# Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

## eMethods

### Patients and study design

After approval from the National Cancer Institute, we obtained clinical and whole-exome sequencing data for total 512 patients with OvCa from the TCGA data portal.[1] The first set of whole-exome sequencing data of total 358 OvCa patients (hereafter referred to as First Batch) were obtained on January 10, 2012 when this study was developed and initiated. The second set of whole-exome sequencing data of total 154 OvCa patients (hereafter referred to as Second Batch) were obtained on March 1, 2014 after it became available in the TCGA database. Each case was reviewed by a board-certified pathologist from both the tissue source site and TCGA's biospecimen core resource, to confirm that the frozen section was histologically consistent with ovarian serous adenocarcinoma and contained an average of 70% tumor cell nuclei with less than 20% necrosis. All cases were of high-grade serous histological type and 95% of tumors were stage III or IV according to the 1988 International Federation of Gynecology and Obstetrics (FIGO) staging system. The specimens had been surgically resected before the patients had undergone systemic treatment. The average age at diagnosis was 60.0 years with a range of 27 to 88 years. All patients received platinum-based chemotherapy treatment; the last primary platinum treatment date was also determined from the available chemotherapy data. Written consent was obtained from all living patients. Among the 358 OvCa patients in the First Batch, the 210 cases with an explicitly defined chemotherapy response status (sensitive or resistant) were used in this study as the discovery cohort. The remaining 148 TCGA OvCa samples for which chemotherapy response status was unavailable were used together with the 154 cases from the Second

Batch as a validation cohort for validation (hereafter referred to validation cohort). The entire TCGA cohort including patients from both the discovery and validation cohorts was hereafter referred to as the combined cohort. Age and tumor clinicopathological characteristics of OvCa patients in these cohorts are described in the **eTable 1 in the Supplement**. Although patients in the Second Batch tend to comprise more women who are living or had grade 2 tumors as compared to those in the First Batch, there is no significant difference in age, tumor stage, and residual tumor size between patients of these two batches (**eTable 2 in the Supplement**). The study was approved by the institutional review board at MD Anderson Cancer Center. The flow chart for the study design was shown in details in **eFigure 1 in the Supplement**.

**Chemotherapy response data analysis**

Two aspects of chemotherapy response were investigated in this study: response status to platinum treatment (sensitive or resistant) and platinum-free duration after treatment. All patients underwent platinum-based chemotherapy treatment; the date of the last primary platinum treatment was determined from the available chemotherapy data and included adjuvant therapy[1] and consolidation treatment when given consecutively following adjuvant therapy.[1] The platinum-free interval was defined as the interval from the date of the last primary platinum treatment to the date of progression, recurrence, or last known contact (censored) if the patient was alive and had not developed recurrent disease. Platinum status was defined as resistant if the platinum-free interval was less than 6 months and the patient experienced progression or recurrence. It was defined as sensitive if the platinum-free interval was 6 months or more, there was no evidence of progression

or recurrence, and the follow-up interval was at least six months from the date of last primary platinum treatment. On the basis of these criteria, 210 cases in the First Batch had an explicitly defined chemotherapy response status and were then used as the discovery cohort, where 141 (67%) cases were designated as sensitive and 69 (33%) as resistant (**eTable 1 in the Supplement**). The distribution of sensitive versus resistant patients in this cohort reflects clinical chemosensitivity rates of approximately 70%.[2] The remaining 148 OvCa cases who had not experienced progression or recurrence and were followed up for less than six months therefore had no explicitly defined chemotherapy response status. These patients were used together with the 154 TCGA OvCa cases from the Second Batch as a validation cohort in this study. A majority of patients in this validation cohort had unknown chemotherapy response status and only 38 (72%) were designated as sensitive and 15 (28%) as resistant. We compared clinicopathologic characteristics of patients with and without chemotherapy response data in the validation cohort. Except that more grade 2 tumors were included in the group with chemotherapy response data, no other differences were observed between these two groups (**eTable 3 in the Supplement**). Taken together in the combined cohort, 179 (68%) were designated as sensitive and 84 (32%) as resistant (**eTable 1 in the Supplement**).

**Mutation data analysis**

Exome capture and massively parallel sequencing on DNA isolated from the 512 TCGA serous OvCa samples and from matched normal samples for each individual were performed on the Illumina GAIIx platform (Illumina Inc., San Diego, California). The sequencing and quality control procedures were described to allow for confident mutation

detection.[1] Variants were annotated as somatic mutations if they were not observed in normal samples. Level 2 somatic mutation data from all three TCGA sequencing centers (The Genome Center at Washington University, Broad Institute, and Human Genome Center at Baylor College of Medicine) were merged into a single non-redundant file which was thus used for subsequent analyses. The germline mutation data for the *BRCA1* and *BRCA2* genes in the First Batch were obtained from a previous TCGA study.[1] Splice-site mutations were restricted to substitutions, deletions, or insertions that overlapped the 2-bp intronic sequence that was defined as the splice donor or acceptor. Mutations that affected the 3'UTR, 5'UTR, intronic and intergenic sequences were excluded from the study. The overall background mutation rate was determined by dividing the total number of mutations by the total number of covered bases. After the highly mutated genes: *TP53, BRCA1, BRCA2, NF1*, and *RB1*, were excluded, the background mutation rate was approximately $1.7x10^{-06}$.[1]

We first analyzed mutation data for the 210 TCGA cases in the discovery cohort that had an explicitly defined response status to chemotherapy (sensitive or resistant). To quantify the association of gene mutation with response status, we calculated for each individual gene the number of mutations in the sensitive ($N_s$) or resistant ($N_r$) samples, respectively. Given the fact that the somatic mutation frequency of any gene except *TP53* is relatively small in high-grade serous ovarian cancer,[1] we further selected the genes associated with chemosensitivity by applying both of the following two criteria: (1) $N_r$ = 0; (2) $N_s$ is greater than or equal to 2. Genes satisfying these two criteria will be mutated in at least two chemosensitive samples (corresponding to a mutation frequency of approximately 1%), but not in any of the chemoresistant cases.

We calculated the mutation frequency in terms of the total number of mutations including single-nucleotide substitution or insertion-deletion (INDEL) per sample. Fractions of mutations (INDELs were excluded) in the six possible mutation classes (i.e., C>T, C>A, C>G, A>G, A>C, and A>T) were calculated for each sample. The scores for the degree of enrichment in hypermutated OvCa cases with ADAMTS status were computed as described previously.[3] The significance of gene mutations was estimated on the basis of the number of patients with mutations in the gene, the gene size and the background mutation rate (approximately $1.7x10^{-06}$) reported in the TCGA OvCa sample cohort.[1]

**Survival analysis**

We determined whether gene mutations or clinical variables were associated with patient outcome by performing survival analysis including overall survival (OS) and progression-free survival (PFS), and platinum-free survival. OS was defined as the interval from the date of initial surgical resection to the date of last known contact (censored) or death. Progression-free survival (PFS) was defined as the interval from the date of initial surgical resection to the date of progression, recurrence, or last known contact (censored) if the patients were alive and had not experienced recurrence. Patients who died for whom no dates of progression or recurrence were available were excluded from PFS analyses. The platinum-free interval was defined as the interval from the date of the last primary platinum treatment to the date of progression, recurrence, or last known contact (censored) if the patient was alive and had not developed recurrent disease. Patients with negative platinum-free intervals (who underwent treatment after

progression or recurrence or who underwent their last treatment after the last follow-up date)[1] were excluded from this analysis. The OS, PFS and platinum-free interval durations were capped at 60, 48 and 36 months, respectively. In the Kaplan-Meier analysis, the patients were either dichotomized into two groups on the basis of gene mutation status or mutation frequency, or divided into three groups on the basis of residual tumor size. The log-rank test was used to assess differences in survival. In the univariate or multivariate Cox proportional hazards model analysis, gene mutation status, stage and surgical outcome were treated as categorical variables, and age was treated as a continuous variable. The Wald test was used to evaluate the survival difference.

**Verification of *ADAMTS* mutations by random selections**

While *ADAMTS* mutations were identified via statistical approaches from the 2118 responder-related genes (**eFigure 2 in the Supplement**), to further determine whether any gene combinations from this gene list were significantly associated with patient outcomes, we randomly selected 8 genes (to match the 8 ADAMTS genes) 100,000 times from the 2118 responder-related genes, and performed Kaplan-Meier analyses of overall survival, progression-free survival and platinum-free survival in patients stratified according to mutation status in those 8 randomly selected genes with the use of the log-rank test. This analysis was performed on the TCGA discovery cohort.

The median number of patients that harbored mutations among these gene combinations is 17 (range, 9 – 30, **eFigure 10 in the Supplement**). These data suggest that the survival difference with different gene combinations as discussed below was less likely due to a difference in the number of mutations. The statistical tests (represented by

–log10(Pvalue)) of gene mutations associated with OS, PFS, and platinum-free survival in all 100,000 randomly selected gene combinations were then visualized via scatter plots (**eFigure 11 in the Supplement**).

In addition, we calculated the p-value histogram that showed the background statistical significance distribution among the 100,000 random selections. The *P* values of these random selections generated a null distribution for association of the 8-gene combination with outcome. The empirical, nominal *P* value of association of *ADAMTS* mutations with outcome was then calculated relative to this null distribution for OS, PFS and platinum-free survival, respectively. Importantly, the random selection of class labels provides a more biologically reasonable assessment of significance than would be obtained by randomly selecting 8 genes.

**Validation of *ADAMTS* mutations in TCGA OvCa cohorts**

As depicted in **eFigure 1 in the Supplement**, the 210 TCGA OvCa samples from the First Batch that had an explicitly defined chemotherapy response status (sensitive or resistant) were used in this study as the discovery cohort for identification of the *ADAMTS* mutations, and the TCGA validation cohort (n = 302) comprised the 148 samples from the First Batch for which chemotherapy response status was unavailable and the 154 patients from the Second Batch to validate the ADAMTS mutations in OvCa. The OvCa samples in the discovery and validation cohorts were contributed from at least 16 different tissue source sites which collected samples from many different hospitals and pathology groups (**eFigure 12 in the Supplement**).[1] Implicit with this heterogeneity of

submitting sites is tumor heterogeneity in OvCa patients in these two TCGA cohorts. The TCGA validation cohort can be therefore used as an independent validation set.

We next validated *ADAMTS* mutations in these additional 302 TCGA OvCa samples, evaluated by the association of *ADAMTS* mutations with *BRCA1/2* mutations, mutation spectra, and patient outcome. 30 (~9.3%) OvCa cases exhibited *ADAMTS* mutations and 38 (~12.6%) had *BRCA1/2* mutations; these two families' mutations were not correlated with each other ($P = 0.24$, Fisher's exact test; only somatic mutation data were available for the second batch) (**eFigures 13** and **14 in the Supplement**). Among those who had known chemotherapy response status (sensitive or resistant), all the *ADAMTS* mutated cases are sensitive and none of them were resistant (**Figure 4A** and **eFigure 13 in the Supplement**). *ADAMTS* mutations were significantly associated with hypermutated samples ($P < 0.0001$, Mann-Whitney test, **eFigure 15 in the Supplement**), and had significantly lower percentage of C>T transition ($P < 0.0001$) but higher percentage of A>T transversion ($P = 0.0028$) (**eFigure 16 in the Supplement**). The mutation frequency (log10 scale) was negatively correlated with C>T transition but positively correlated with A>T transversion (**eFigure 17 in the Supplement**). These results were consistent with findings from the discovery cohort. Except for a significant correlation with tumor stage, *ADAMTS* mutations were not correlated with age or other patient characteristics in the validation cohort (**eTable 7 in the Supplement**).

Correlation with patient outcome showed that *ADAMTS* mutated patients had significantly better PFS than *ADAMTS* wild-type cases (Log-rank $P = 0.0076$, HR [95%CI] = 0.36 [0.27 – 0.81) (**Figure 4B**). Although *ADAMTS* mutations exhibited a discernible trend toward better OS and a longer platinum-free interval (**eFigure 18 in the**

**Supplement**), the statistical significance was compromised likely because of the relatively short clinical follow-ups and the smaller size of analyzed samples (**eTable 8 in the Supplement**). The median OS follow-up in the validation cohort was less than half of that in the discovery cohort and only 83 cases were used in the platinum-free survival analysis among which only 7 harbored *ADAMTS* mutations. With these limitations, the known outcome predictor, *BRCA1/2* mutation status, was not significantly associated with overall survival or platinum-free survival in this validation cohort (**eFigure 19 in the Supplement**). The short clinical follow-up also contributes to the missing chemotherapy response status in majority of patients in this validation cohort.

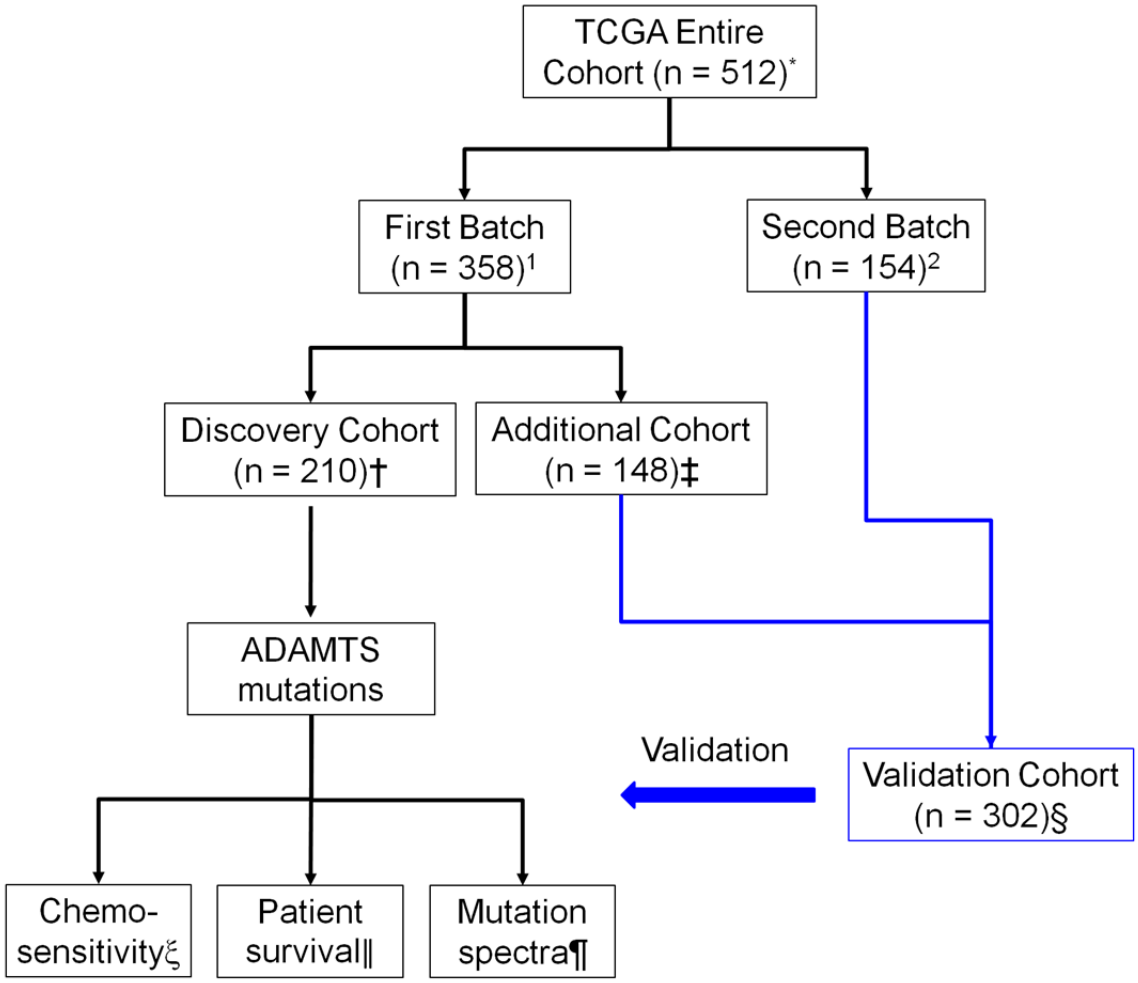
We also analyzed *ADAMTS* mutations in the TCGA combined cohort of total 512 OvCa patients. A total of 53 (~10.4%) cases had *ADAMTS* mutations and 80 (~15.6%) had *BRCA1/2* mutations (**eFigure 20 in the Supplement**) but both families' mutations were not correlated with each other ($P = 0.07$, Fisher's exact test, **eFigure 21 in the Supplement**). Except for a significant correlation with tumor stage, patients with *ADAMTS* mutations were not correlated with age or other patient characteristics in this combined cohort (**eTable 9 in the Supplement**). Consistently, *ADAMTS* mutations were significantly associated with hypermutated samples ($P < 0.0001$, Mann-Whitney test), and had significantly lower percentage of C>T transition ($P < 0.0001$) but higher percentage of A>T transversion ($P = 0.0003$). In contrast to the validation cohort, the combined cohort had longer clinical follow-ups that were comparable to those in the discovery cohort (**eTable 8 in the Supplement**). *BRCA1/2* mutations, as anticipated, exhibited significant correlation with overall survival, progression-free survival and platinum-free survival in this combined cohort (**eFigure 22 in the Supplement**). With an

increased clinical follow-up and more samples included in the platinum-free survival analysis, patients with *ADAMTS* mutations not only had better PFS (Log-rank $P < 0.0001$, HR [95%CI] = 0.42 [0.38 – 0.70]), but also exhibited better OS (Log-rank $P = 0.01$, HR [95%CI] = 0.54 [0.42 – 0.89]) and a longer platinum-free survival (Log-rank $P = 0.0014$, HR [95%CI] = 0.48 [0.39 – 0.80]) than those without *ADAMTS* mutations (**Figure 4C** and **eFigure 23 in the Supplement**). Compared to the discovery cohort, the combined cohort added 231 more cases into the overall survival analysis, 156 more cases into the progression-free survival analysis, and 83 more cases into the platinum-free survival analysis.

**Statistical analysis**

Survival differences were assessed with the use of either log-rank test or Wald test. Differences in cell viability were assessed via the two-tailed unpaired *t*-test. Other standard statistical tests were used to analyze the clinical and genomic data, including the Mann-Whitney *U* test, Fisher's exact test, and Chi-square test. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed using scientific software such as Matlab (MathWorks, Natick, Massachusetts), SPSS version 18 (SPSS Inc, Chicago, Illinois) and GraphPad Prism 6 (Graphpad Software Inc, La Jolla, CA).

**eFigure 1. Analysis flow chart for identification and validation of *ADAMTS* mutations in TCGA OvCa Cases**




* Whole-exome sequencing data of total 512 OvCa patients were obtained from The Cancer Genome Atlas (TCGA) data portal, https://tcga-data.nci.nih.gov/tcga/.

[1] The first set of whole-exome sequencing data of total 358 OvCa patients (referred to as First Batch) were obtained on January 10, 2012 when this study was developed and initiated.

[2] The second set of whole-exome sequencing data of total 154 OvCa patients (referred to as Second Batch) were obtained on March 1, 2014 from the TCGA database.

† Total 210 patients who had explicitly defined platinum-based drug response status (sensitive or resistant) were used as the discovery cohort for identification of ADAMTS mutations and clinical / molecular associations.

‡ The 148 remaining patients from the First Batch had unknown platinum-based chemotherapy response status and were used together with the 154 cases from the Second Batch for validation.

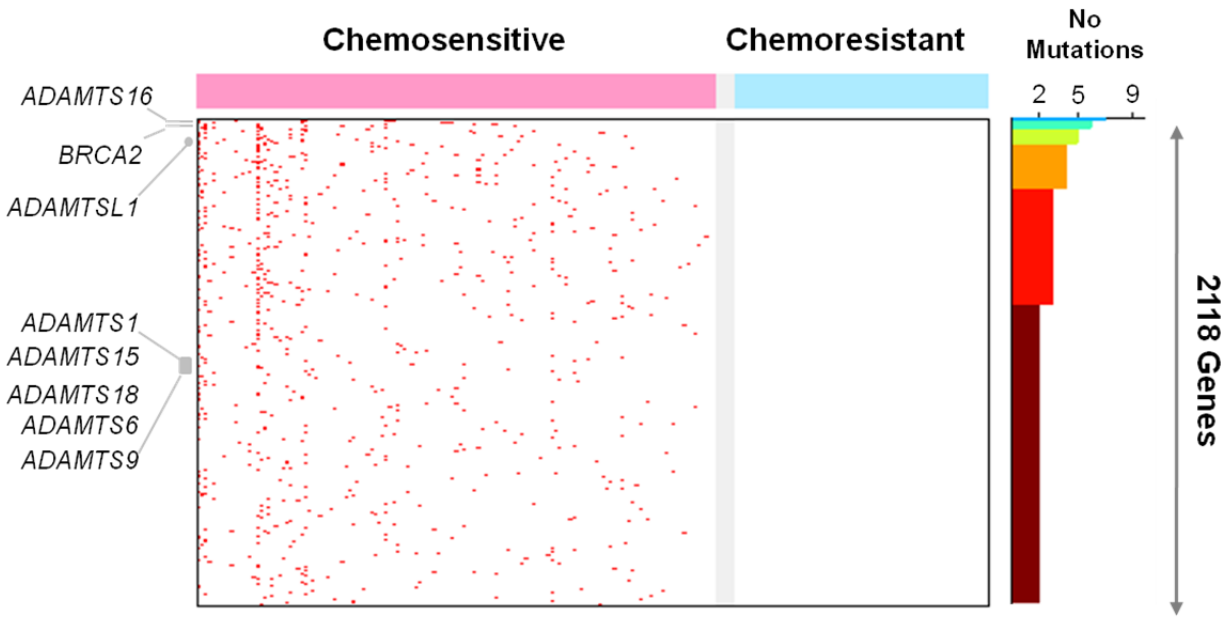
§ The validation cohort included the 148 cases from the First batch and the 154 cases from the Second Batch.

ξ Including chemotherapy response status (sensitive or resistant) and platinum-free survival.

‖ Including overall survival, and progression-free survival.

