% | chr19:41352371-41397661 (45) | 8/16665 | 3% | chr19:41337301-41394407 (57) | Gain+ Loss | 6 | 450 |
| 19q13.42 | Dup | LILRA6 | chr19:54731679-54845802 (114) | 2% | chr19:54716840-54748342 (32) | 10/17552 | 5.6% | chr19:54718938-54761735 (43) | Gain+ Loss | 12 | 561 |
| 2q34 | Del | ERBB4 | chr2:213187034-213191389 (4) | 3% | chr2:213183409-213194322 (4.6%) | 13/8095 | 4.6% | chr2:213183409-213192660 (9) | Loss | 7 | 78 |
| 5p15.2 | Del | Intergenic | Chr5:12812336-12888815 (76) | 13% | chr5:12810778-12820827 (10) | 11/4193 | 40.9% | chr5:12809645-12821242 (12) | Loss | 7 | 502 |

a DGV Gold Standard Variants, largest study was selected and reported.

b Human CNV Map among presumably healthy individuals of various ethnicities. Developed from DGV content based on high-resolution studies only.

c Carriers from study (160k, 2.5Mk) where CNVR was associated with risk. 2q34 and 5p15 are relative to 2.5M set and all others are 610k set.

**Supplemental Table 6. Mixed type CNVR merging and alternative logistic regression models for all EOC susceptibility**

| Array | Locus | Gene | N Del/Dup | | CNVR (KB)[a] | Alternative Regression Models[b] | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Deletion | | Duplication | | Mixed Type | |
| | | | *Case* | *Control* | | P-value | OR (95% CI) | P-value | OR (95% CI) | P-value | OR (95% CI) |
| 610k | 8p21.2 | DOCK5 | 113/0 | 168/0 | Chr8: 25061807-25079502 (18) | **0.004** | **0.69 (0.54-0.88)** | NA | NA | NA | NA |
| | 19q13.2 | CYP2A7 | 49/3 | 29/9 | chr19:41349732-41393760 (44) | **0.01** | **1.83 (1.15-2.92)** | 0.12 | 0.35 (0.09-1.30) | 0.07 | 1.48 (0.96-2.23) |
| | 19q13.42 | LILRA6 | 14/37 | 26/17 | chr19:54731679-54743217 (12) | 0.09 | 0.57 (0.30-1.09) | **0.004** | **2.35 (1.32-4.19)** | 0.26 | 1.27 (0.84-1.92) |
| 2.5M | 2q34 | ERBB4 | 8/0 | 18/0 | chr2:213187034-213191389 (4) | **0.009** | **0.32 (0.14-0.76)** | NA | NA | NA | NA |

[a] CNVR were constructed by merging deletion and duplication segments into a singular CNVR. The primary analysis constructed deletion and duplication CNVR separately and therefore the region boundaries may differ. Overall, smaller regions were constructed due to more extensive trimming of long segments that were (now) present in <10% of subjects.

[b] Each column lists the CNV group that was compared to diploid reference group. Mixed type was defined as any CNV (deletion or duplication). Models were adjusted for the first principal component (PC). PCs were constructed from copy number matrix of CNVR. PC's differed from primary analysis PCs constructed on deletion or duplication regions alone and thus estimates vary even when CNVR size, counts, and type are the same as primary analysis.

**Supplemental Table 7. Mixed type CNVR merging and alternative logistic regression models for HGSOC susceptibility**

| Array | Locus | Gene | N Del/Dup | | CNVR (KB)[a] | Alternative Regression Models[b] | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Deletion | | Duplication | | Mixed Type | |
| | | | *Case* | *Control* | | P-value | OR (95% CI) | P-value | OR (95% CI) | P-value | OR (95% CI) |
| 610k | 1p36.33 | DVL1 | 7/4 | 82/6 | Chr1:1106473-1356550 (250) | **0.002** | **0.29 (0.13-0.63)** | 0.16 | 2.47 (0.69-8.82) | **0.009** | **0.43 (0.23-0.80)** |
| | 1p13.3 | Intergenic | 23/0 | 40/0 | Chr1: 111374827-111391381 (17) | **0.009** | **2.02 (1.19-3.42)** | NA | NA | NA | NA |
| | 8p21.2 | DOCK5 | 27/0 | 168/0 | Chr8: 25061807-25074361 (13) | **0.004** | **0.53 (0.35-0.81)** | NA | NA | NA | NA |
| | 12p11.21 | RP11-428G5.5 | 0/19 | 3/32 | Chr12: 31997981-32063002 (65) | 0.97 | NE | **0.01** | **2.14 (1.20-3.82)** | **0.02** | **1.96 (1.11-3.46)** |
| | 19q13.2 | CYP2A7 | 24/1 | 29/9 | chr19:41349732-41393760 (44) | **9.6E-05** | **3.01 (1.73-5.23)** | 0.38 | 0.39 (0.05-3.12) | 9.8E-04 | 2.40 (1.42-4.01) |
| | 19q13.42 | LILRA6 | 3/14 | 26/17 | chr19:54731679-54743217 (12) | 0.12 | 0.38 (0.12-1.27) | **0.004** | **2.90 (1.42-5.94)** | 0.29 | 1.36 (0.77-2.42) |
| 2.5M | 2q34 | ERBB4 | 3/0 | 18/0 | chr2:213187034-213191389 (4) | **0.006** | **0.17 (0.05-0.60)** | NA | NA | NA | NA |
| | 5p15.2 | Intergenic | 55/0 | 36/0 | Chr5: 12812336-12822959 (11) | **0.005** | **1.92 (1.42-2.79)** | NA | NA | NA | NA |