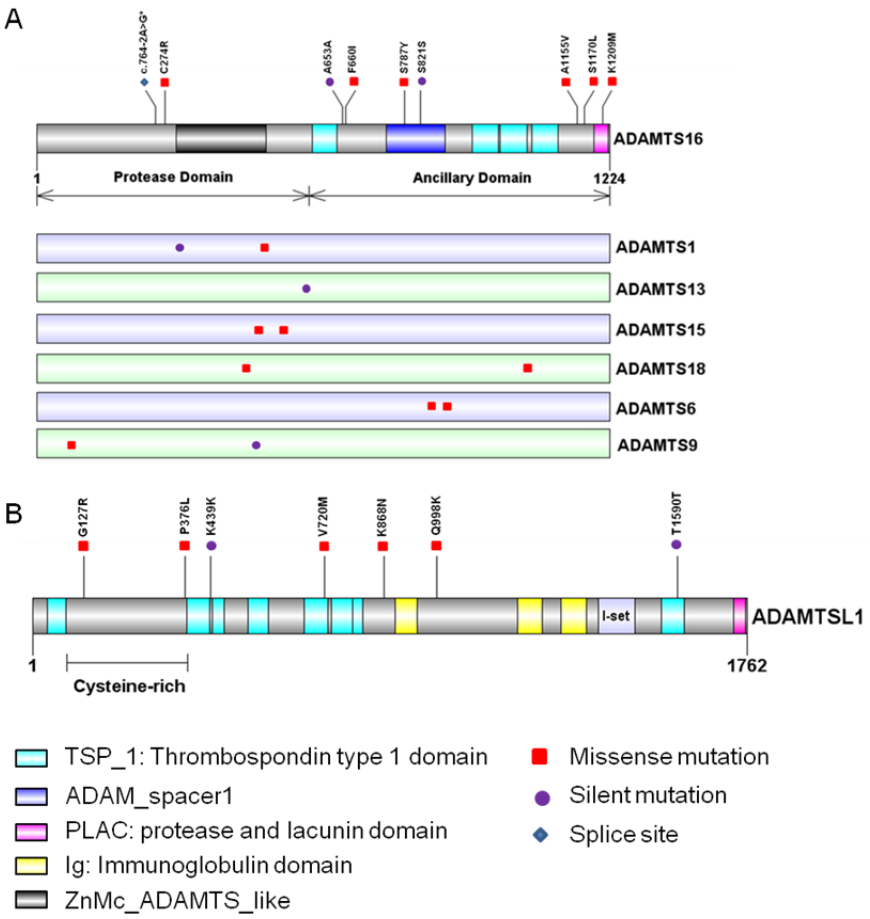
¶ Including patient mutation frequency and mutation spectrum.

**eFigure 2. Responder-related genes identified in the TCGA discovery cohort**



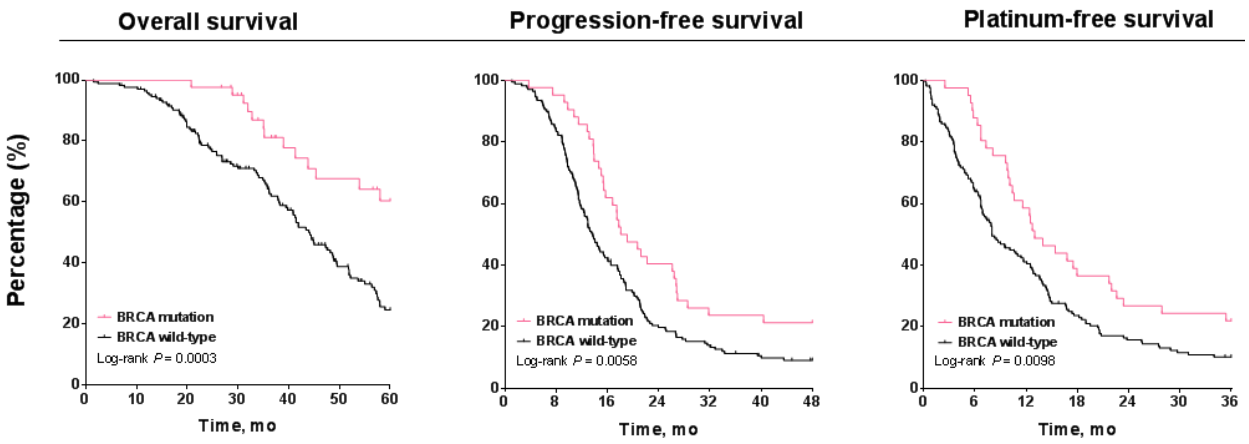

Genes mutated in at least two chemosensitive samples but not in any chemoresistant samples, resulting in a total of 2118 responder-related genes. Columns denote the TCGA OvCa samples stratified according to the chemotherapy response status (chemosensitive or chemoresistant) and rows denote the 2118 responder-related genes that are sorted by the number of patients harboring mutations. The right panel on the plot showed the numbers of mutations for each of the 2118 genes. *ADAMTS16* and *BRCA2* were the most frequently mutated genes in the list, each were mutated in 9 OvCa cases (refer to **eTable 2 in the Supplement**). In addition to *ADAMTS16*, six other members from the *ADAMTS* gene family were identified in the responder-related gene list including *ADAMTSL1*, *ADAMTS1*, *ADAMTS15*, *ADAMTS6*, *ADAMTS9*, and *ADAMTS18*.

**eFigure 3. Distribution of protein alterations encoded in the *ADAMTS* genes in the TCGA discovery cohort**



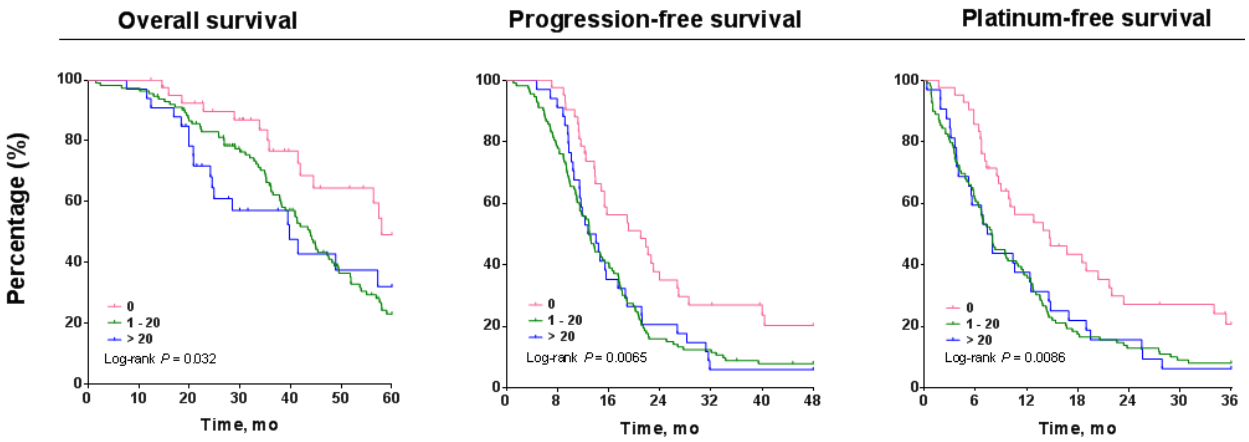

(**A**, **B**) Positional distribution of somatic mutations across ADAMTS16 (**A**) and ADAMTSL1 (**B**) proteins. Somatic mutations in additional ADAMTS family members were mapped onto the ADAMTS16 protein, on the basis of the sequence alignment. The protease domain, ancillary domain, cysteine-rich domain, thrombospondin type domain, signal peptide, immunoglobulin domain, ADAM spacer, and PLAC (protease and lacunin) domain are depicted. Red squares indicate missense mutations, purple bullets silent mutations, and blue diamonds mutations at splice sites.

**eFigure 4. Association of *BRCA* mutations with clinical outcome and chemotherapy response in the TCGA discovery cohort.**



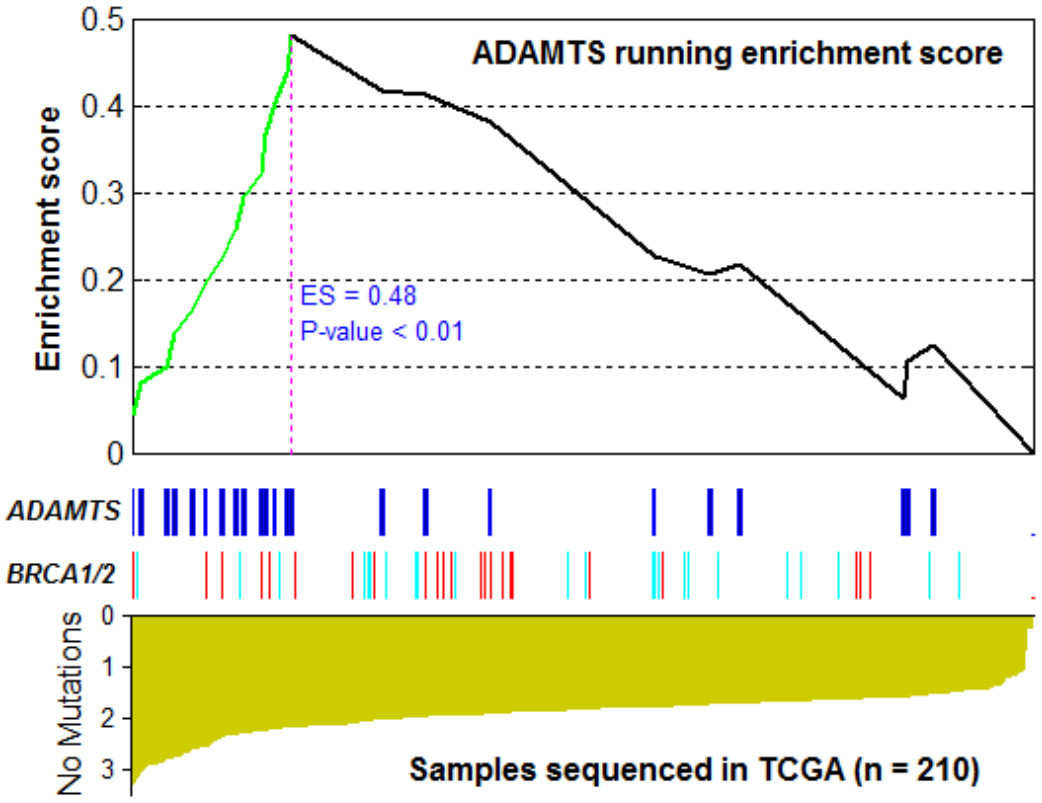

Estimates of clinical outcome (in terms of overall survival and progression-free survival), and chemotherapy response (i.e., platinum-free interval) were performed among patients that were stratified on the basis of *BRCA* (including *BRCA1* and *BRCA2*) mutations. Subgroups were compared with the use of the log-rank test. The Kaplan-Meier analysis shows that patients with BRCA mutations had longer overall survival ($P$ = 0.0003), progression-free survival ($P$ = 0.0058) and platinum-free survival ($P$ = 0.0098) than those without, which is consistent with previous reports.[1] For both overall survival and progression-free survival, the percentage probability is plotted versus the time since diagnosis in months. For platinum-free survival, the percentage probability is plotted versus the time since the end of adjuvant therapy.

**eFigure 5. Association of residual tumor size with clinical outcome and chemotherapy response in the TCGA discovery cohort**



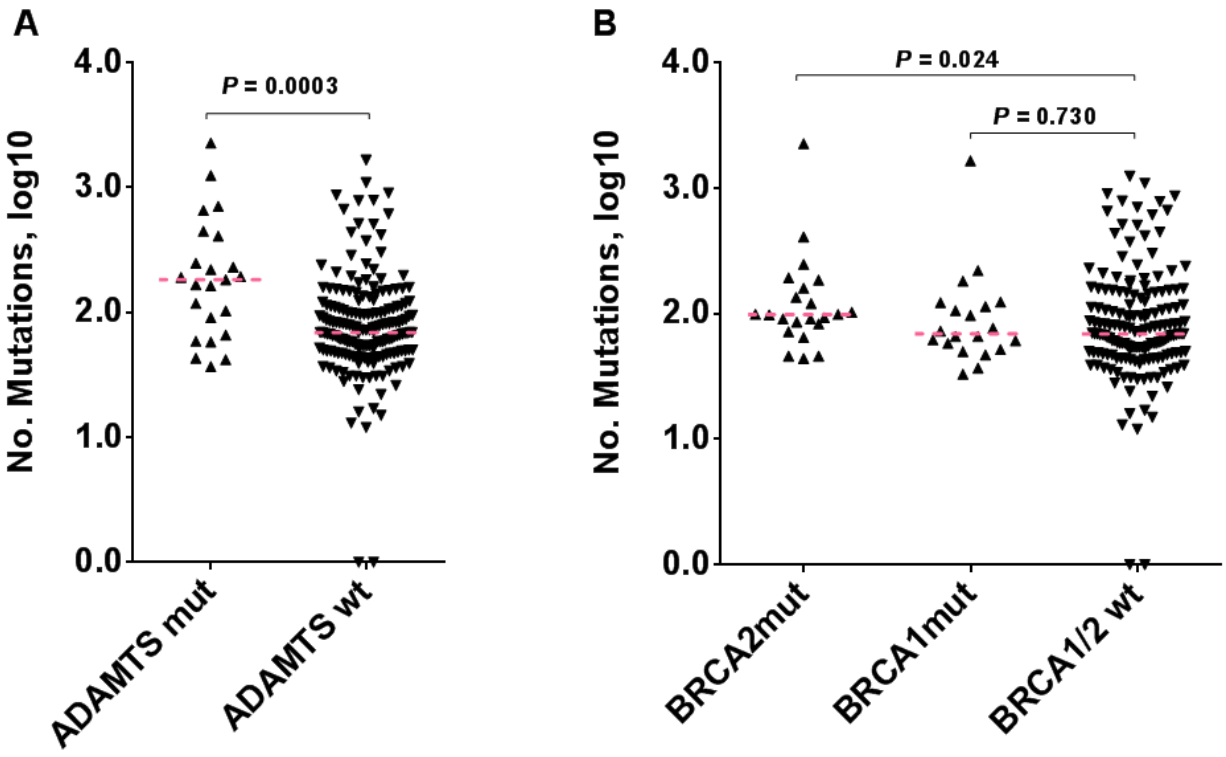

Estimates of clinical outcome (in terms of overall survival and progression-free survival), and chemotherapy response (i.e., platinum-free interval) were performed among patients that were stratified on the basis of residual tumor size defined as the size of residual disease at the conclusion of the primary surgical procedure. The subgroups are described in **eTable 1 in the Supplement** and were compared with the use of the log-rank test. The Kaplan-Meier analysis shows residual disease was significantly correlated with overall survival ($P = 0.032$), progression-free survival ($P = 0.0066$) and platinum-free survival ($P = 0.0086$). For both overall survival and progression-free survival, the percentage probability is plotted versus the time since diagnosis in months. For platinum-free survival, the percentage probability is plotted versus the time since the end of adjuvant therapy.

**eFigure 6. Association of *ADAMTS* mutations with genetic instability in the TCGA discovery cohort**



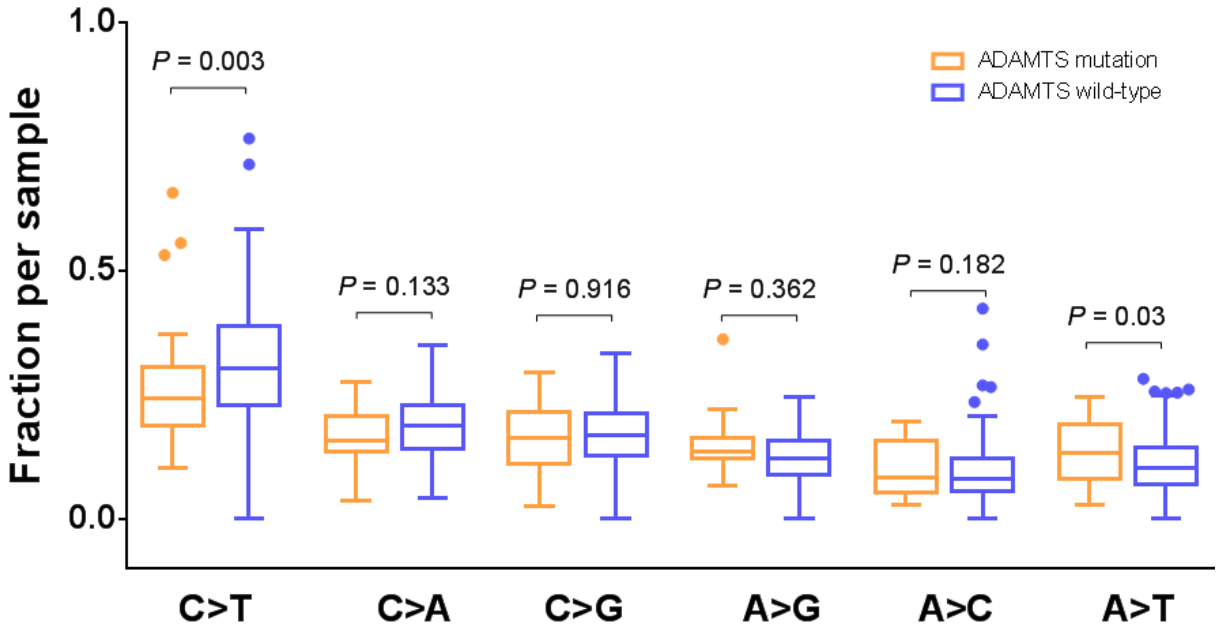

The top portion shows the running enrichment score (ES) test of *ADAMTS* mutations in the hyper-mutated samples. The bottom portion shows the total numbers of mutations (log10 scale) in 210 decreasingly ranked OvCa cases in the TCGA discovery cohort. The height of each discrete line indicates the number of mutations ($\log_{10}$) for each tumor. The middle portion of the plot shows where the samples with *ADAMTS* or *BRCA1/2* mutations appear in the ranked list of samples. Blue lines indicate *ADAMTS* mutations, red lines *BRCA2* mutations and cyan lines *BRCA1* mutations. Consistent with *BRCA2* mutation,[3] *ADAMTS* mutated cases were significantly enriched in the hypermutated samples (maximum ES, 0.48, $P < 0.01$).

**eFigure 7. Comparison of association of *ADAMTS* and *BRCA1/2* mutations with mutation frequency in the TCGA discovery cohort**



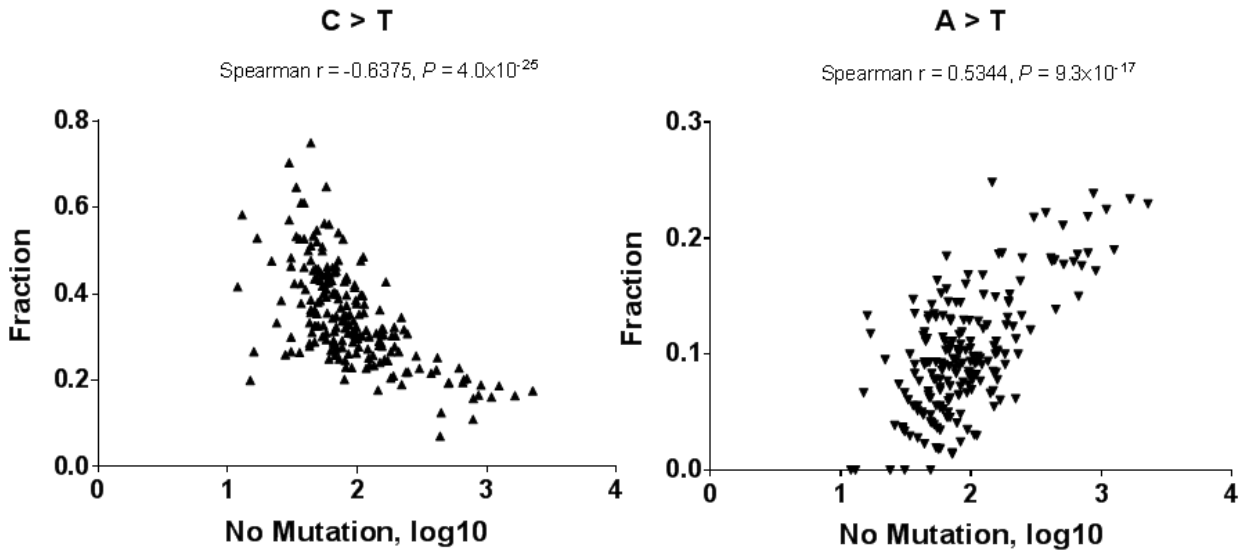

(**A**) The *ADAMTS* mutation carriers had a significantly higher mutation rate than did the *ADAMTS* wild-type cases in the TCGA discovery cohort ($P$ = 0.0003, Mann-Whitney test). The dashed pink line indicates the median value. The median mutation number per sample was approximately 111 for *ADAMTS*-mutated cases versus 69 for wild-type cases. This result was consistent with that in the discovery cohort. (**B**) *BRCA2* mutations ($P$ = 0.024) are more significantly correlated with mutation frequency than *BRCA1* mutations ($P$ = 0.730), consistent with the previous report.[3]

**eFigure 8. Association of *ADAMTS* mutations with mutation spectra in the TCGA discovery cohort**



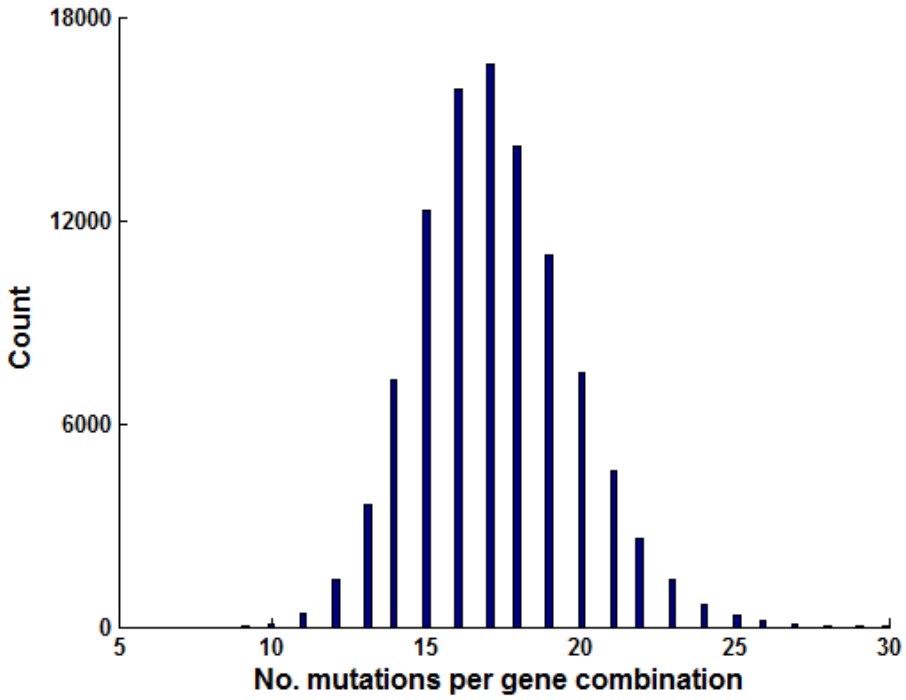

We calculated fractions of single nucleotide substitutions (INDELs were excluded) in the six possible mutation classes (i.e., C>T, C>A, C>G, A>G, A>C and A>T) for each sample. Data are represented as box-and-whiskers (Tukey) plots. The central line of each box is the median and edges are the 25$^{th}$ and 75$^{th}$ percentile. The outliers outside the Tukey whiskers are plotted individually as dots and excluded from the statistical test. The Mann-Whitney test was performed on these mutation categories in patients stratified according to *ADAMTS* mutation status. The *ADAMTS* mutated samples had a significantly lower percentage of C>T transition ($P$ = 0.003), but a significantly higher percentage of A>T transversion ($P$ = 0.03) than the *ADAMTS* wild-type samples. No significant difference was observed for other mutation classes in this cohort.

**eFigure 9. Correlation of mutation frequency with C>T or A>T fractions in the TCGA discovery cohort**



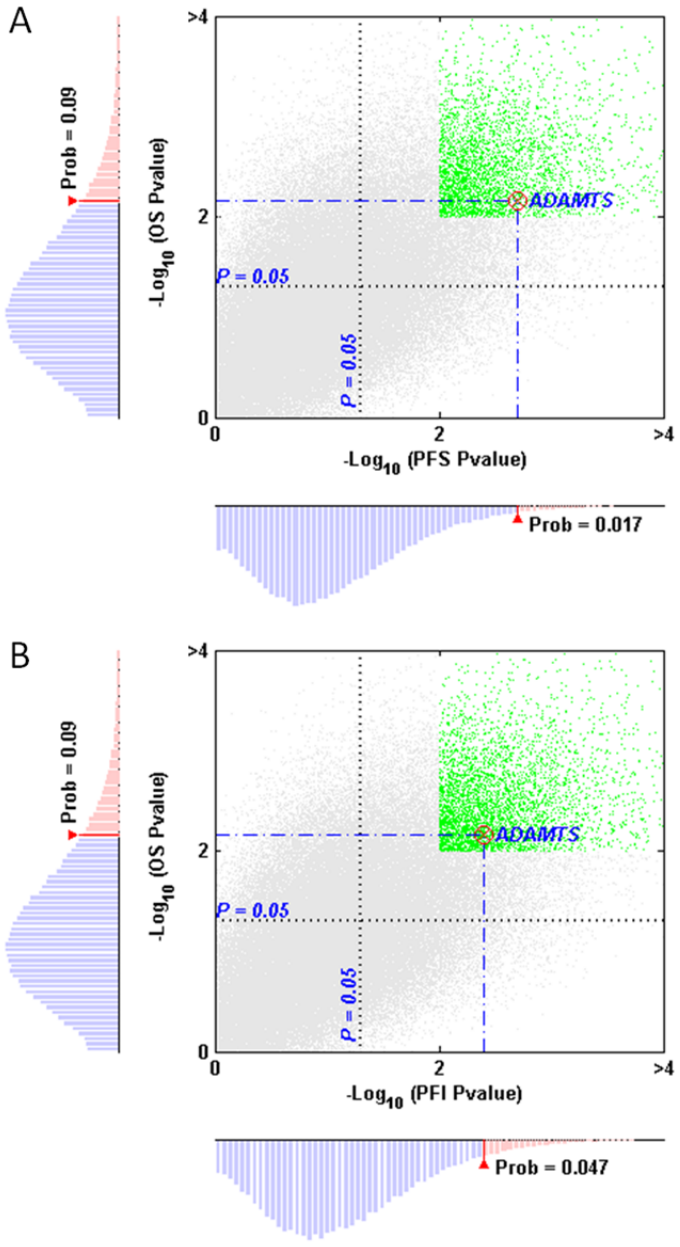

The mutation frequency (log10 scale) was negatively correlated with C>T transition (Spearman r = -0.6375, $P = 4.0 \times 10^{-25}$) and positively correlated with A>T transversion (Spearman r = 0.5344, $P = 9.3 \times 10^{-17}$).

**eFigure 10. Distribution of the number of patients harboring gene mutations among the 100,000 random gene selections**




We randomly selected eight genes (to match the eight *ADAMTS* genes) over 100,1000 times from the 2118 responder-related genes as shown in the **eFigure 2 in the Supplement**, and performed Kaplan-Meier analysis of overall survival, progression-free survival and platinum-free interval in patients stratified according to mutation status in each gene combination. The median number of patients harboring gene mutations among these combinations was 17 (range, 9 – 30). These data suggested that survival differences in different gene combinations as discussed below was not due to differences in the patient size in the mutated group. This analysis was performed on the TCGA discovery cohort.

**eFigure 11. Statistical significance (*P* value) of outcome association among the 100,000 random gene selections**




OS Pvalue: p-value of overall survival difference in patients stratified according to gene mutations.
PFS Pvalue: p-value of progression-free survival difference in patients stratified according to gene mutations.
PFI Pvalue: p-value of platinum-free survival difference in patients stratified according to gene mutations.
Prob: Probability

While *ADAMTS* mutations were identified via a statistical approach (with a statistical significance) from the 2118 responder-related genes, to further reduce the possibility of a significant difference in outcomes as a result of a self-fulfilling prophecy or tautological model, we randomly selected eight genes (to match the 8 *ADAMTS* genes) over 100,000 times from the 2118 responder-related genes (Supplementary Fig. 2), and performed Kaplan-Meier analysis of overall survival, progression-free survival and platinum-free survival in patients stratified according to mutation status in each of randomly selected gene combinations with the use of the log-rank test. This analysis was performed on the TCGA discovery cohort.

(**A**) *P* values (represented by –log10(Pvalue)) of association of gene mutations with progression-free survival (x-axis) and overall survival (y-axis) in the 100,000 randomly selected gene combinations. Each dot represents a gene combination consisting of 8 genes that were randomly selected from the 2118 responder-related genes. The dashed lines indicate a *P* value of 0.05. The green dots denote the gene combinations with a *P* value of $< 0.01$ for both overall survival and progression-free survival. The *ADAMTS* gene combination is indicated by the symbol, x, in the plot.

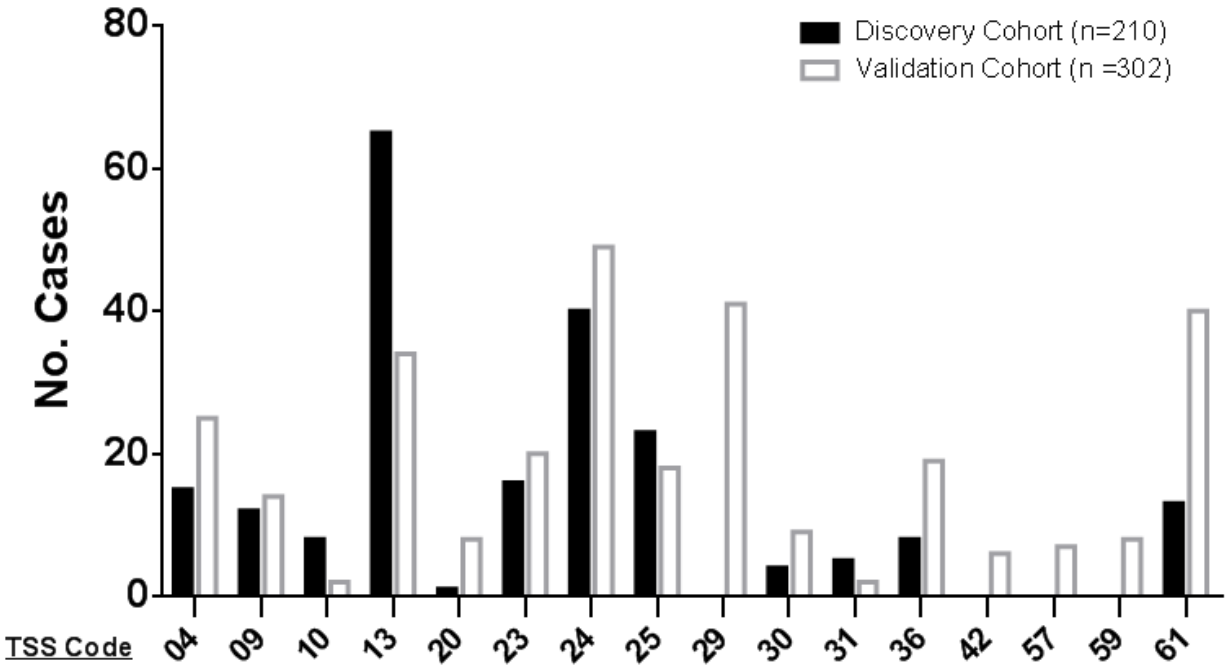
The univariate histogram on the horizontal axis shows the *P* value distribution for progression-free survival among the 100,000 randomly selected gene combinations. The *P* values of these random selections generated a null distribution for association of the 8-gene combination with progression-free survival. From this histogram, we can calculate the empirical, nominal *P* value of association of *ADAMTS* mutations with progression-free survival (*P* value = 0.0022, -log10(*P* value) = 2.6576, **Figure 2B**) relative to this null distribution (nominal *P* = 0.017, equivalent to the percentage of the pink area).

The univariate histogram on the vertical axis shows the *P* value distribution for overall survival among the 100,000 randomly selected gene combinations. The *P* values of these random selections generated a null distribution for association of the 8-gene combination with overall survival. From this histogram, we can calculate the empirical, nominal *P* value of association of *ADAMTS* mutations with overall survival (*P* value = 0.0073, -log10(*P* value) = 2.1367, **Figure 2A**) relative to this null distribution (nominal *P* = 0.09, equivalent to the percentage of the pink area).

(**B**) *P* value (represented by –log10(Pvalue)) of gene mutations associated with platinum-free survival (x-axis) and overall survival (y-axis) in the 100,000 randomly selected gene combinations. Each dot represents a gene combination consisting of 8 genes that are randomly selected from the 2118 responder-related genes. The dashed lines indicate a *P* value of 0.05. The green dots denote the gene combinations with a *P* value of < 0.01 in for both overall survival and platinum-free survival. The *ADAMTS* gene combination is indicated by the symbol, x, in the plot.

The univariate histogram on the vertical axis is the same as that in Panel A. The univariate histogram on the horizontal axis shows the *P* value distribution for platinum-free survival among the 100,000 randomly selected gene combinations. The *P* values of these random selections generated a null distribution for association of the 8-gene combination with platinum-free survival. From this histogram, we can calculate the empirical, nominal *P* value of association of *ADAMTS* mutations with platinum-free survival (*P* value = 0.004, -log10(*P* value) = 2.3979, **Figure 2C**) relative to this null distribution (nominal *P* = 0.047, equivalent to the percentage of the pink area).

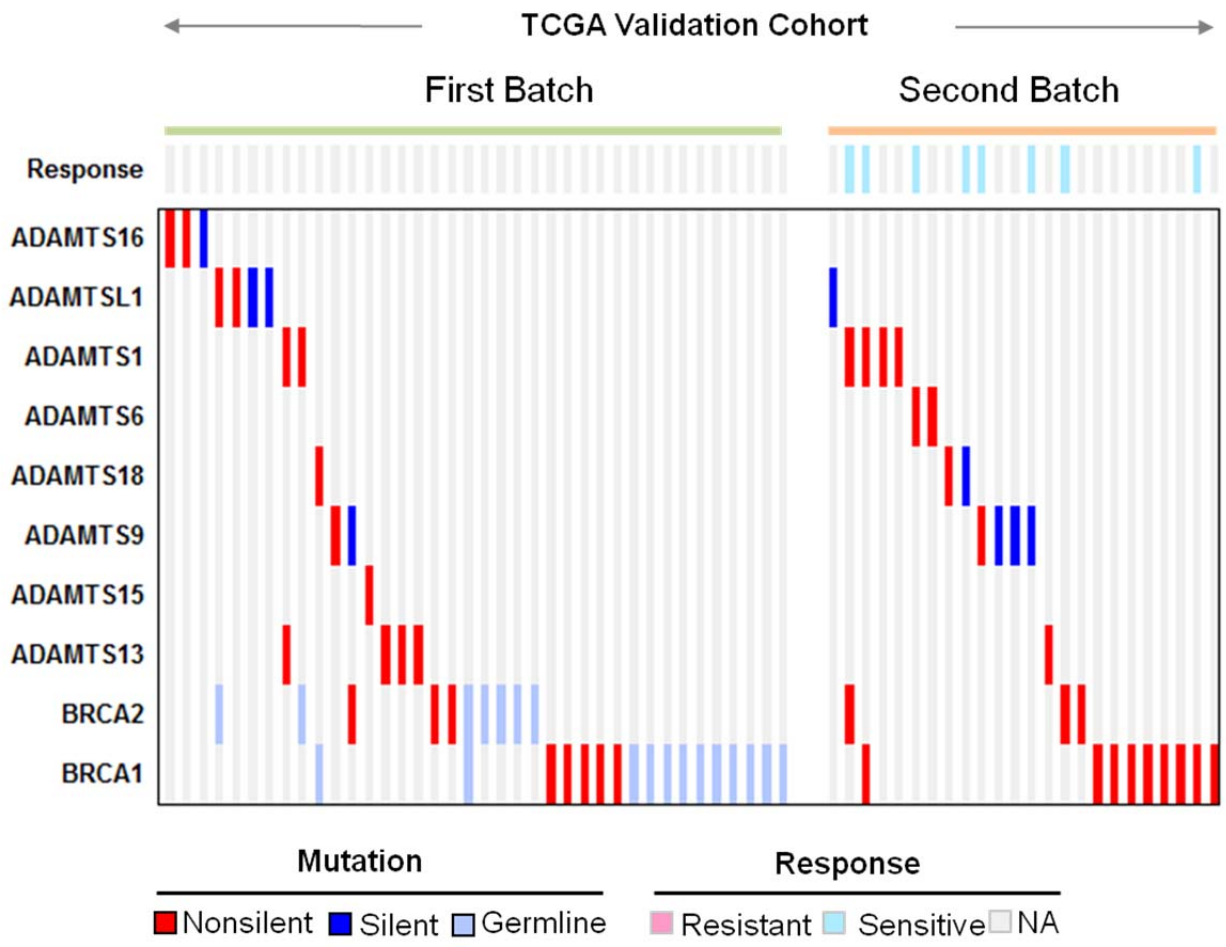
**eFigure 12. Distribution of TCGA OvCa patients from different tissue source sites in the discovery cohort and validation cohort**




| TSS Code | Source Site | TSS Code | Source Site |
|---|---|---|---|
| *04* | Gynecologic Oncology Group | *29* | Duke |
| *09* | UCSF | *30* | Harvard |
| *10* | MD Anderson Cancer Center | *31* | Imperial College |
| *13* | Memorial Sloan Kettering | *36* | BC Cancer Agency |
| *20* | Fox Chase Cancer Center | *42* | Christiana Healthcare |
| *23* | Cedars Sinai | *57* | International Genomics Consortium |
| *24* | Washington University | *59* | Roswell Park |
| *25* | Mayo Clinic - Rochester | *61* | University of Pittsburgh |

The top panel shows the number of TCGA OvCa patients contributed from different tissue source sites (TSS) in the discovery cohort (n = 210, black bar) and in the validation cohort (n = 302, white bar). The table on the bottom maps the TSS code with the tissue source sites.

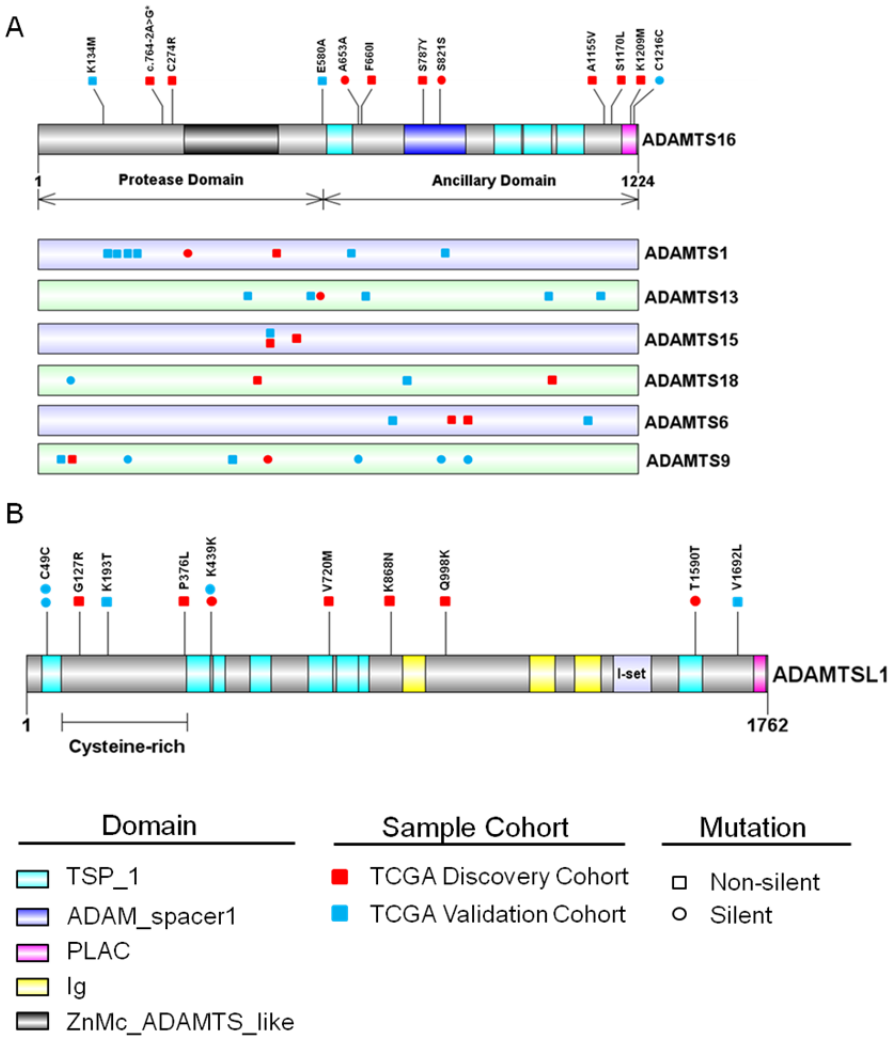
**eFigure 13. *ADAMTS* and *BRCA1/2* mutations in the TCGA validation cohort.**




This plot shows *ADAMTS* and *BRCA1/2* mutations that were detected in the TCGA validation cohort that comprised 302 patients with ovarian cancer. For each gene (row) indicated, tumors (columns) with mutations are labeled in red (nonsilent mutations), dark blue (silent mutations), or light blue (germline mutations) bars. Note that only somatic mutation data were available for the second batch. Distribution of protein alterations encoded in the *ADAMTS* genes in this validation cohort is detailed in **eFigure 14 in the Supplement**. In this validation cohort, 30 (~9.3%) OvCa cases exhibited *ADAMTS*

mutations and 38 (~12.6%) had *BRCA1/2* mutations; these two families' mutations were not correlated with each other ($P = 0.24$, Fisher's exact test).