NE=Non-estimable

[a] CNVR were constructed by merging deletion and duplication segments into a singular CNVR. The primary analysis constructed deletion and duplication CNVR separately and therefore the region boundaries may differ. Overall, smaller regions were constructed due to more extensive trimming of long segments that were (now) present in <10% of subjects.

[b] Each column lists the CNV group that was compared to diploid reference group. Mixed type was defined as any CNV (deletion or duplication). Models were adjusted for the first principal component (PC). PCs were constructed from copy number matrix of CNVR. PC's differed from primary analysis PCs constructed on deletion or duplication regions alone and thus estimates may vary even when CNVR size, counts, and type are the same as primary analysis.

**Supplemental Table 8. Differential gene expression by somatic copy number in primary ovarian tumors**
Linear regression was used to model SCNA (deletion, diploid, duplication) onto gene expression (log2 transformed FPKM) values.

| | | | SCNA Fold Change[a] | |
|---|---|---|---|---|
| Region | Gene | SCNA Pval | Deletion | Duplication |
| 1p13 | CEPT1 | 9.58E-22 | 2.0 | 1.2 |
| | DRAM2 | 1.18E-13 | 1.9 | 1.2 |
| | DENND2D | 2.75E-11 | 2.1 | 1.2 |
| | RBM15 | 5.39E-11 | 1.5 | 1.4 |
| 2q34 | ERBB4 | 4.67E-05 | 4.2 | 1.2 |
| 8p21 | GNRH1 | 5.86E-05 | 1.7 | 4.2 |
| 12p11 | FGD4 | 3.00E-08 | 3.7 | 1.5 |
| | DENND5B | 1.01E-03 | 1.7 | 1.7 |
| | BICD1 | 2.40E-04 | 3.1 | 1.7 |
| | AMN1 | 2.72E-04 | 2.5 | 1.6 |
| 19q13.2 | C19orf47 | 8.37E-62 | 1.6 | 3.2 |
| | EGLN2 | 1.17E-49 | 1.7 | 2.7 |
| | CCDC97 | 4.26E-38 | 1.7 | 1.9 |
| | HNRNPUL1 | 3.54E-36 | 1.8 | 1.8 |
| | SERTAD3 | 8.26E-36 | 1.5 | 2.4 |
| | ITPKC | 8.22E-35 | 1.8 | 2.9 |
| | ADCK4 | 4.98E-34 | 1.6 | 2.9 |
| | SHKBP1 | 6.72E-32 | 1.6 | 3.0 |
| | EXOSC5 | 2.23E-25 | 1.8 | 1.7 |
| | SERTAD1 | 1.52E-22 | 1.7 | 2.2 |
| | BCKDHA | 5.43E-21 | 1.6 | 1.6 |
| | RAB4B | 1.21E-20 | 1.6 | 2.2 |
| | NUMBL | 6.30E-18 | 1.5 | 2.6 |
| | B9D2 | 3.26E-16 | 1.6 | 1.8 |
| | MIA | 2.57E-14 | 1.5 | 2.2 |
| | TMEM91 | 6.43E-14 | 1.6 | 1.5 |
| | BLVRB | 2.05E-13 | 1.5 | 2.0 |
| | B3GNT8 | 1.77E-10 | 2.0 | 1.7 |
| | HIPK4 | 1.33E-05 | 1.6 | 3.4 |
| | CYP2S1 | 7.70E-04 | 1.6 | 1.6 |
| | CYP2B7P1 | 5.78E-03 | 2.4 | 1.7 |
| 19q13.42 | PRPF31 | 1.21E-30 | 1.6 | 2.0 |
| | LENG1 | 1.31E-28 | 1.8 | 1.9 |
| | TFPT | 7.13E-27 | 1.7 | 2.5 |
| | CNOT3 | 7.05E-26 | 1.6 | 2.1 |
| | NDUFA3 | 3.83E-14 | 1.9 | 2.6 |
| | LENG9 | 6.51E-14 | 1.8 | 1.9 |
| | MYADM | 4.09E-11 | 1.7 | 1.7 |
| | TMC4 | 7.81E-08 | 1.9 | 2.0 |
| | TARM1 | 1.89E-03 | 1.3 | 3.3 |
| | CACNG8 | 4.72E-03 | 4.4 | 4.5 |
| | TSEN34 | 9.78E-24 | 1.7 | 2.1 |
| | MBOAT7 | 1.98E-20 | 1.8 | 2.1 |

a Fold-change is in reference to diploid. All deletions were underregulated (i.e. negative fold-change) and duplications were upregulated (i.e. positive fold-change).