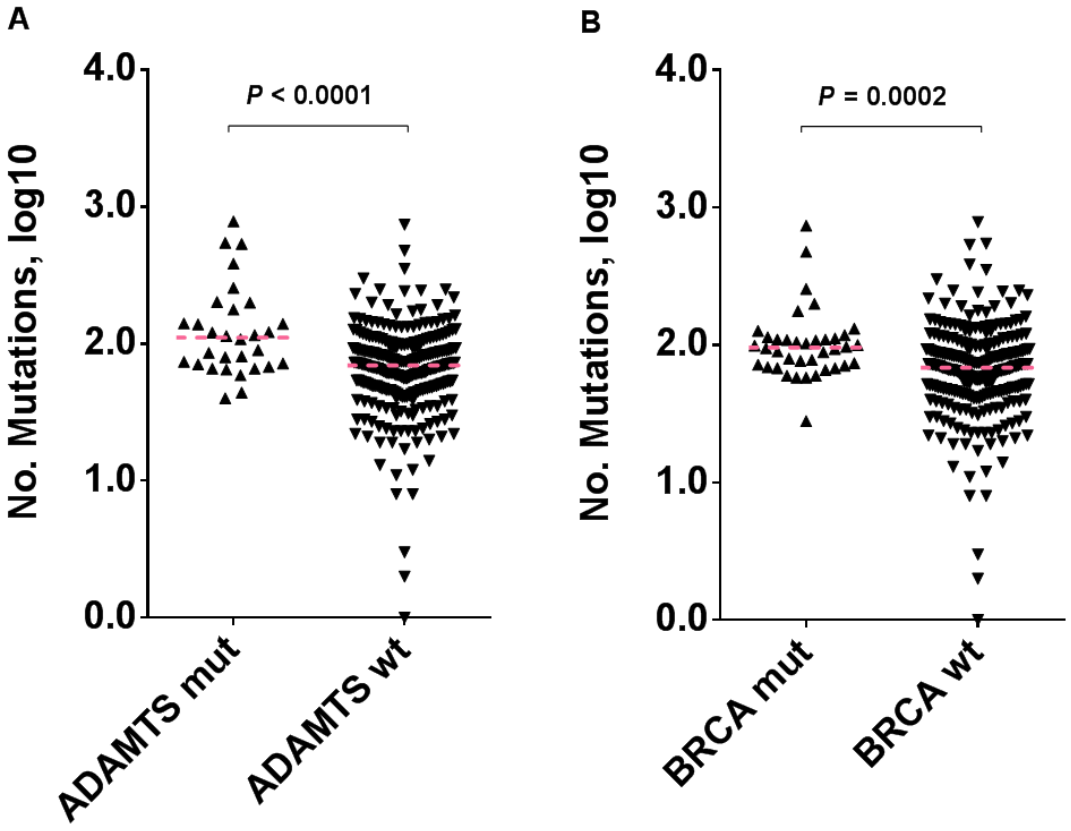
**eFigure 14. Distribution of protein alterations encoded in the *ADAMTS* genes in the TCGA validation cohort**




(**A**, **B**) Positional distribution of somatic mutations across ADAMTS16 (**A**) and ADAMTSL1 (**B**) proteins. Somatic mutations in additional ADAMTS family members were mapped onto ADAMTS16 protein, on the basis of sequence alignment. The protease domain, ancillary domain, cysteine-rich domain, thrombospondin type domain, signal peptide, immunoglobulin domain, ADAM spacer, and PLAC (protease and lacunin) domain are depicted. Mutations from different sample cohorts are indicated by different colors: red color indicates mutations from the TCGA discovery cohort (n =

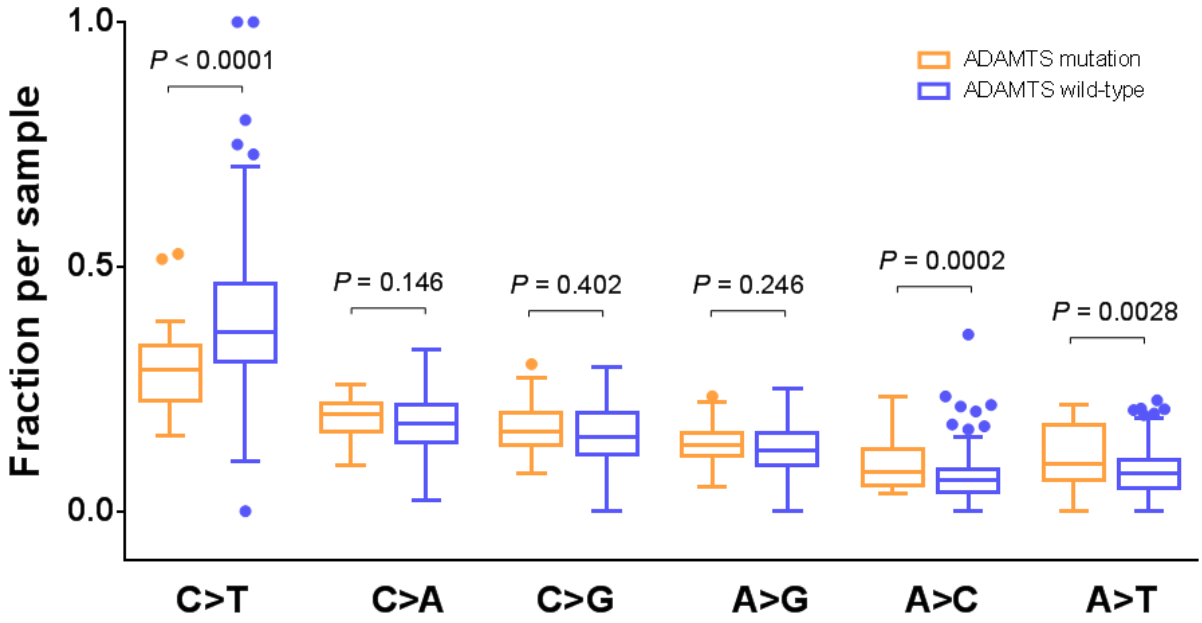
210), and cyan color from the TCGA validation cohort (n = 302). Mutation types are indicated by different symbol shapes: rectangular represents non-silent mutations and circular silent mutations.

**eFigure 15. Comparison of association of *ADAMTS* and *BRCA1/2* mutations with mutation frequency in the TCGA validation cohort**



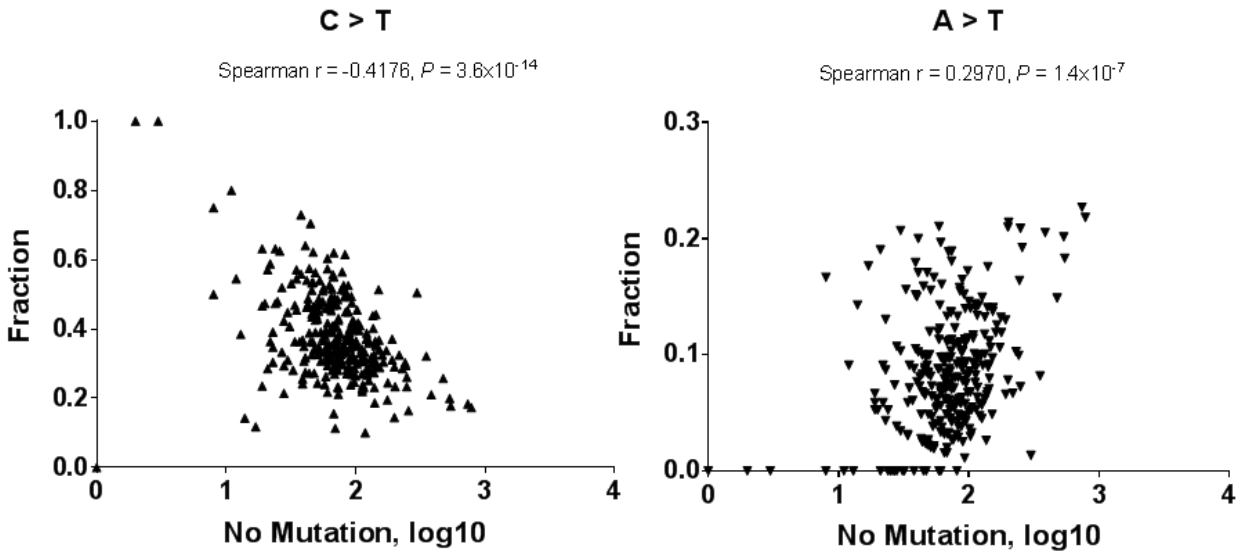

(**A**) The *ADAMTS* mutation carriers had a significantly higher mutation rate than did the *ADAMTS* wild-type cases in the TCGA validation cohort ($P < 0.0001$, Mann-Whitney test). The dashed pink line indicates the median value. The median mutation number per sample was approximately 111 for *ADAMTS*-mutated cases versus 69 for wild-type cases. (B) *BRCA1/2* mutated cases had a significantly higher mutation frequency than *BRCA1/2* wild-type cases ($P = 0.0002$). More significant association of mutation frequency with *ADAMTS* mutations than with *BRCA1/2* mutations is consistent with that in the discovery cohort.

**eFigure 16. Association of *ADAMTS* mutations with mutation spectra in the TCGA validation cohort**



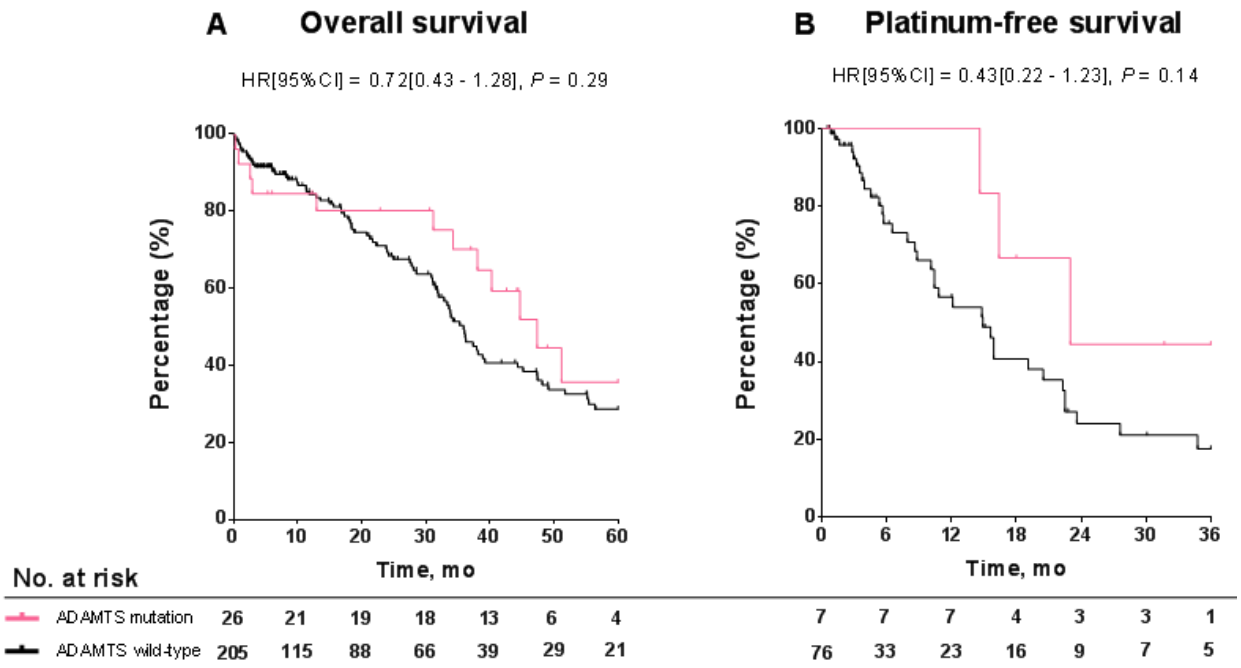

We calculated fractions of single nucleotide substitutions (INDELs were excluded) in the six possible mutation classes (i.e., C>T, C>A, C>G, A>G, A>C and A>T) for each sample. Data are represented as box-and-whiskers (Tukey) plots. The central line of each box is the median and edges are the 25$^{th}$ and 75$^{th}$ percentile. The outliers outside the Tukey whiskers are plotted individually as dots and excluded from the statistical test. The Mann-Whitney test was performed on these mutation categories in patients stratified according to *ADAMTS* mutations. The *ADAMTS* mutated samples had a significantly lower percentage of C>T transition ($P < 0.0001$), but a significantly higher percentage of A>T transversion ($P = 0.0028$) than the *ADAMTS* wild-type samples, consistent with the findings from the discovery cohort.

**eFigure 17. Correlation of mutation frequency with C>T or A>T fractions in the TCGA validation Cohort**



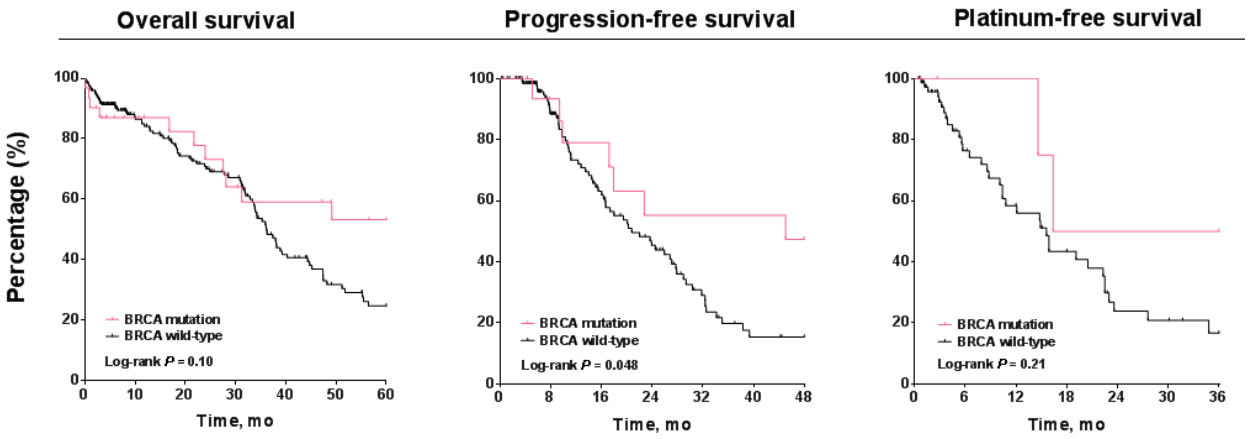

The mutation frequency (log10 scale) was negatively correlated with C>T transition (Spearman r = -0.4176, $P = 3.6 \times 10^{-14}$) but positively correlated with A>T transversion (Spearman r = 0.2970, $P = 1.4 \times 10^{-7}$), consistent with the findings from the discovery cohort.

**eFigure 18. Association of *ADAMTS* Mutations with overall survival and platinum-free survival in the validation cohort**



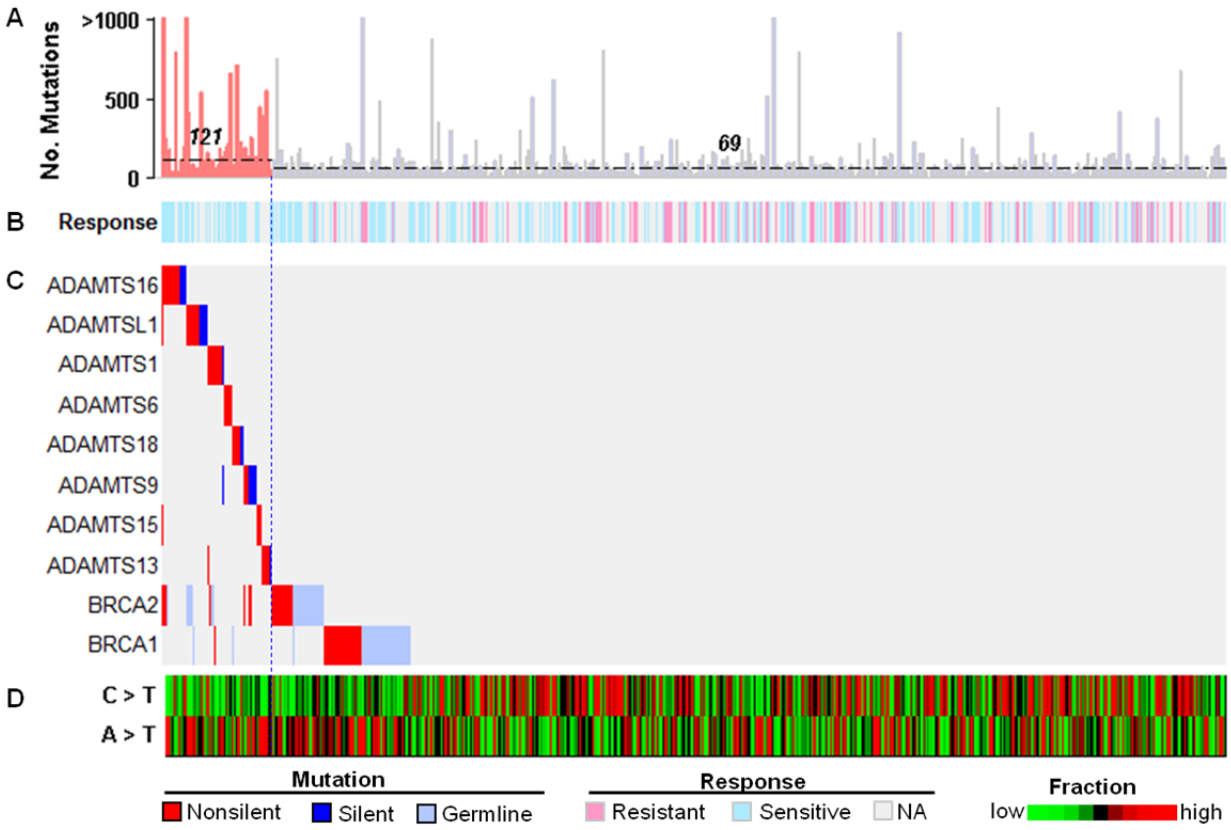

*ADAMTS* mutations exhibited a discernible trend toward better OS and a longer platinum-free interval, however, the statistical significance was compromised likely because of the relatively short clinical follow-ups and the smaller size of analyzed samples (**eTable 5 in the Supplement**). The median OS follow-up in the validation was less than half of that in the discovery cohort and only 83 cases were used in the platinum-free survival analysis.

**eFigure 19. Association of *BRCA1/2* mutations with overall survival, progression-free survival, and platinum-free survival in the validation cohort**




As a positive control, we performed Kaplan-Meier analysis on those known outcome predictors such as *BRCA1/2* mutation status. Similar to *ADAMTS* mutations (**Figure 4B**), *BRCA1/2* mutations were significantly correlated with PFS (Log-rank $P = 0.048$), but not with OS (Log-rank $P = 0.10$) or platinum-free survival (Log-rank $P = 0.21$) in the validation cohort, likely because of the relatively short OS follow-ups and the smaller size of analyzed samples in the platinum-free survival analysis (**eTable 5 in the Supplement**).

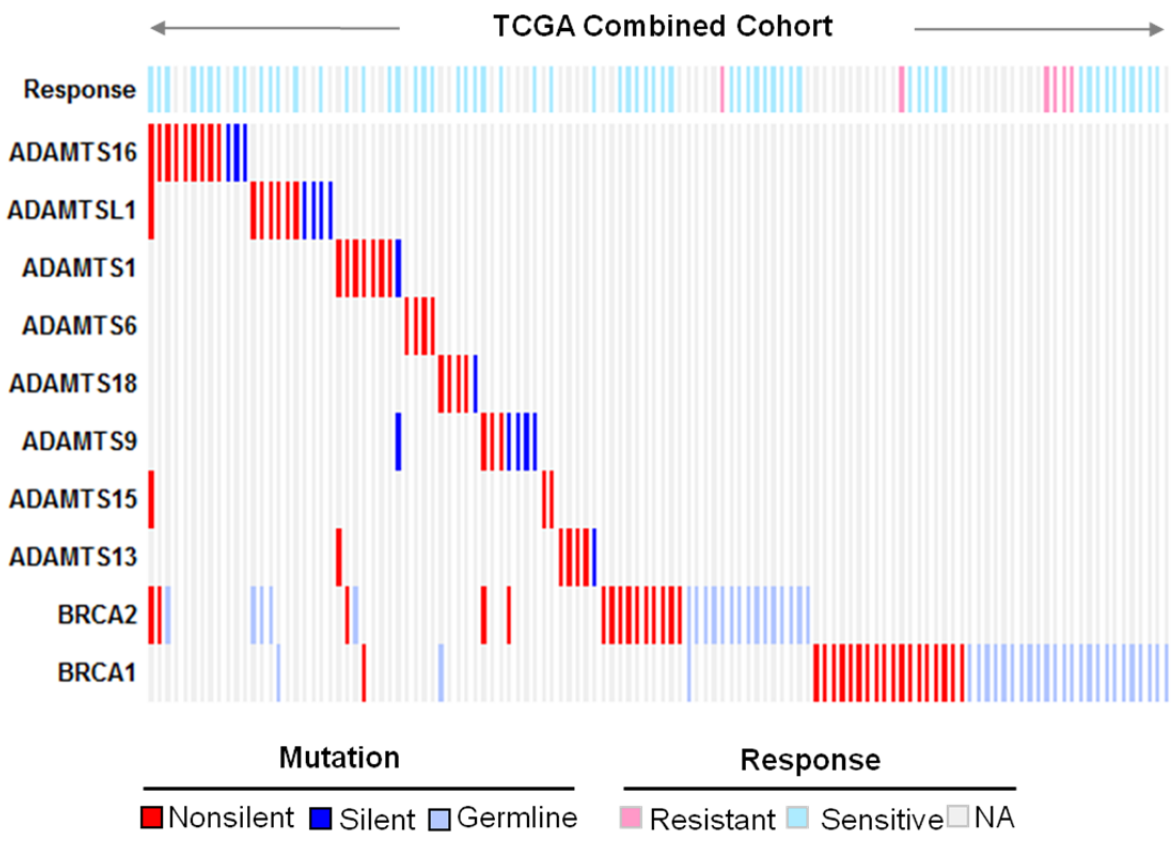
**eFigure 20. *ADAMTS* mutation and its association with chemotherapy response status and mutation spectra in the TCGA combined cohort**




(**A**) Genome-wide mutation frequencies in terms of number of mutations (vertical axis) detected for each tumor (horizontal axis) within each patient group stratified according to *ADAMTS* mutation status. The median mutations for *ADAMTS* mutated and wild-type groups were indicated by the dashed line (121 vs 69, $P < 0.0001$, Mann-Whitney test). (**B**) Response status to chemotherapy (either sensitive or resistant) for each tumor in the same order as in (A): light blue bars indicate sensitive and pink resistant. (**C**) *ADAMTS* and *BRCA1/2* mutations that were detected in the 512 TCGA patients with ovarian cancer. For each gene (row) indicated, tumors (columns) with mutations are labeled in red (nonsilent mutations), dark blue (silent mutations), or light blue (germline mutations)

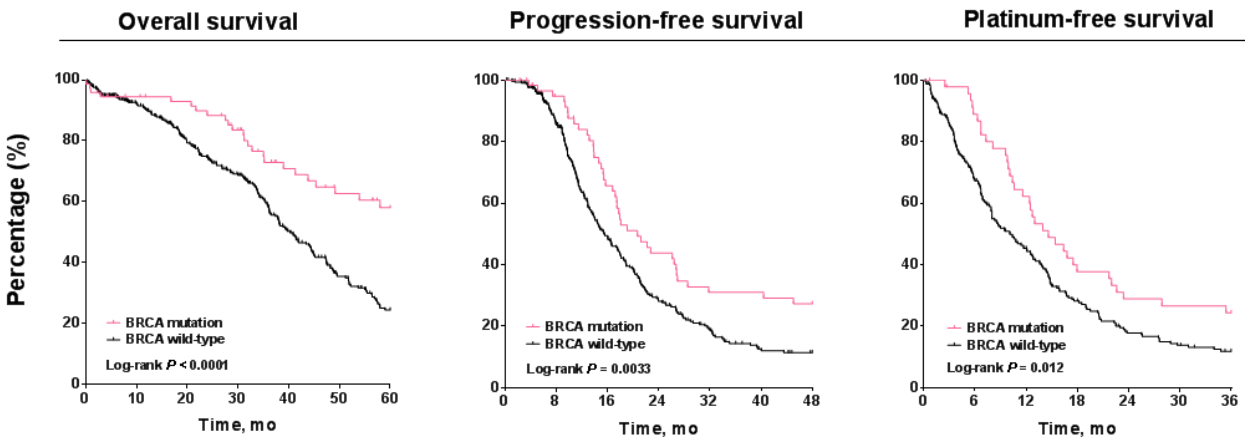
bars. Distribution of protein alterations encoded in the *ADAMTS* genes in this validation cohort is detailed in **eFigure 14 in the Supplement**. (**D**) Heat map of C>T and A>T fractions across the tumors where blue indicates low fraction and red high fraction. The *ADAMTS* mutated samples had a significantly lower percentage of C>T transition ($P < 0.0001$, Mann-Whitney test), but a significantly higher fraction of A>T transversion ($P = 0.0003$) than the *ADAMTS* wild-type samples.

**eFigure 21. *ADAMTS* and *BRCA1/2* mutations in the TCGA combined cohort**



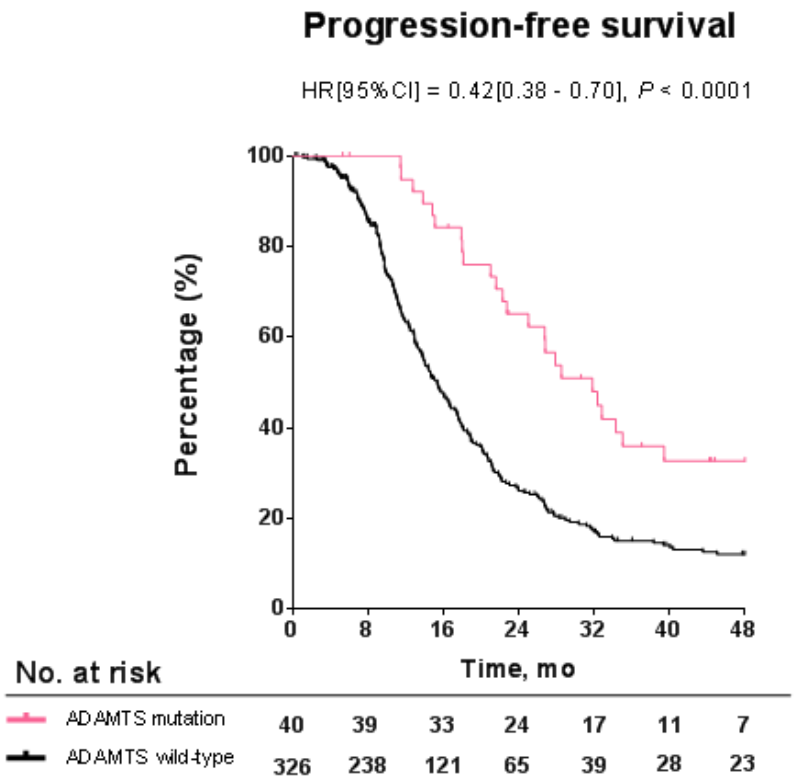

This plot shows *ADAMTS* and *BRCA1/2* mutations that were detected in the TCGA combined cohort that comprised 512 patients with ovarian cancer. For each gene (row) indicated, tumors (columns) with mutations are labeled in red (nonsilent mutations), dark blue (silent mutations), or light blue (germline mutations) bars. Note that only somatic mutation data were available for the second batch. In this combined cohort, 53 (~10.4%) OvCa cases exhibited *ADAMTS* mutations and 80 (~15.6%) had *BRCA1/2* mutations; these two families' mutations were not correlated with each other ($P$ = 0.07, Fisher's exact test).

**eFigure 22. Association of BRCA mutations with clinical outcome in the TCGA combined cohort (n = 512)**



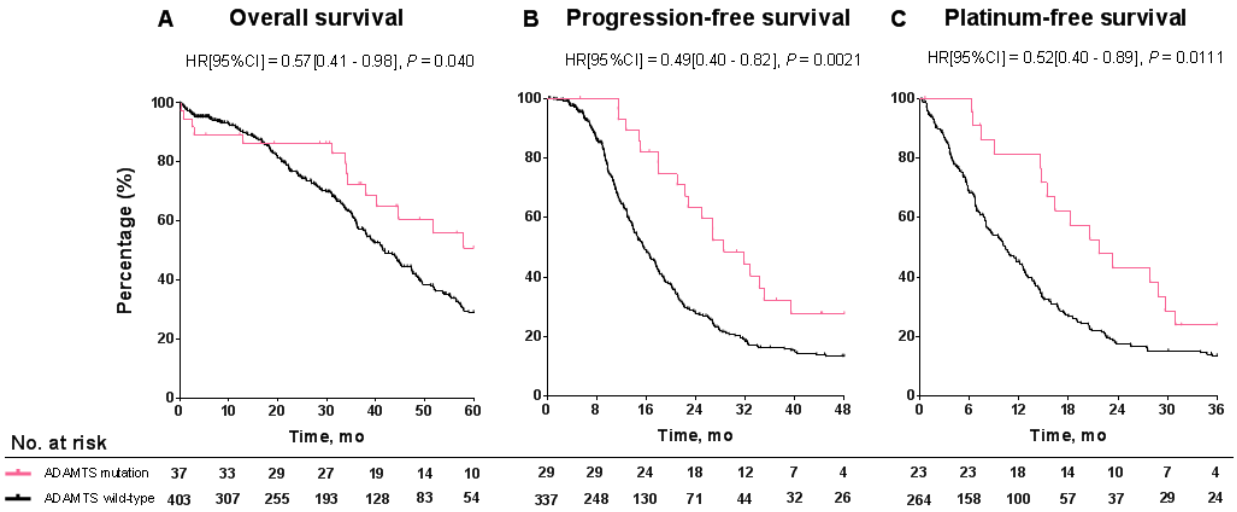

Estimates of clinical outcome (in terms of overall survival and progression-free survival), and chemotherapy response (i.e., platinum-free interval) were performed among patients that were stratified on the basis of *BRCA* (including *BRCA1* and *BRCA2*) mutations. Subgroups were compared with the use of the log-rank test. In contrast to the validation cohort, the TCGA combined cohort had longer clinical follow-ups that were comparable to those in the discovery cohort (**eTable 5 in the Supplement**). With increased clinical follow-ups and more samples included in the platinum-free survival analysis, *BRCA1/2* mutations, as anticipated, exhibited significant correlation with overall survival ($P < 0.0001$), progression-free survival ($P = 0.0033$) and platinum-free survival ($P = 0.012$) in this combined cohort, consistent with previous reports.[1] For both overall survival and progression-free survival, the percentage probability is plotted versus the time since diagnosis in months. For platinum-free survival, the percentage probability is plotted versus the time since the end of adjuvant therapy.

**eFigure 23. Association of *ADAMTS* mutations with progression-free survival in the TCGA combined cohort**




Patients with *ADAMTS* mutations had significantly better progression-free survival than those without in the TCGA combined cohort (median, 31.8 months vs. 15.3 months, $P < 0.0001$, hazard ratio (HR), 0.42, 95% confidence interval (CI), 0.38 to 0.70).

**eFigure 24. Association of *ADAMTS* nonsilent mutations with overall survival, progression-free survival, and platinum-free survival in the TCGA combined cohort**




In this analysis, we excluded the cases with ADAMTS silent mutations from the ADAMTS mutation group. Consistently, patients with *ADAMTS* nonsilent mutations exhibited significant association with longer OS, PFS and platinum-free survival.

**eTable 1. Chemotherapy response status and clinicopathologic characteristics of OvCa patients in different TCGA cohorts.***

| | Discovery Cohort[a] (n = 210) | Validation Cohort[b] (n=302) | Combined Cohort[c] (n=512) |
|---|---|---|---|
| **Chemotherapy Response†** | | | |
| Resistant | 69 (33) | 15 (28) | 84 (32) |
| Sensitive | 141 (67) | 38 (72) | 179 (68) |
| Unknown | 0 | 249 | 249 |
| **Age** | | | |
| Mean, years [SD] | 60.3 [11.3] | 59.8 [11.6] | 60.0 [11.5] |
| Range | 30.5 – 87.5 | 27.2-84.7 | 27.2-87.5 |
| **FIGO Stage‡** | | | |
| II | 7 (3) | 15 (6) | 22 (5) |
| III / IV | 203 (97) | 219 (94) | 422 (95) |
| Unknown | 0 | 68 | 68 |
| **WHO Grade** | | | |
| 2 | 16 (8) | 34 (15) | 50 (11) |
| 3 | 189 (92) | 196 (85) | 385 (89) |
| Unknown | 5 | 72 | 77 |
| **Residual tumor size, mm§** | | | |
| 0 | 42 (22) | 40 (20) | 82 (21) |
| 1 - 20 | 113 (60) | 118 (58) | 231 (59) |
| > 20 | 34 (18) | 45 (22) | 79 (20) |
| Unknown | 21 | 99 | 120 |

Abbreviations: TCGA, The Cancer Genome Atlas; SD, standard deviation; FIGO, International Federation of Gynecology and Obstetrics; WHO, World Health Organization.

* Values are reported as No. (%). Missing values are excluded from the percentage calculation and statistical test.

[a] Among the first set of whole-exome sequencing data of total 358 OvCa patients downloaded on January 10, 2012, 210 patients that had an explicitly defined platinum-based chemotherapy response status (resistant or sensitive) were used as the discovery cohort in this study.

[b] The validation cohort included the 148 patients from the first batch that had no explicitly defined platinum-based chemotherapy response status and the 154 cases from the second batch.

[c] Whole exome sequencing data of total 512 OvCa patients were obtained and downloaded from the TCGA data portal..

† Platinum status was defined as resistant if the platinum-free interval was less than 6 months and the patient had experienced progression or recurrence. Platinum status was defined as sensitive if the platinum-free interval was 6 months or more, there was no evidence of progression or recurrence, and the follow-up interval was at least 6 months from the date of the last primary platinum treatment.

‡ Cases were staged according to the 1988 FIGO staging system.

§ Residual tumor size was defined as the size of residual disease at the conclusion of the primary surgical procedure. Patients with no macroscopic disease were labeled as 0 mm. Patients were divided into three groups on the basis of this parameter, patients with no macroscopic disease (0 mm), patients with residual tumor size between 1 and 20 mm (1 – 20), and patients with residual tumor size of greater than 20 mm (> 20).

**eTable 2. Clinicopathologic characteristics of OvCa patients in the First and Second Batches.***

| | **Combined cohort** (n=512) | **First Batch** (n=358) | **Second Batch** (n=154) | ***P*†** |
|---|---|---|---|---|
| **Age** | | | | |
| Mean, years [SD] | 60.0 [11.5] | 60.3 [11.4] | 58.9 [11.6] | |
| Range | 27.2-87.5 | 27.2 – 87.5 | 39.9 – 84.7 | 0.232** |
| **FIGO Stage§** | | | | |
| II | 22 (5) | 16 (4) | 6 (7) | |
| III / IV | 422 (95) | 341 (96) | 81 (93) | 0.406¶ |
| Unknown | 68 | 1 | 67 | |
| **WHO Grade** | | | | |
| 2 | 50 (11) | 30 (9) | 20 (24) | |
| 3 | 385 (89) | 320 (91) | 65 (76) | 0.0004¶ |
| Unknown | 77 | 8 | 69 | |
| **Residual tumor size, mm‖** | | | | |
| 0 | 82 (21) | 68 (22) | 14 (18) | |
| 1 - 20 | 231 (59) | 187 (59) | 44 (58) | |
| > 20 | 79 (20) | 61 (19) | 18 (24) | 0.364¶# |
| Unknown | 120 | 42 | 78 | |
| **Vital status** | | | | |
| Living | 205 (46) | 152 (43) | 53 (61) | |
| Deceased | 236 (54) | 202 (57) | 34 (39) | 0.0028¶ |
| Unknown | 71 | 4 | 67 | |

Abbreviations: TCGA, The Cancer Genome Atlas; SD, standard deviation; FIGO, the International Federation of Gynecology and Obstetrics; WHO, World Health Organization.

* Values are reported as No. (%). Missing values are excluded from the percentage calculation and statistical test.

† Statistical test (*P* value) between OvCa patients in the First and Second Batches.

§ Cases were staged according to the 1988 FIGO staging system.

‖ Residual tumor size was defined as the size of residual disease at the conclusion of the primary surgical procedure. Patients with no macroscopic disease were labeled as 0 mm. Patients were divided into three groups on the basis of this parameter, patients with no macroscopic disease (0 mm), patients with residual tumor size between 1 and 20 mm (1 – 20), and patients with residual tumor size of greater than 20 mm (> 20).

¶ Fisher's exact test.

# tumors with no macroscopic disease versus tumors with macroscopic disease.

** Mann-Whitney test.

**eTable 3. Clinicopathologic characteristics of OvCa patients with or without chemotherapy response data in the TCGA validation cohort.***

| | **Validation cohort** (n=302) | **with Chemo data** (n=53) | **without Chemo data** (n=249) | ***P*†** |
|---|---|---|---|---|
| **Age** | | | | |
| Mean, years [SD] | 59.8 [11.6] | 57.7 [11.3] | 60.4 [11.6] | |
| Range | 27.2-84.7 | 40.4 – 84.7 | 27.2 – 83.8 | 0.10** |
| **FIGO Stage§** | | | | |
| II | 15 (6) | 5 (9) | 10 (6) | |
| III / IV | 219 (94) | 48 (91) | 171 (94) | 0.34¶ |
| Unknown | 68 | 0 | 68 | |
| **WHO Grade** | | | | |
| 2 | 34 (15) | 15 (29) | 19 (11) | |
| 3 | 196 (85) | 37 (71) | 159 (89) | 0.003¶ |
| Unknown | 72 | 1 | 71 | |
| **Residual tumor size, mm‖** | | | | |
| 0 | 40 (20) | 9 (19) | 31 (20) | |
| 1 - 20 | 118 (58) | 27 (58) | 91 (58) | |
| > 20 | 45 (22) | 11 (23) | 34 (22) | 1.00¶# |
| Unknown | 99 | 6 | 93 | |

Abbreviations: TCGA, The Cancer Genome Atlas; SD, standard deviation; FIGO, the International Federation of Gynecology and Obstetrics; WHO, World Health Organization.

* Values are reported as No. (%). Missing values are excluded from the percentage calculation and statistical test.

† Statistical test (*P* value) between OvCa patients with and without chemotherapy response data.

§ Cases were staged according to the 1988 FIGO staging system.

‖ Residual tumor size was defined as the size of residual disease at the conclusion of the primary surgical procedure. Patients with no macroscopic disease were labeled as 0 mm. Patients were divided into three groups on the basis of this parameter, patients with no macroscopic disease (0 mm), patients with residual tumor size between 1 and 20 mm (1 – 20), and patients with residual tumor size of greater than 20 mm (> 20).

¶ Fisher's exact test.

# tumors with no macroscopic disease versus tumors with macroscopic disease.

** Mann-Whitney test.

**eTable 4. The 2,118 responder-related genes and their mutation data in the chemosensitive and chemoresistant samples**

| Genes | Total mutations | No. Res | No. Sens |
|---|---|---|---|
| ADAMTS16 | 9 | 0 | 9 |
| BRCA2 | 9 | 0 | 9 |
| MAGEC1 | 8 | 0 | 8 |
| VPS11 | 8 | 0 | 8 |
| ZNFX1 | 8 | 0 | 8 |
| CENPF | 7 | 0 | 7 |
| DMBT1 | 7 | 0 | 7 |
| DOCK2 | 7 | 0 | 7 |
| DSCAM | 7 | 0 | 7 |
| ITK | 7 | 0 | 7 |
| KNTC1 | 7 | 0 | 7 |
| MLLT4 | 7 | 0 | 7 |
| NAV3 | 7 | 0 | 7 |
| NRAP | 7 | 0 | 7 |
| NRXN2 | 7 | 0 | 7 |
| OR2AG1 | 7 | 0 | 7 |
| USP4 | 7 | 0 | 7 |
| YSK4 | 7 | 0 | 7 |
| ZNF236 | 7 | 0 | 7 |
| ZNF521 | 7 | 0 | 7 |
| ABCA4 | 6 | 0 | 6 |
| ADAMTSL1 | 6 | 0 | 6 |
| ALMS1 | 6 | 0 | 6 |
| CACNA1E | 6 | 0 | 6 |
| CCDC88C | 6 | 0 | 6 |
| CHD9 | 6 | 0 | 6 |
| COL12A1 | 6 | 0 | 6 |
| CPAMD8 | 6 | 0 | 6 |
| CREB3L2 | 6 | 0 | 6 |
| FCRL1 | 6 | 0 | 6 |
| GAB2 | 6 | 0 | 6 |
| GPRIN3 | 6 | 0 | 6 |
| ITSN1 | 6 | 0 | 6 |
| KIAA1797 | 6 | 0 | 6 |
| MAGEB6 | 6 | 0 | 6 |
| MAPKBP1 | 6 | 0 | 6 |
| MAST4 | 6 | 0 | 6 |

| | | | |
|---|---|---|---|
| MED13L | 6 | 0 | 6 |
| MYLK | 6 | 0 | 6 |
| NCKAP1L | 6 | 0 | 6 |
| NFKB1 | 6 | 0 | 6 |
| NLRP3 | 6 | 0 | 6 |
| PIGG | 6 | 0 | 6 |
| PLCH1 | 6 | 0 | 6 |
| SEC23A | 6 | 0 | 6 |
| SNTG1 | 6 | 0 | 6 |
| TNPO3 | 6 | 0 | 6 |
| TNS1 | 6 | 0 | 6 |
| TUBB1 | 6 | 0 | 6 |
| UGGT2 | 6 | 0 | 6 |
| UGT1A9 | 6 | 0 | 6 |
| UHRF1BP1 | 6 | 0 | 6 |
| AARS2 | 5 | 0 | 5 |
| ACIN1 | 5 | 0 | 5 |
| AFF2 | 5 | 0 | 5 |
| AMBN | 5 | 0 | 5 |
| AP3B2 | 5 | 0 | 5 |
| C6orf170 | 5 | 0 | 5 |
| CBLL1 | 5 | 0 | 5 |
| CILP | 5 | 0 | 5 |
| COL3A1 | 5 | 0 | 5 |
| DACH2 | 5 | 0 | 5 |
| EDC4 | 5 | 0 | 5 |
| ELMO2 | 5 | 0 | 5 |
| EPHX1 | 5 | 0 | 5 |
| EVL | 5 | 0 | 5 |
| FANCE | 5 | 0 | 5 |
| FBLN7 | 5 | 0 | 5 |
| FBXO18 | 5 | 0 | 5 |
| FGD1 | 5 | 0 | 5 |
| FNTB | 5 | 0 | 5 |
| GPR179 | 5 | 0 | 5 |
| GRIP1 | 5 | 0 | 5 |
| HSD17B13 | 5 | 0 | 5 |
| IKBKAP | 5 | 0 | 5 |
| INSC | 5 | 0 | 5 |
| INVS | 5 | 0 | 5 |
| ITPR3 | 5 | 0 | 5 |

| | | | |
|---|---|---|---|
| KCNQ5 | 5 | 0 | 5 |
| KDM4C | 5 | 0 | 5 |
| KIAA0319L | 5 | 0 | 5 |
| KIAA0406 | 5 | 0 | 5 |
| KIRREL2 | 5 | 0 | 5 |
| KIT | 5 | 0 | 5 |
| KRT82 | 5 | 0 | 5 |
| KRT9 | 5 | 0 | 5 |
| LILRB4 | 5 | 0 | 5 |
| LTA | 5 | 0 | 5 |
| MAP3K15 | 5 | 0 | 5 |
| MIB1 | 5 | 0 | 5 |
| MYO10 | 5 | 0 | 5 |
| NPHP4 | 5 | 0 | 5 |
| OR2T3 | 5 | 0 | 5 |
| OSBP | 5 | 0 | 5 |
| PALM2-AKAP2 | 5 | 0 | 5 |
| PEX5 | 5 | 0 | 5 |
| PHC1 | 5 | 0 | 5 |
| PLEKHG1 | 5 | 0 | 5 |
| POLR3B | 5 | 0 | 5 |
| PRKD2 | 5 | 0 | 5 |
| PTPRH | 5 | 0 | 5 |
| RAP1GAP | 5 | 0 | 5 |
| RAPGEF1 | 5 | 0 | 5 |
| RGS3 | 5 | 0 | 5 |
| RHBG | 5 | 0 | 5 |
| RICTOR | 5 | 0 | 5 |
| SLC12A2 | 5 | 0 | 5 |
| SNX27 | 5 | 0 | 5 |
| SPANXN3 | 5 | 0 | 5 |
| TMPO | 5 | 0 | 5 |
| TMPRSS6 | 5 | 0 | 5 |
| TRIM23 | 5 | 0 | 5 |
| TRPC1 | 5 | 0 | 5 |
| UNC13C | 5 | 0 | 5 |
| ZNF132 | 5 | 0 | 5 |
| ZNF212 | 5 | 0 | 5 |
| ZNF333 | 5 | 0 | 5 |
| ZNF699 | 5 | 0 | 5 |
| ZNF792 | 5 | 0 | 5 |

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|---|---|---|---|
| AASDH | 4 | 0 | 4 |
| ACAD11 | 4 | 0 | 4 |
| ACCN1 | 4 | 0 | 4 |
| ACSM4 | 4 | 0 | 4 |
| AKR1C1 | 4 | 0 | 4 |
| ALDH1L1 | 4 | 0 | 4 |
| ALS2 | 4 | 0 | 4 |
| ANGPT1 | 4 | 0 | 4 |
| ANGPT4 | 4 | 0 | 4 |
| APAF1 | 4 | 0 | 4 |
| APBB1 | 4 | 0 | 4 |
| ARAP2 | 4 | 0 | 4 |
| ARHGEF17 | 4 | 0 | 4 |
| ARMC2 | 4 | 0 | 4 |
| ARNTL2 | 4 | 0 | 4 |
| ASNA1 | 4 | 0 | 4 |
| ATP2A3 | 4 | 0 | 4 |
| BCOR | 4 | 0 | 4 |
| BDH1 | 4 | 0 | 4 |
| BMP2K | 4 | 0 | 4 |
| BPIL3 | 4 | 0 | 4 |
| BRSK1 | 4 | 0 | 4 |
| C15orf40 | 4 | 0 | 4 |
| C18orf34 | 4 | 0 | 4 |
| C1orf125 | 4 | 0 | 4 |
| C21orf63 | 4 | 0 | 4 |
| CAPN6 | 4 | 0 | 4 |
| CAPN7 | 4 | 0 | 4 |
| CCDC46 | 4 | 0 | 4 |
| CCDC64 | 4 | 0 | 4 |
| CDH6 | 4 | 0 | 4 |
| CDRT4 | 4 | 0 | 4 |
| CHI3L1 | 4 | 0 | 4 |
| CKAP5 | 4 | 0 | 4 |
| CLCA1 | 4 | 0 | 4 |
| CLEC18B | 4 | 0 | 4 |
| CLTC | 4 | 0 | 4 |
| CNTNAP2 | 4 | 0 | 4 |
| CPEB1 | 4 | 0 | 4 |
| CPT1A | 4 | 0 | 4 |
| CPZ | 4 | 0 | 4 |

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|---|---|---|---|
| CREG2 | 4 | 0 | 4 |
| CSE1L | 4 | 0 | 4 |
| CUEDC1 | 4 | 0 | 4 |
| CUX2 | 4 | 0 | 4 |
| CYFIP2 | 4 | 0 | 4 |
| CYP2C9 | 4 | 0 | 4 |
| DCST2 | 4 | 0 | 4 |
| DLC1 | 4 | 0 | 4 |
| DNAH7 | 4 | 0 | 4 |
| DOC2A | 4 | 0 | 4 |
| DPP10 | 4 | 0 | 4 |
| DUSP10 | 4 | 0 | 4 |
| EPHB4 | 4 | 0 | 4 |
| ETV1 | 4 | 0 | 4 |
| EXTL1 | 4 | 0 | 4 |
| FAM104B | 4 | 0 | 4 |
| FAM187B | 4 | 0 | 4 |
| FAM59A | 4 | 0 | 4 |
| FAM83B | 4 | 0 | 4 |
| FAM83D | 4 | 0 | 4 |
| FAP | 4 | 0 | 4 |
| FBXO28 | 4 | 0 | 4 |
| FGF10 | 4 | 0 | 4 |
| FIP1L1 | 4 | 0 | 4 |
| FLT1 | 4 | 0 | 4 |
| FMO2 | 4 | 0 | 4 |
| FOXM1 | 4 | 0 | 4 |
| GAPDHS | 4 | 0 | 4 |
| GCNT2 | 4 | 0 | 4 |
| GGCT | 4 | 0 | 4 |
| GGT1 | 4 | 0 | 4 |
| GPATCH3 | 4 | 0 | 4 |
| GPR81 | 4 | 0 | 4 |
| GRID2 | 4 | 0 | 4 |
| GRIPAP1 | 4 | 0 | 4 |
| H2AFY2 | 4 | 0 | 4 |
| HLA-B | 4 | 0 | 4 |
| IFRD2 | 4 | 0 | 4 |
| IL18R1 | 4 | 0 | 4 |
| IL7R | 4 | 0 | 4 |
| ITGAL | 4 | 0 | 4 |

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|---|---|---|---|
| JRK | 4 | 0 | 4 |
| KDM2A | 4 | 0 | 4 |
| KDM2B | 4 | 0 | 4 |
| KIAA0802 | 4 | 0 | 4 |
| KIAA1310 | 4 | 0 | 4 |
| KIAA1751 | 4 | 0 | 4 |
| KIAA1919 | 4 | 0 | 4 |
| KIF6 | 4 | 0 | 4 |
| KIRREL3 | 4 | 0 | 4 |
| KRT6A | 4 | 0 | 4 |
| LACE1 | 4 | 0 | 4 |
| LAIR1 | 4 | 0 | 4 |
| LBR | 4 | 0 | 4 |
| LPAR4 | 4 | 0 | 4 |
| LRRC36 | 4 | 0 | 4 |
| LRRC50 | 4 | 0 | 4 |
| LRRFIP1 | 4 | 0 | 4 |
| LTF | 4 | 0 | 4 |
| MACC1 | 4 | 0 | 4 |
| MAGI2 | 4 | 0 | 4 |
| MAP1A | 4 | 0 | 4 |
| MAP3K2 | 4 | 0 | 4 |
| MASP1 | 4 | 0 | 4 |
| MC5R | 4 | 0 | 4 |
| MCM2 | 4 | 0 | 4 |
| MEP1B | 4 | 0 | 4 |
| MICALCL | 4 | 0 | 4 |
| MKL1 | 4 | 0 | 4 |
| MOSPD3 | 4 | 0 | 4 |
| MX1 | 4 | 0 | 4 |
| MYH8 | 4 | 0 | 4 |
| MYOM1 | 4 | 0 | 4 |
| MYT1 | 4 | 0 | 4 |
| NCKAP5 | 4 | 0 | 4 |
| NECAP1 | 4 | 0 | 4 |
| NES | 4 | 0 | 4 |
| NOL6 | 4 | 0 | 4 |
| NPHS1 | 4 | 0 | 4 |
| OR1K1 | 4 | 0 | 4 |
| OR5D16 | 4 | 0 | 4 |
| OR8K1 | 4 | 0 | 4 |

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|---|---|---|---|
| OTOF | 4 | 0 | 4 |
| PARD3 | 4 | 0 | 4 |
| PARP10 | 4 | 0 | 4 |
| PAX8 | 4 | 0 | 4 |
| PCDHB16 | 4 | 0 | 4 |
| PIK3AP1 | 4 | 0 | 4 |
| PLXNB2 | 4 | 0 | 4 |
| PNLIPRP2 | 4 | 0 | 4 |
| POGK | 4 | 0 | 4 |
| POLR2A | 4 | 0 | 4 |
| PPFIBP2 | 4 | 0 | 4 |
| PPIL2 | 4 | 0 | 4 |
| PRKAG1 | 4 | 0 | 4 |
| PRKD3 | 4 | 0 | 4 |
| PTPRA | 4 | 0 | 4 |
| RAB11FIP1 | 4 | 0 | 4 |
| RBM19 | 4 | 0 | 4 |
| RGL3 | 4 | 0 | 4 |
| RING1 | 4 | 0 | 4 |
| RXFP2 | 4 | 0 | 4 |
| RYK | 4 | 0 | 4 |
| SEC14L1 | 4 | 0 | 4 |
| SEL1L | 4 | 0 | 4 |
| SEMA4B | 4 | 0 | 4 |
| SGCD | 4 | 0 | 4 |
| SIK3 | 4 | 0 | 4 |
| SLC47A2 | 4 | 0 | 4 |
| SLC4A9 | 4 | 0 | 4 |
| SLC6A3 | 4 | 0 | 4 |
| SLFN5 | 4 | 0 | 4 |
| SNAP91 | 4 | 0 | 4 |
| SNCAIP | 4 | 0 | 4 |
| SNX19 | 4 | 0 | 4 |
| SPATA21 | 4 | 0 | 4 |
| ST6GALNAC3 | 4 | 0 | 4 |
| STRBP | 4 | 0 | 4 |
| SUPT5H | 4 | 0 | 4 |
| SYNM | 4 | 0 | 4 |
| TACR1 | 4 | 0 | 4 |
| TBC1D2 | 4 | 0 | 4 |
| TGM1 | 4 | 0 | 4 |

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|---|---|---|---|
| THADA | 4 | 0 | 4 |
| TMEM132A | 4 | 0 | 4 |
| TMEM67 | 4 | 0 | 4 |
| TNC | 4 | 0 | 4 |
| TRAK2 | 4 | 0 | 4 |
| TRAPPC10 | 4 | 0 | 4 |
| TTC15 | 4 | 0 | 4 |
| TTK | 4 | 0 | 4 |
| TUBB8 | 4 | 0 | 4 |
| TXNDC16 | 4 | 0 | 4 |
| UNC13B | 4 | 0 | 4 |
| USP2 | 4 | 0 | 4 |
| VPS33A | 4 | 0 | 4 |
| WDHD1 | 4 | 0 | 4 |
| WDR35 | 4 | 0 | 4 |
| WDR49 | 4 | 0 | 4 |
| WWC1 | 4 | 0 | 4 |
| XRN2 | 4 | 0 | 4 |
| ZC3H11A | 4 | 0 | 4 |
| ZDHHC23 | 4 | 0 | 4 |
| ZKSCAN4 | 4 | 0 | 4 |
| ZNF211 | 4 | 0 | 4 |
| ZNF398 | 4 | 0 | 4 |
| ZNF407 | 4 | 0 | 4 |
| ZNF43 | 4 | 0 | 4 |
| ZNF7 | 4 | 0 | 4 |
| ZNF718 | 4 | 0 | 4 |
| ZNF772 | 4 | 0 | 4 |
| ZNF81 | 4 | 0 | 4 |
| ZNF816A | 4 | 0 | 4 |
| ABCC11 | 3 | 0 | 3 |
| ABCF3 | 3 | 0 | 3 |
| ACADM | 3 | 0 | 3 |
| ACADSB | 3 | 0 | 3 |
| ADAM29 | 3 | 0 | 3 |
| ADCY4 | 3 | 0 | 3 |
| ADRA2B | 3 | 0 | 3 |
| AIFM1 | 3 | 0 | 3 |
| AIM2 | 3 | 0 | 3 |
| AKNAD1 | 3 | 0 | 3 |
| AKR1C4 | 3 | 0 | 3 |

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|---|---|---|---|
| AKT1 | 3 | 0 | 3 |
| ALDH1A1 | 3 | 0 | 3 |
| ALOX12 | 3 | 0 | 3 |
| ALS2CL | 3 | 0 | 3 |
| AMPH | 3 | 0 | 3 |
| ANGPTL5 | 3 | 0 | 3 |
| ANO10 | 3 | 0 | 3 |
| ANO3 | 3 | 0 | 3 |
| ANXA7 | 3 | 0 | 3 |
| ARHGEF10 | 3 | 0 | 3 |
| ARHGEF5 | 3 | 0 | 3 |
| ARID1A | 3 | 0 | 3 |
| ASB11 | 3 | 0 | 3 |
| ASTL | 3 | 0 | 3 |
| ATAD5 | 3 | 0 | 3 |
| ATP11A | 3 | 0 | 3 |
| ATXN3 | 3 | 0 | 3 |
| ATXN7L2 | 3 | 0 | 3 |
| BANK1 | 3 | 0 | 3 |
| BIRC3 | 3 | 0 | 3 |
| BLZF1 | 3 | 0 | 3 |
| BMX | 3 | 0 | 3 |
| BOLL | 3 | 0 | 3 |
| BPIL1 | 3 | 0 | 3 |
| BST2 | 3 | 0 | 3 |
| BTRC | 3 | 0 | 3 |
| BZRAP1 | 3 | 0 | 3 |
| C10orf111 | 3 | 0 | 3 |
| C10orf140 | 3 | 0 | 3 |
| C10orf84 | 3 | 0 | 3 |
| C12orf42 | 3 | 0 | 3 |
| C16orf73 | 3 | 0 | 3 |
| C1QTNF7 | 3 | 0 | 3 |
| C20orf117 | 3 | 0 | 3 |
| C21orf29 | 3 | 0 | 3 |
| C2orf67 | 3 | 0 | 3 |
| C4orf35 | 3 | 0 | 3 |
| C5orf24 | 3 | 0 | 3 |
| C6 | 3 | 0 | 3 |
| C7orf58 | 3 | 0 | 3 |
| C8orf41 | 3 | 0 | 3 |

| | | | |
|---|---|---|---|
| C9orf135 | 3 | 0 | 3 |
| C9orf3 | 3 | 0 | 3 |
| CACNG3 | 3 | 0 | 3 |
| CASP7 | 3 | 0 | 3 |
| CATSPERG | 3 | 0 | 3 |
| CCDC135 | 3 | 0 | 3 |
| CCDC15 | 3 | 0 | 3 |
| CCDC41 | 3 | 0 | 3 |
| CCDC62 | 3 | 0 | 3 |
| CCDC70 | 3 | 0 | 3 |
| CCDC80 | 3 | 0 | 3 |
| CCNG1 | 3 | 0 | 3 |
| CCR2 | 3 | 0 | 3 |
| CCR3 | 3 | 0 | 3 |
| CD209 | 3 | 0 | 3 |
| CD22 | 3 | 0 | 3 |
| CD276 | 3 | 0 | 3 |
| CD59 | 3 | 0 | 3 |
| CDH16 | 3 | 0 | 3 |
| CDH2 | 3 | 0 | 3 |
| CEACAM1 | 3 | 0 | 3 |
| CECR2 | 3 | 0 | 3 |
| CES3 | 3 | 0 | 3 |
| CETP | 3 | 0 | 3 |
| CFHR4 | 3 | 0 | 3 |
| CHIT1 | 3 | 0 | 3 |
| CHM | 3 | 0 | 3 |
| CHRNA1 | 3 | 0 | 3 |
| CHST2 | 3 | 0 | 3 |
| CHSY3 | 3 | 0 | 3 |
| CLCA4 | 3 | 0 | 3 |
| CLCN5 | 3 | 0 | 3 |
| CLEC14A | 3 | 0 | 3 |
| CLEC16A | 3 | 0 | 3 |
| CLP1 | 3 | 0 | 3 |
| CNKSR2 | 3 | 0 | 3 |
| COL6A2 | 3 | 0 | 3 |
| CP110 | 3 | 0 | 3 |
| CPB2 | 3 | 0 | 3 |
| CPNE3 | 3 | 0 | 3 |
| CPXCR1 | 3 | 0 | 3 |

| | | | |
|---|---|---|---|
| CRHR2 | 3 | 0 | 3 |
| CRKRS | 3 | 0 | 3 |
| CSF1R | 3 | 0 | 3 |
| CSF2RA | 3 | 0 | 3 |
| CSRNP1 | 3 | 0 | 3 |
| CTNS | 3 | 0 | 3 |
| CXCR3 | 3 | 0 | 3 |
| CYP27C1 | 3 | 0 | 3 |
| CYP2C19 | 3 | 0 | 3 |
| DAOA | 3 | 0 | 3 |
| DAXX | 3 | 0 | 3 |
| DBC1 | 3 | 0 | 3 |
| DBH | 3 | 0 | 3 |
| DCST1 | 3 | 0 | 3 |
| DDX58 | 3 | 0 | 3 |
| DERL2 | 3 | 0 | 3 |
| DHCR7 | 3 | 0 | 3 |
| DHX9 | 3 | 0 | 3 |
| DIP2A | 3 | 0 | 3 |
| DKK2 | 3 | 0 | 3 |
| DLG1 | 3 | 0 | 3 |
| DNMT3B | 3 | 0 | 3 |
| DOCK10 | 3 | 0 | 3 |
| DSC1 | 3 | 0 | 3 |
| DYM | 3 | 0 | 3 |
| DYNC1LI1 | 3 | 0 | 3 |
| DYNC2LI1 | 3 | 0 | 3 |
| ECM2 | 3 | 0 | 3 |
| EEF2K | 3 | 0 | 3 |
| EFEMP1 | 3 | 0 | 3 |
| EFTUD2 | 3 | 0 | 3 |
| ELF3 | 3 | 0 | 3 |
| EMILIN1 | 3 | 0 | 3 |
| ENO2 | 3 | 0 | 3 |
| ENOSF1 | 3 | 0 | 3 |
| EPB41L3 | 3 | 0 | 3 |
| EPB41L5 | 3 | 0 | 3 |
| EPHB6 | 3 | 0 | 3 |
| EPHX2 | 3 | 0 | 3 |
| EPS15L1 | 3 | 0 | 3 |
| EPX | 3 | 0 | 3 |

| | | | |
|---|---|---|---|
| ERBB2 | 3 | 0 | 3 |
| ESYT1 | 3 | 0 | 3 |
| EVI2B | 3 | 0 | 3 |
| FAM120C | 3 | 0 | 3 |
| FAM123A | 3 | 0 | 3 |
| FAM160B2 | 3 | 0 | 3 |
| FAM53C | 3 | 0 | 3 |
| FANCA | 3 | 0 | 3 |
| FANCM | 3 | 0 | 3 |
| FBLN5 | 3 | 0 | 3 |
| FBXL20 | 3 | 0 | 3 |
| FCGR2B | 3 | 0 | 3 |
| FCHSD2 | 3 | 0 | 3 |
| FER1L5 | 3 | 0 | 3 |
| FGGY | 3 | 0 | 3 |
| FHOD1 | 3 | 0 | 3 |
| FLJ10357 | 3 | 0 | 3 |
| FSTL4 | 3 | 0 | 3 |
| GABRE | 3 | 0 | 3 |
| GALNT1 | 3 | 0 | 3 |
| GDF9 | 3 | 0 | 3 |
| GGCX | 3 | 0 | 3 |
| GGT7 | 3 | 0 | 3 |
| GIMAP1 | 3 | 0 | 3 |
| GINS4 | 3 | 0 | 3 |
| GJB4 | 3 | 0 | 3 |
| GLT8D2 | 3 | 0 | 3 |
| GNAI2 | 3 | 0 | 3 |
| GNB2 | 3 | 0 | 3 |
| GOLGA4 | 3 | 0 | 3 |
| GOLGA6B | 3 | 0 | 3 |
| GPR110 | 3 | 0 | 3 |
| GPR114 | 3 | 0 | 3 |
| GPR116 | 3 | 0 | 3 |
| GPR124 | 3 | 0 | 3 |
| GPR171 | 3 | 0 | 3 |
| GPX2 | 3 | 0 | 3 |
| GRID1 | 3 | 0 | 3 |
| GRIN2D | 3 | 0 | 3 |
| GSTA1 | 3 | 0 | 3 |
| GSTA3 | 3 | 0 | 3 |

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|---|---|---|---|
| GSTCD | 3 | 0 | 3 |
| GSTM5 | 3 | 0 | 3 |
| GTF2IRD2B | 3 | 0 | 3 |
| GTF3C3 | 3 | 0 | 3 |
| HBS1L | 3 | 0 | 3 |
| HEATR5A | 3 | 0 | 3 |
| HELQ | 3 | 0 | 3 |
| HELZ | 3 | 0 | 3 |
| HIST1H1A | 3 | 0 | 3 |
| HM13 | 3 | 0 | 3 |
| HMGCL | 3 | 0 | 3 |
| HORMAD2 | 3 | 0 | 3 |
| HOXA1 | 3 | 0 | 3 |
| HOXA6 | 3 | 0 | 3 |
| HOXD10 | 3 | 0 | 3 |
| HSF5 | 3 | 0 | 3 |
| HSPA5 | 3 | 0 | 3 |
| ICA1 | 3 | 0 | 3 |
| IK | 3 | 0 | 3 |
| IL1F7 | 3 | 0 | 3 |
| IL1RN | 3 | 0 | 3 |
| INHBC | 3 | 0 | 3 |
| INPP5F | 3 | 0 | 3 |
| INTS3 | 3 | 0 | 3 |
| INTS5 | 3 | 0 | 3 |
| ISLR2 | 3 | 0 | 3 |
| ITGA3 | 3 | 0 | 3 |
| ITIH3 | 3 | 0 | 3 |
| IVD | 3 | 0 | 3 |
| JHDM1D | 3 | 0 | 3 |
| KBTBD3 | 3 | 0 | 3 |
| KCNH1 | 3 | 0 | 3 |
| KCNH2 | 3 | 0 | 3 |
| KCNK17 | 3 | 0 | 3 |
| KCNMB1 | 3 | 0 | 3 |
| KCNN4 | 3 | 0 | 3 |
| KCNS3 | 3 | 0 | 3 |
| KCNT1 | 3 | 0 | 3 |
| KIAA0141 | 3 | 0 | 3 |
| KIAA0319 | 3 | 0 | 3 |
| KIAA0556 | 3 | 0 | 3 |

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|---|---|---|---|
| KIAA1614 | 3 | 0 | 3 |
| KIAA1704 | 3 | 0 | 3 |
| KIAA2026 | 3 | 0 | 3 |
| KIF3B | 3 | 0 | 3 |
| KIF4A | 3 | 0 | 3 |
| KIF5A | 3 | 0 | 3 |
| KLHL7 | 3 | 0 | 3 |
| KNG1 | 3 | 0 | 3 |
| KRTAP9-3 | 3 | 0 | 3 |
| KTELC1 | 3 | 0 | 3 |
| LAMC2 | 3 | 0 | 3 |
| LDB3 | 3 | 0 | 3 |
| LENG8 | 3 | 0 | 3 |
| LGALS2 | 3 | 0 | 3 |
| LOC153328 | 3 | 0 | 3 |
| LOC402116 | 3 | 0 | 3 |
| LOC81691 | 3 | 0 | 3 |
| LONP1 | 3 | 0 | 3 |
| LPAR3 | 3 | 0 | 3 |
| LPHN3 | 3 | 0 | 3 |
| LRCH1 | 3 | 0 | 3 |
| LRCH3 | 3 | 0 | 3 |
| LRRC15 | 3 | 0 | 3 |
| LRRC23 | 3 | 0 | 3 |
| LRRC30 | 3 | 0 | 3 |
| LRRC3B | 3 | 0 | 3 |
| LRRC52 | 3 | 0 | 3 |
| MAGEA11 | 3 | 0 | 3 |
| MALL | 3 | 0 | 3 |
| MAP1LC3C | 3 | 0 | 3 |
| MAP7D2 | 3 | 0 | 3 |
| MARCO | 3 | 0 | 3 |
| MAS1L | 3 | 0 | 3 |
| MBOAT1 | 3 | 0 | 3 |
| MC3R | 3 | 0 | 3 |
| MCM10 | 3 | 0 | 3 |
| MDGA2 | 3 | 0 | 3 |
| MED14 | 3 | 0 | 3 |
| MFSD2A | 3 | 0 | 3 |
| MFSD2B | 3 | 0 | 3 |
| MGRN1 | 3 | 0 | 3 |

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|---|---|---|---|
| MID2 | 3 | 0 | 3 |
| MOV10L1 | 3 | 0 | 3 |
| MPND | 3 | 0 | 3 |
| MRRF | 3 | 0 | 3 |
| MS4A1 | 3 | 0 | 3 |
| MTBP | 3 | 0 | 3 |
| MTMR2 | 3 | 0 | 3 |
| MTO1 | 3 | 0 | 3 |
| MTUS1 | 3 | 0 | 3 |
| MUSK | 3 | 0 | 3 |
| MX2 | 3 | 0 | 3 |
| MYOF | 3 | 0 | 3 |
| NACA | 3 | 0 | 3 |
| NAT10 | 3 | 0 | 3 |
| NBEAL2 | 3 | 0 | 3 |
| NBPF7 | 3 | 0 | 3 |
| NCOA7 | 3 | 0 | 3 |
| NDFIP2 | 3 | 0 | 3 |
| NDST4 | 3 | 0 | 3 |
| NEK8 | 3 | 0 | 3 |
| NLK | 3 | 0 | 3 |
| NOTCH1 | 3 | 0 | 3 |
| NOX1 | 3 | 0 | 3 |
| NOX3 | 3 | 0 | 3 |
| NR1D2 | 3 | 0 | 3 |
| NR3C1 | 3 | 0 | 3 |
| NR5A1 | 3 | 0 | 3 |
| NT5C1A | 3 | 0 | 3 |
| NTNG1 | 3 | 0 | 3 |
| OAZ2 | 3 | 0 | 3 |
| OGDH | 3 | 0 | 3 |
| OLFM2 | 3 | 0 | 3 |
| OPCML | 3 | 0 | 3 |
| OR10J3 | 3 | 0 | 3 |
| OR10X1 | 3 | 0 | 3 |
| OR2M3 | 3 | 0 | 3 |
| OR2T4 | 3 | 0 | 3 |
| OR4B1 | 3 | 0 | 3 |
| OR4D10 | 3 | 0 | 3 |
| OR51B2 | 3 | 0 | 3 |
| OR51F2 | 3 | 0 | 3 |

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|---|---|---|---|
| OR5AK2 | 3 | 0 | 3 |
| OR6S1 | 3 | 0 | 3 |
| OR8B12 | 3 | 0 | 3 |
| OXGR1 | 3 | 0 | 3 |
| PAK3 | 3 | 0 | 3 |
| PAPOLG | 3 | 0 | 3 |
| PAPPA | 3 | 0 | 3 |
| PARVB | 3 | 0 | 3 |
| PCDHA10 | 3 | 0 | 3 |
| PCDHB12 | 3 | 0 | 3 |
| PCDHB3 | 3 | 0 | 3 |
| PCDHB5 | 3 | 0 | 3 |
| PCDHGA5 | 3 | 0 | 3 |
| PCOLCE2 | 3 | 0 | 3 |
| PCSK1 | 3 | 0 | 3 |
| PDIA3 | 3 | 0 | 3 |
| PDPR | 3 | 0 | 3 |
| PDZRN3 | 3 | 0 | 3 |
| PEX3 | 3 | 0 | 3 |
| PGK1 | 3 | 0 | 3 |
| PHF6 | 3 | 0 | 3 |
| PKP1 | 3 | 0 | 3 |
| PLCD4 | 3 | 0 | 3 |
| PLEKHA8 | 3 | 0 | 3 |
| PLIN1 | 3 | 0 | 3 |
| PNCK | 3 | 0 | 3 |
| PNPLA6 | 3 | 0 | 3 |
| POGZ | 3 | 0 | 3 |
| POLA1 | 3 | 0 | 3 |
| POLG | 3 | 0 | 3 |
| POLM | 3 | 0 | 3 |
| POLR2B | 3 | 0 | 3 |
| POMGNT1 | 3 | 0 | 3 |
| PORCN | 3 | 0 | 3 |
| POT1 | 3 | 0 | 3 |
| PPFIA4 | 3 | 0 | 3 |
| PPP2R2C | 3 | 0 | 3 |
| PROM2 | 3 | 0 | 3 |
| PRPF3 | 3 | 0 | 3 |
| PRR14 | 3 | 0 | 3 |
| PRSS36 | 3 | 0 | 3 |

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| PSIP1 | 3 | 0 | 3 |
| PSMC5 | 3 | 0 | 3 |
| PSMD2 | 3 | 0 | 3 |
| PSME4 | 3 | 0 | 3 |
| PTCD2 | 3 | 0 | 3 |
| PTCHD1 | 3 | 0 | 3 |
| PTCHD2 | 3 | 0 | 3 |
| PTK2B | 3 | 0 | 3 |
| PTPN14 | 3 | 0 | 3 |
| PTPRC | 3 | 0 | 3 |
| PTPRR | 3 | 0 | 3 |
| PXN | 3 | 0 | 3 |
| R3HDM2 | 3 | 0 | 3 |
| RAB1B | 3 | 0 | 3 |
| RAB5B | 3 | 0 | 3 |
| RAD23B | 3 | 0 | 3 |
| RALY | 3 | 0 | 3 |
| RAPGEF2 | 3 | 0 | 3 |
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| RCOR1 | 3 | 0 | 3 |
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| RGAG4 | 3 | 0 | 3 |
| RHOBTB2 | 3 | 0 | 3 |
| RHPN2 | 3 | 0 | 3 |
| RNF130 | 3 | 0 | 3 |
| RNF150 | 3 | 0 | 3 |
| RPA2 | 3 | 0 | 3 |
| RRH | 3 | 0 | 3 |
| RRP9 | 3 | 0 | 3 |
| RSPH3 | 3 | 0 | 3 |
| RSPRY1 | 3 | 0 | 3 |
| SASH1 | 3 | 0 | 3 |
| SBF2 | 3 | 0 | 3 |
| SCAF1 | 3 | 0 | 3 |
| SCGB3A2 | 3 | 0 | 3 |
| SEC16A | 3 | 0 | 3 |
| SELE | 3 | 0 | 3 |
| SELP | 3 | 0 | 3 |
| SEMA3E | 3 | 0 | 3 |
| SEZ6 | 3 | 0 | 3 |
| SFMBT1 | 3 | 0 | 3 |

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| SFTPD | 3 | 0 | 3 |
| SFXN3 | 3 | 0 | 3 |
| SGSM3 | 3 | 0 | 3 |
| SGTA | 3 | 0 | 3 |
| SH3PXD2B | 3 | 0 | 3 |
| SIRT5 | 3 | 0 | 3 |
| SKA1 | 3 | 0 | 3 |
| SKA3 | 3 | 0 | 3 |
| SLC12A8 | 3 | 0 | 3 |
| SLC16A7 | 3 | 0 | 3 |
| SLC17A5 | 3 | 0 | 3 |
| SLC25A44 | 3 | 0 | 3 |
| SLC30A6 | 3 | 0 | 3 |
| SLC38A4 | 3 | 0 | 3 |
| SLC39A11 | 3 | 0 | 3 |
| SLC4A5 | 3 | 0 | 3 |
| SLC6A14 | 3 | 0 | 3 |
| SLC7A14 | 3 | 0 | 3 |
| SLCO1B1 | 3 | 0 | 3 |
| SLCO1B3 | 3 | 0 | 3 |
| SLCO5A1 | 3 | 0 | 3 |
| SMARCD2 | 3 | 0 | 3 |
| SMC1B | 3 | 0 | 3 |
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| SMPDL3B | 3 | 0 | 3 |
| SMTN | 3 | 0 | 3 |
| SNRPA | 3 | 0 | 3 |
| SNX1 | 3 | 0 | 3 |
| SP2 | 3 | 0 | 3 |
| SPAG8 | 3 | 0 | 3 |
| SPTBN4 | 3 | 0 | 3 |
| SPTLC1 | 3 | 0 | 3 |
| SQSTM1 | 3 | 0 | 3 |
| SRPX2 | 3 | 0 | 3 |
| SSBP3 | 3 | 0 | 3 |
| SSTR1 | 3 | 0 | 3 |
| SSX2IP | 3 | 0 | 3 |
| ST3GAL3 | 3 | 0 | 3 |
| ST8SIA1 | 3 | 0 | 3 |
| STYK1 | 3 | 0 | 3 |
| SUV420H1 | 3 | 0 | 3 |

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| SYVN1 | 3 | 0 | 3 |
| TAF1L | 3 | 0 | 3 |
| TAS2R41 | 3 | 0 | 3 |
| TBC1D1 | 3 | 0 | 3 |
| TBC1D29 | 3 | 0 | 3 |
| TBCCD1 | 3 | 0 | 3 |
| TBCD | 3 | 0 | 3 |
| TBL1X | 3 | 0 | 3 |
| TBX22 | 3 | 0 | 3 |
| TEKT2 | 3 | 0 | 3 |
| TEX14 | 3 | 0 | 3 |
| TEX2 | 3 | 0 | 3 |
| TFRC | 3 | 0 | 3 |
| THAP9 | 3 | 0 | 3 |
| THBS1 | 3 | 0 | 3 |
| THNSL2 | 3 | 0 | 3 |
| TIMD4 | 3 | 0 | 3 |
| TLR8 | 3 | 0 | 3 |
| TMC2 | 3 | 0 | 3 |
| TMC5 | 3 | 0 | 3 |
| TMCC2 | 3 | 0 | 3 |
| TMCC3 | 3 | 0 | 3 |
| TMEM143 | 3 | 0 | 3 |
| TMEM63B | 3 | 0 | 3 |
| TPK1 | 3 | 0 | 3 |
| TRAPPC4 | 3 | 0 | 3 |
| TRHR | 3 | 0 | 3 |
| TRIM44 | 3 | 0 | 3 |
| TRIT1 | 3 | 0 | 3 |
| TRPC6 | 3 | 0 | 3 |
| TRPM1 | 3 | 0 | 3 |
| TRPM6 | 3 | 0 | 3 |
| TRPV5 | 3 | 0 | 3 |
| TSGA14 | 3 | 0 | 3 |
| TSHZ2 | 3 | 0 | 3 |
| TTC21A | 3 | 0 | 3 |
| TTC7A | 3 | 0 | 3 |
| TTLL7 | 3 | 0 | 3 |
| TUBB2C | 3 | 0 | 3 |
| TXLNA | 3 | 0 | 3 |
| UAP1 | 3 | 0 | 3 |

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| UBAC2 | 3 | 0 | 3 |
| UGT1A8 | 3 | 0 | 3 |
| UNC5CL | 3 | 0 | 3 |
| USP11 | 3 | 0 | 3 |
| USP19 | 3 | 0 | 3 |
| USP33 | 3 | 0 | 3 |
| USP35 | 3 | 0 | 3 |
| VAMP8 | 3 | 0 | 3 |
| VSIG2 | 3 | 0 | 3 |
| WDR25 | 3 | 0 | 3 |
| WDR60 | 3 | 0 | 3 |
| WDR66 | 3 | 0 | 3 |
| WDR70 | 3 | 0 | 3 |
| WDTC1 | 3 | 0 | 3 |
| WFDC10A | 3 | 0 | 3 |
| WFIKKN2 | 3 | 0 | 3 |
| WIF1 | 3 | 0 | 3 |
| WRN | 3 | 0 | 3 |
| XPC | 3 | 0 | 3 |
| XPNPEP3 | 3 | 0 | 3 |
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| ZDHHC19 | 3 | 0 | 3 |
| ZGLP1 | 3 | 0 | 3 |
| ZNF124 | 3 | 0 | 3 |
| ZNF14 | 3 | 0 | 3 |
| ZNF141 | 3 | 0 | 3 |
| ZNF167 | 3 | 0 | 3 |
| ZNF193 | 3 | 0 | 3 |
| ZNF28 | 3 | 0 | 3 |
| ZNF282 | 3 | 0 | 3 |
| ZNF35 | 3 | 0 | 3 |
| ZNF417 | 3 | 0 | 3 |
| ZNF429 | 3 | 0 | 3 |
| ZNF493 | 3 | 0 | 3 |
| ZNF514 | 3 | 0 | 3 |
| ZNF569 | 3 | 0 | 3 |
| ZNF608 | 3 | 0 | 3 |
| ZNF652 | 3 | 0 | 3 |
| ZNF654 | 3 | 0 | 3 |
| ZNF667 | 3 | 0 | 3 |
| ZNF677 | 3 | 0 | 3 |

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| ZNF746 | 3 | 0 | 3 |
| ZNF831 | 3 | 0 | 3 |
| ZNF839 | 3 | 0 | 3 |
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| AARS | 2 | 0 | 2 |
| ABCB7 | 2 | 0 | 2 |
| ABCG4 | 2 | 0 | 2 |
| ABL1 | 2 | 0 | 2 |
| ABT1 | 2 | 0 | 2 |
| ACAT2 | 2 | 0 | 2 |
| ACLY | 2 | 0 | 2 |
| ACOT8 | 2 | 0 | 2 |
| ACRBP | 2 | 0 | 2 |
| ACSL6 | 2 | 0 | 2 |
| ACSM5 | 2 | 0 | 2 |
| ACTG2 | 2 | 0 | 2 |
| ACTN1 | 2 | 0 | 2 |
| ACTN4 | 2 | 0 | 2 |
| ACTRT1 | 2 | 0 | 2 |
| ACVR1C | 2 | 0 | 2 |
| ACVR2B | 2 | 0 | 2 |
| ADAM12 | 2 | 0 | 2 |
| ADAM32 | 2 | 0 | 2 |
| ADAMTS1 | 2 | 0 | 2 |
| ADAMTS15 | 2 | 0 | 2 |
| ADAMTS18 | 2 | 0 | 2 |
| ADAMTS6 | 2 | 0 | 2 |
| ADAMTS9 | 2 | 0 | 2 |
| ADAP2 | 2 | 0 | 2 |
| ADARB1 | 2 | 0 | 2 |
| ADC | 2 | 0 | 2 |
| ADCK5 | 2 | 0 | 2 |
| ADRB2 | 2 | 0 | 2 |
| ADSS | 2 | 0 | 2 |
| AFAP1 | 2 | 0 | 2 |
| AFG3L2 | 2 | 0 | 2 |
| AGAP3 | 2 | 0 | 2 |
| AGAP8 | 2 | 0 | 2 |
| AGTPBP1 | 2 | 0 | 2 |
| AKAP14 | 2 | 0 | 2 |
| AKD1 | 2 | 0 | 2 |

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| AKR7A3 | 2 | 0 | 2 |
| ALCAM | 2 | 0 | 2 |
| ALDOC | 2 | 0 | 2 |
| ALG1 | 2 | 0 | 2 |
| ALG2 | 2 | 0 | 2 |
| ALG8 | 2 | 0 | 2 |
| ALOX15B | 2 | 0 | 2 |
| ALPK3 | 2 | 0 | 2 |
| ALS2CR12 | 2 | 0 | 2 |
| ALX4 | 2 | 0 | 2 |
| AMDHD1 | 2 | 0 | 2 |
| AMOT | 2 | 0 | 2 |
| AMPD3 | 2 | 0 | 2 |
| ANAPC7 | 2 | 0 | 2 |
| ANKRD24 | 2 | 0 | 2 |
| ANKRD52 | 2 | 0 | 2 |
| ANO8 | 2 | 0 | 2 |
| AP1S1 | 2 | 0 | 2 |
| AP3B1 | 2 | 0 | 2 |
| APLF | 2 | 0 | 2 |
| APOBEC3C | 2 | 0 | 2 |
| APOD | 2 | 0 | 2 |
| APPL2 | 2 | 0 | 2 |
| ARG1 | 2 | 0 | 2 |
| ARHGAP15 | 2 | 0 | 2 |
| ARHGAP20 | 2 | 0 | 2 |
| ARHGAP28 | 2 | 0 | 2 |
| ARID4A | 2 | 0 | 2 |
| ARL13A | 2 | 0 | 2 |
| ARSG | 2 | 0 | 2 |
| ARSH | 2 | 0 | 2 |
| ASAP3 | 2 | 0 | 2 |
| ASB18 | 2 | 0 | 2 |
| ASB7 | 2 | 0 | 2 |
| ASNSD1 | 2 | 0 | 2 |
| ASTE1 | 2 | 0 | 2 |
| ATF1 | 2 | 0 | 2 |
| ATF7IP | 2 | 0 | 2 |
| ATG2B | 2 | 0 | 2 |
| ATP12A | 2 | 0 | 2 |
| ATP1A3 | 2 | 0 | 2 |

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| ATP2A1 | 2 | 0 | 2 |
| ATP6V0A4 | 2 | 0 | 2 |
| ATP7B | 2 | 0 | 2 |
| ATPAF1 | 2 | 0 | 2 |
| AWAT2 | 2 | 0 | 2 |
| B3GAT2 | 2 | 0 | 2 |
| B3GNT2 | 2 | 0 | 2 |
| BCAM | 2 | 0 | 2 |
| BCDIN3D | 2 | 0 | 2 |
| BCL2L2 | 2 | 0 | 2 |
| BCL3 | 2 | 0 | 2 |
| BCL7C | 2 | 0 | 2 |
| BCS1L | 2 | 0 | 2 |
| BDH2 | 2 | 0 | 2 |
| BEND7 | 2 | 0 | 2 |
| BFSP1 | 2 | 0 | 2 |
| BHLHB9 | 2 | 0 | 2 |
| BHMT | 2 | 0 | 2 |
| BRS3 | 2 | 0 | 2 |
| BSND | 2 | 0 | 2 |
| BTBD9 | 2 | 0 | 2 |
| BTD | 2 | 0 | 2 |
| BTN2A2 | 2 | 0 | 2 |
| BUB1B | 2 | 0 | 2 |
| BZW2 | 2 | 0 | 2 |
| C10orf119 | 2 | 0 | 2 |
| C10orf32 | 2 | 0 | 2 |
| C10orf55 | 2 | 0 | 2 |
| C11orf24 | 2 | 0 | 2 |
| C11orf80 | 2 | 0 | 2 |
| C12orf29 | 2 | 0 | 2 |
| C12orf74 | 2 | 0 | 2 |
| C13orf31 | 2 | 0 | 2 |
| C14orf106 | 2 | 0 | 2 |
| C14orf138 | 2 | 0 | 2 |
| C14orf21 | 2 | 0 | 2 |
| C15orf39 | 2 | 0 | 2 |
| C16orf62 | 2 | 0 | 2 |
| C17orf42 | 2 | 0 | 2 |
| C18orf1 | 2 | 0 | 2 |
| C18orf22 | 2 | 0 | 2 |

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|---|---|---|---|
| C19orf46 | 2 | 0 | 2 |
| C1D | 2 | 0 | 2 |
| C1orf111 | 2 | 0 | 2 |
| C1orf127 | 2 | 0 | 2 |
| C1orf158 | 2 | 0 | 2 |
| C1orf168 | 2 | 0 | 2 |
| C1orf172 | 2 | 0 | 2 |
| C1orf9 | 2 | 0 | 2 |
| C20orf11 | 2 | 0 | 2 |
| C20orf12 | 2 | 0 | 2 |
| C20orf54 | 2 | 0 | 2 |
| C21orf33 | 2 | 0 | 2 |
| C2orf53 | 2 | 0 | 2 |
| C2orf65 | 2 | 0 | 2 |
| C2orf71 | 2 | 0 | 2 |
| C2orf86 | 2 | 0 | 2 |
| C3orf17 | 2 | 0 | 2 |
| C4A | 2 | 0 | 2 |
| C4orf22 | 2 | 0 | 2 |
| C4orf29 | 2 | 0 | 2 |
| C4orf31 | 2 | 0 | 2 |
| C5orf22 | 2 | 0 | 2 |
| C6orf10 | 2 | 0 | 2 |
| C6orf192 | 2 | 0 | 2 |
| C6orf26 | 2 | 0 | 2 |
| C7orf10 | 2 | 0 | 2 |
| C7orf44 | 2 | 0 | 2 |
| C8orf45 | 2 | 0 | 2 |
| C9orf116 | 2 | 0 | 2 |
| C9orf84 | 2 | 0 | 2 |
| C9orf93 | 2 | 0 | 2 |
| CA1 | 2 | 0 | 2 |
| CACNA1H | 2 | 0 | 2 |
| CACNA1I | 2 | 0 | 2 |
| CACNA2D3 | 2 | 0 | 2 |
| CADM1 | 2 | 0 | 2 |
| CADM4 | 2 | 0 | 2 |
| CALD1 | 2 | 0 | 2 |
| CAMK2A | 2 | 0 | 2 |
| CAP2 | 2 | 0 | 2 |
| CAPN10 | 2 | 0 | 2 |

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| CAPN13 | 2 | 0 | 2 |
| CAPN3 | 2 | 0 | 2 |
| CAPS2 | 2 | 0 | 2 |
| CARHSP1 | 2 | 0 | 2 |
| CARS2 | 2 | 0 | 2 |
| CARTPT | 2 | 0 | 2 |
| CASC3 | 2 | 0 | 2 |
| CASKIN1 | 2 | 0 | 2 |
| CASP10 | 2 | 0 | 2 |
| CASP8AP2 | 2 | 0 | 2 |
| CASP9 | 2 | 0 | 2 |
| CBWD1 | 2 | 0 | 2 |
| CBX8 | 2 | 0 | 2 |
| CC2D1A | 2 | 0 | 2 |
| CCDC102A | 2 | 0 | 2 |
| CCDC105 | 2 | 0 | 2 |
| CCDC109A | 2 | 0 | 2 |
| CCDC112 | 2 | 0 | 2 |
| CCDC129 | 2 | 0 | 2 |
| CCDC144NL | 2 | 0 | 2 |
| CCDC146 | 2 | 0 | 2 |
| CCDC27 | 2 | 0 | 2 |
| CCDC28A | 2 | 0 | 2 |
| CCDC30 | 2 | 0 | 2 |
| CCDC57 | 2 | 0 | 2 |
| CCDC87 | 2 | 0 | 2 |
| CCDC93 | 2 | 0 | 2 |
| CCKBR | 2 | 0 | 2 |
| CCL27 | 2 | 0 | 2 |
| CCNA1 | 2 | 0 | 2 |
| CCNA2 | 2 | 0 | 2 |
| CCNY | 2 | 0 | 2 |
| CCR9 | 2 | 0 | 2 |
| CCT7 | 2 | 0 | 2 |
| CD180 | 2 | 0 | 2 |
| CD300LB | 2 | 0 | 2 |
| CD38 | 2 | 0 | 2 |
| CD3E | 2 | 0 | 2 |
| CD72 | 2 | 0 | 2 |
| CDC14B | 2 | 0 | 2 |
| CDC16 | 2 | 0 | 2 |

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| CDC2 | 2 | 0 | 2 |
| CDC7 | 2 | 0 | 2 |
| CDCA7 | 2 | 0 | 2 |
| CDH19 | 2 | 0 | 2 |
| CDH26 | 2 | 0 | 2 |
| CDK2 | 2 | 0 | 2 |
| CDKN3 | 2 | 0 | 2 |
| CDON | 2 | 0 | 2 |
| CDR2 | 2 | 0 | 2 |
| CEACAM18 | 2 | 0 | 2 |
| CECR1 | 2 | 0 | 2 |
| CECR5 | 2 | 0 | 2 |
| CENPB | 2 | 0 | 2 |
| CEP78 | 2 | 0 | 2 |
| CEPT1 | 2 | 0 | 2 |
| CETN1 | 2 | 0 | 2 |
| CGRRF1 | 2 | 0 | 2 |
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| CHMP4C | 2 | 0 | 2 |
| CHRM5 | 2 | 0 | 2 |
| CHRNA10 | 2 | 0 | 2 |
| CHRNA3 | 2 | 0 | 2 |
| CIDEA | 2 | 0 | 2 |
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| CLCN2 | 2 | 0 | 2 |
| CLDN14 | 2 | 0 | 2 |
| CLDN16 | 2 | 0 | 2 |
| CLDN17 | 2 | 0 | 2 |
| CLDN18 | 2 | 0 | 2 |
| CLEC1B | 2 | 0 | 2 |
| CLK2 | 2 | 0 | 2 |
| CLNK | 2 | 0 | 2 |
| CLNS1A | 2 | 0 | 2 |
| CLPTM1 | 2 | 0 | 2 |
| CLPTM1L | 2 | 0 | 2 |
| CLUL1 | 2 | 0 | 2 |
| CMTM1 | 2 | 0 | 2 |
| CMTM5 | 2 | 0 | 2 |
| CNDP2 | 2 | 0 | 2 |
| CNIH4 | 2 | 0 | 2 |
| CNTROB | 2 | 0 | 2 |

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| COG1 | 2 | 0 | 2 |
| COG6 | 2 | 0 | 2 |
| COL25A1 | 2 | 0 | 2 |
| COL8A1 | 2 | 0 | 2 |
| COPB1 | 2 | 0 | 2 |
| CORO2A | 2 | 0 | 2 |
| COX11 | 2 | 0 | 2 |
| CPNE6 | 2 | 0 | 2 |
| CRHBP | 2 | 0 | 2 |
| CRISP2 | 2 | 0 | 2 |
| CRTAP | 2 | 0 | 2 |
| CRTC2 | 2 | 0 | 2 |
| CRYBB1 | 2 | 0 | 2 |
| CRYZL1 | 2 | 0 | 2 |
| CSAD | 2 | 0 | 2 |
| CSK | 2 | 0 | 2 |
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| CSPG4 | 2 | 0 | 2 |
| CSRP3 | 2 | 0 | 2 |
| CST8 | 2 | 0 | 2 |
| CSTF2 | 2 | 0 | 2 |
| CTBP1 | 2 | 0 | 2 |
| CTCFL | 2 | 0 | 2 |
| CTDSP1 | 2 | 0 | 2 |
| CTNNA2 | 2 | 0 | 2 |
| CTNNAL1 | 2 | 0 | 2 |
| CTPS2 | 2 | 0 | 2 |
| CTSG | 2 | 0 | 2 |
| CUL3 | 2 | 0 | 2 |
| CWF19L2 | 2 | 0 | 2 |
| CXCR5 | 2 | 0 | 2 |
| CXorf67 | 2 | 0 | 2 |
| CYB5D2 | 2 | 0 | 2 |
| CYBASC3 | 2 | 0 | 2 |
| CYLD | 2 | 0 | 2 |
| CYP1A2 | 2 | 0 | 2 |
| CYP20A1 | 2 | 0 | 2 |
| CYP27B1 | 2 | 0 | 2 |
| CYP4A11 | 2 | 0 | 2 |
| CYP4B1 | 2 | 0 | 2 |
| CYTH2 | 2 | 0 | 2 |

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| CYTH4 | 2 | 0 | 2 |
| CYTSB | 2 | 0 | 2 |
| DAND5 | 2 | 0 | 2 |
| DCAF12L1 | 2 | 0 | 2 |
| DCAF4 | 2 | 0 | 2 |
| DCAF4L2 | 2 | 0 | 2 |
| DCBLD1 | 2 | 0 | 2 |
| DCP2 | 2 | 0 | 2 |
| DCPS | 2 | 0 | 2 |
| DCT | 2 | 0 | 2 |
| DCTN3 | 2 | 0 | 2 |
| DCTN6 | 2 | 0 | 2 |
| DDC | 2 | 0 | 2 |
| DDX19B | 2 | 0 | 2 |
| DDX23 | 2 | 0 | 2 |
| DDX24 | 2 | 0 | 2 |
| DDX27 | 2 | 0 | 2 |
| DENND1C | 2 | 0 | 2 |
| DENND2A | 2 | 0 | 2 |
| DENND2D | 2 | 0 | 2 |
| DHRS1 | 2 | 0 | 2 |
| DHRS4L2 | 2 | 0 | 2 |
| DHX40 | 2 | 0 | 2 |
| DLGAP1 | 2 | 0 | 2 |
| DLK1 | 2 | 0 | 2 |
| DLK2 | 2 | 0 | 2 |
| DLST | 2 | 0 | 2 |
| DLX5 | 2 | 0 | 2 |
| DMBX1 | 2 | 0 | 2 |
| DMP1 | 2 | 0 | 2 |
| DMRT1 | 2 | 0 | 2 |
| DMRT3 | 2 | 0 | 2 |
| DMTF1 | 2 | 0 | 2 |
| DNAJB13 | 2 | 0 | 2 |
| DNAJC1 | 2 | 0 | 2 |
| DNAJC22 | 2 | 0 | 2 |
| DNAJC6 | 2 | 0 | 2 |
| DPP9 | 2 | 0 | 2 |
| DPY19L3 | 2 | 0 | 2 |
| DPYS | 2 | 0 | 2 |
| DPYSL3 | 2 | 0 | 2 |

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| DPYSL5 | 2 | 0 | 2 |
| DTD1 | 2 | 0 | 2 |
| DTX2 | 2 | 0 | 2 |
| DZIP1L | 2 | 0 | 2 |
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| EBP | 2 | 0 | 2 |
| ECHDC2 | 2 | 0 | 2 |
| EFNA4 | 2 | 0 | 2 |
| EGF | 2 | 0 | 2 |
| EGLN1 | 2 | 0 | 2 |
| EGR2 | 2 | 0 | 2 |
| EHD1 | 2 | 0 | 2 |
| EHD4 | 2 | 0 | 2 |
| EHMT2 | 2 | 0 | 2 |
| EIF2AK2 | 2 | 0 | 2 |
| EIF3IP1 | 2 | 0 | 2 |
| ELAVL4 | 2 | 0 | 2 |
| ELMOD2 | 2 | 0 | 2 |
| EMR1 | 2 | 0 | 2 |
| EMR2 | 2 | 0 | 2 |
| ENPP1 | 2 | 0 | 2 |
| ENPP7 | 2 | 0 | 2 |
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| EP300 | 2 | 0 | 2 |
| EPB41 | 2 | 0 | 2 |
| EPB41L2 | 2 | 0 | 2 |
| EPC2 | 2 | 0 | 2 |
| EPHA10 | 2 | 0 | 2 |
| EPHA4 | 2 | 0 | 2 |
| EPOR | 2 | 0 | 2 |
| EPS8 | 2 | 0 | 2 |
| ERICH1 | 2 | 0 | 2 |
| ERN1 | 2 | 0 | 2 |
| ERO1LB | 2 | 0 | 2 |
| ERRFI1 | 2 | 0 | 2 |
| ESX1 | 2 | 0 | 2 |
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| EVC2 | 2 | 0 | 2 |
| EVI5L | 2 | 0 | 2 |
| EVPL | 2 | 0 | 2 |

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| EVX2 | 2 | 0 | 2 |
| EXOC2 | 2 | 0 | 2 |
| EXT1 | 2 | 0 | 2 |
| EZH1 | 2 | 0 | 2 |
| FABP12 | 2 | 0 | 2 |
| FAF1 | 2 | 0 | 2 |
| FAM111A | 2 | 0 | 2 |
| FAM155B | 2 | 0 | 2 |
| FAM166A | 2 | 0 | 2 |
| FAM169A | 2 | 0 | 2 |
| FAM178A | 2 | 0 | 2 |
| FAM190A | 2 | 0 | 2 |
| FAM198B | 2 | 0 | 2 |
| FAM20B | 2 | 0 | 2 |
| FAM38B | 2 | 0 | 2 |
| FAM46D | 2 | 0 | 2 |
| FAM49A | 2 | 0 | 2 |
| FAM50A | 2 | 0 | 2 |
| FAM65A | 2 | 0 | 2 |
| FAM73B | 2 | 0 | 2 |
| FAM78A | 2 | 0 | 2 |
| FAM82A1 | 2 | 0 | 2 |
| FAM98C | 2 | 0 | 2 |
| FANCC | 2 | 0 | 2 |
| FANK1 | 2 | 0 | 2 |
| FARP2 | 2 | 0 | 2 |
| FBXL2 | 2 | 0 | 2 |
| FBXL7 | 2 | 0 | 2 |
| FBXO10 | 2 | 0 | 2 |
| FBXO22 | 2 | 0 | 2 |
| FBXO46 | 2 | 0 | 2 |
| FBXW2 | 2 | 0 | 2 |
| FBXW8 | 2 | 0 | 2 |
| FCGR1A | 2 | 0 | 2 |
| FECH | 2 | 0 | 2 |
| FERMT2 | 2 | 0 | 2 |
| FGL1 | 2 | 0 | 2 |
| FKBP5 | 2 | 0 | 2 |
| FKTN | 2 | 0 | 2 |
| FNDC8 | 2 | 0 | 2 |
| FNIP2 | 2 | 0 | 2 |

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| FOXG1 | 2 | 0 | 2 |
| FOXJ2 | 2 | 0 | 2 |
| FOXJ3 | 2 | 0 | 2 |
| FOXN4 | 2 | 0 | 2 |
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| FRMD8 | 2 | 0 | 2 |
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| FZD5 | 2 | 0 | 2 |
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| GABRR3 | 2 | 0 | 2 |
| GAGE12H | 2 | 0 | 2 |
| GALNT13 | 2 | 0 | 2 |
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| GDF15 | 2 | 0 | 2 |
| GEFT | 2 | 0 | 2 |
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| GGT5 | 2 | 0 | 2 |
| GHITM | 2 | 0 | 2 |
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| GLYATL1 | 2 | 0 | 2 |
| GM2A | 2 | 0 | 2 |
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| GNAS | 2 | 0 | 2 |
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| GPI | 2 | 0 | 2 |
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| GPR155 | 2 | 0 | 2 |
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| GYPA | 2 | 0 | 2 |
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| IL29 | 2 | 0 | 2 |
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| IL4I1 | 2 | 0 | 2 |
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| KRTAP10-9 | 2 | 0 | 2 |
| KRTAP26-1 | 2 | 0 | 2 |
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| LEPRE1 | 2 | 0 | 2 |
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| LRRN2 | 2 | 0 | 2 |
| LRRTM4 | 2 | 0 | 2 |
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| LUZP2 | 2 | 0 | 2 |
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| MAB21L2 | 2 | 0 | 2 |
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| MAP6 | 2 | 0 | 2 |
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| MAPK14 | 2 | 0 | 2 |
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| MED19 | 2 | 0 | 2 |
| MEFV | 2 | 0 | 2 |
| MEIS2 | 2 | 0 | 2 |
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| NGLY1 | 2 | 0 | 2 |
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| NKTR | 2 | 0 | 2 |
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| NLRP10 | 2 | 0 | 2 |
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| NOL8 | 2 | 0 | 2 |
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| NONO | 2 | 0 | 2 |
| NOP2 | 2 | 0 | 2 |
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| NR2C2 | 2 | 0 | 2 |
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| OR2J2 | 2 | 0 | 2 |
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| OR4C46 | 2 | 0 | 2 |
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| OR56B1 | 2 | 0 | 2 |
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| OR5H2 | 2 | 0 | 2 |
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| P2RY2 | 2 | 0 | 2 |
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| PAICS | 2 | 0 | 2 |
| PAK7 | 2 | 0 | 2 |
| PAMR1 | 2 | 0 | 2 |
| PAPLN | 2 | 0 | 2 |
| PAPSS2 | 2 | 0 | 2 |
| PAQR5 | 2 | 0 | 2 |
| PAXIP1 | 2 | 0 | 2 |
| PBX2 | 2 | 0 | 2 |
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| PCBP2 | 2 | 0 | 2 |
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| PCDHA12 | 2 | 0 | 2 |
| PCDHA13 | 2 | 0 | 2 |
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| PCDHAC2 | 2 | 0 | 2 |
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| PDE3B | 2 | 0 | 2 |
| PDE6B | 2 | 0 | 2 |
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| PDIA4 | 2 | 0 | 2 |
| PDSS2 | 2 | 0 | 2 |
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| PELI3 | 2 | 0 | 2 |
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| PFKL | 2 | 0 | 2 |
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| PODXL2 | 2 | 0 | 2 |
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| POP7 | 2 | 0 | 2 |
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| PREP | 2 | 0 | 2 |
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| RBM12B | 2 | 0 | 2 |
| RBMS2 | 2 | 0 | 2 |
| RBMX | 2 | 0 | 2 |
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| RDH8 | 2 | 0 | 2 |
| RECK | 2 | 0 | 2 |
| REL | 2 | 0 | 2 |
| RELL2 | 2 | 0 | 2 |
| REST | 2 | 0 | 2 |
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| SHE | 2 | 0 | 2 |
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| SIRT3 | 2 | 0 | 2 |
| SKP2 | 2 | 0 | 2 |
| SLC11A2 | 2 | 0 | 2 |
| SLC15A4 | 2 | 0 | 2 |
| SLC17A2 | 2 | 0 | 2 |
| SLC17A8 | 2 | 0 | 2 |
| SLC18A1 | 2 | 0 | 2 |
| SLC1A2 | 2 | 0 | 2 |
| SLC22A12 | 2 | 0 | 2 |
| SLC22A9 | 2 | 0 | 2 |
| SLC25A15 | 2 | 0 | 2 |
| SLC25A5 | 2 | 0 | 2 |
| SLC29A3 | 2 | 0 | 2 |
| SLC29A4 | 2 | 0 | 2 |
| SLC2A11 | 2 | 0 | 2 |
| SLC2A14 | 2 | 0 | 2 |
| SLC2A3 | 2 | 0 | 2 |
| SLC2A4 | 2 | 0 | 2 |
| SLC2A5 | 2 | 0 | 2 |
| SLC37A2 | 2 | 0 | 2 |
| SLC38A1 | 2 | 0 | 2 |
| SLC38A11 | 2 | 0 | 2 |
| SLC38A5 | 2 | 0 | 2 |

| | | | |
|---|---|---|---|
| SLC38A7 | 2 | 0 | 2 |
| SLC38A8 | 2 | 0 | 2 |
| SLC44A3 | 2 | 0 | 2 |
| SLC45A1 | 2 | 0 | 2 |
| SLC4A1 | 2 | 0 | 2 |
| SLC5A1 | 2 | 0 | 2 |
| SLC5A10 | 2 | 0 | 2 |
| SLC5A12 | 2 | 0 | 2 |
| SLC7A6OS | 2 | 0 | 2 |
| SLC9A10 | 2 | 0 | 2 |
| SLC9A9 | 2 | 0 | 2 |
| SLCO2A1 | 2 | 0 | 2 |
| SLCO4A1 | 2 | 0 | 2 |
| SLFNL1 | 2 | 0 | 2 |
| SLITRK2 | 2 | 0 | 2 |
| SLITRK4 | 2 | 0 | 2 |
| SLITRK6 | 2 | 0 | 2 |
| SMC5 | 2 | 0 | 2 |
| SMPD1 | 2 | 0 | 2 |
| SMS | 2 | 0 | 2 |
| SMYD2 | 2 | 0 | 2 |
| SMYD3 | 2 | 0 | 2 |
| SNAP23 | 2 | 0 | 2 |
| SNX11 | 2 | 0 | 2 |
| SNX13 | 2 | 0 | 2 |
| SNX16 | 2 | 0 | 2 |
| SNX29 | 2 | 0 | 2 |
| SNX8 | 2 | 0 | 2 |
| SOAT1 | 2 | 0 | 2 |
| SOX15 | 2 | 0 | 2 |
| SPA17 | 2 | 0 | 2 |
| SPAG5 | 2 | 0 | 2 |
| SPG20 | 2 | 0 | 2 |
| SPINK5 | 2 | 0 | 2 |
| SPINK7 | 2 | 0 | 2 |
| SPINT1 | 2 | 0 | 2 |
| SPOP | 2 | 0 | 2 |
| SPRYD4 | 2 | 0 | 2 |
| SQRDL | 2 | 0 | 2 |
| SRA1 | 2 | 0 | 2 |
| SREBF2 | 2 | 0 | 2 |

| | | | |
|---|---|---|---|
| SRGAP2 | 2 | 0 | 2 |
| SRM | 2 | 0 | 2 |
| SRPK2 | 2 | 0 | 2 |
| SRRM4 | 2 | 0 | 2 |
| SRRT | 2 | 0 | 2 |
| SSH2 | 2 | 0 | 2 |
| ST3GAL6 | 2 | 0 | 2 |
| ST7 | 2 | 0 | 2 |
| STAMBPL1 | 2 | 0 | 2 |
| STARD3NL | 2 | 0 | 2 |
| STAT5A | 2 | 0 | 2 |
| STC2 | 2 | 0 | 2 |
| STEAP3 | 2 | 0 | 2 |
| STK36 | 2 | 0 | 2 |
| STK38L | 2 | 0 | 2 |
| STXBP3 | 2 | 0 | 2 |
| SULT2A1 | 2 | 0 | 2 |
| SULT4A1 | 2 | 0 | 2 |
| SURF1 | 2 | 0 | 2 |
| SVOPL | 2 | 0 | 2 |
| SWAP70 | 2 | 0 | 2 |
| SYK | 2 | 0 | 2 |
| SYMPK | 2 | 0 | 2 |
| SYNRG | 2 | 0 | 2 |
| SYT17 | 2 | 0 | 2 |
| SYT5 | 2 | 0 | 2 |
| SYTL1 | 2 | 0 | 2 |
| TACC3 | 2 | 0 | 2 |
| TAF15 | 2 | 0 | 2 |
| TAF3 | 2 | 0 | 2 |
| TAF4B | 2 | 0 | 2 |
| TAP1 | 2 | 0 | 2 |
| TAPBP | 2 | 0 | 2 |
| TAS1R2 | 2 | 0 | 2 |
| TAS2R39 | 2 | 0 | 2 |
| TAS2R9 | 2 | 0 | 2 |
| TBC1D10A | 2 | 0 | 2 |
| TBC1D21 | 2 | 0 | 2 |
| TBC1D8 | 2 | 0 | 2 |
| TBC1D9B | 2 | 0 | 2 |
| TBX10 | 2 | 0 | 2 |

| | | | |
|---|---|---|---|
| TCF12 | 2 | 0 | 2 |
| TCF7L1 | 2 | 0 | 2 |
| TCP10L | 2 | 0 | 2 |
| TCP11 | 2 | 0 | 2 |
| TDG | 2 | 0 | 2 |
| TDRD10 | 2 | 0 | 2 |
| TDRD6 | 2 | 0 | 2 |
| TDRKH | 2 | 0 | 2 |
| TECTB | 2 | 0 | 2 |
| TEDDM1 | 2 | 0 | 2 |
| TFDP1 | 2 | 0 | 2 |
| TGFB2 | 2 | 0 | 2 |
| TGIF1 | 2 | 0 | 2 |
| THAP8 | 2 | 0 | 2 |
| THBS4 | 2 | 0 | 2 |
| THEM5 | 2 | 0 | 2 |
| THEMIS | 2 | 0 | 2 |
| THOC1 | 2 | 0 | 2 |
| THOC5 | 2 | 0 | 2 |
| THUMPD2 | 2 | 0 | 2 |
| THUMPD3 | 2 | 0 | 2 |
| TIAF1 | 2 | 0 | 2 |
| TIAM1 | 2 | 0 | 2 |
| TIGD6 | 2 | 0 | 2 |
| TINAG | 2 | 0 | 2 |
| TJP1 | 2 | 0 | 2 |
| TLL1 | 2 | 0 | 2 |
| TLL2 | 2 | 0 | 2 |
| TLR10 | 2 | 0 | 2 |
| TM2D1 | 2 | 0 | 2 |
| TM6SF2 | 2 | 0 | 2 |
| TM7SF2 | 2 | 0 | 2 |
| TM9SF1 | 2 | 0 | 2 |
| TM9SF4 | 2 | 0 | 2 |
| TMC3 | 2 | 0 | 2 |
| TMC4 | 2 | 0 | 2 |
| TMC6 | 2 | 0 | 2 |
| TMEM100 | 2 | 0 | 2 |
| TMEM132B | 2 | 0 | 2 |
| TMEM150C | 2 | 0 | 2 |
| TMEM156 | 2 | 0 | 2 |

| | | | |
|---|---|---|---|
| TMEM198 | 2 | 0 | 2 |
| TMEM214 | 2 | 0 | 2 |
| TMEM30A | 2 | 0 | 2 |
| TMEM45B | 2 | 0 | 2 |
| TMEM53 | 2 | 0 | 2 |
| TMLHE | 2 | 0 | 2 |
| TNFRSF11B | 2 | 0 | 2 |
| TNFRSF1B | 2 | 0 | 2 |
| TNFSF13B | 2 | 0 | 2 |
| TNKS1BP1 | 2 | 0 | 2 |
| TOB1 | 2 | 0 | 2 |
| TOM1L1 | 2 | 0 | 2 |
| TOP2A | 2 | 0 | 2 |
| TOR1AIP1 | 2 | 0 | 2 |
| TP53TG5 | 2 | 0 | 2 |
| TPH2 | 2 | 0 | 2 |
| TPR | 2 | 0 | 2 |
| TPST1 | 2 | 0 | 2 |
| TRIM10 | 2 | 0 | 2 |
| TRIM11 | 2 | 0 | 2 |
| TRIM17 | 2 | 0 | 2 |
| TRIM29 | 2 | 0 | 2 |
| TRIM31 | 2 | 0 | 2 |
| TRIM36 | 2 | 0 | 2 |
| TRIM38 | 2 | 0 | 2 |
| TRIM6-TRIM34 | 2 | 0 | 2 |
| TRIP10 | 2 | 0 | 2 |
| TRMT1 | 2 | 0 | 2 |
| TRMT2B | 2 | 0 | 2 |
| TRNT1 | 2 | 0 | 2 |
| TRPC4AP | 2 | 0 | 2 |
| TSC22D1 | 2 | 0 | 2 |
| TSNARE1 | 2 | 0 | 2 |
| TSPAN3 | 2 | 0 | 2 |
| TSSK1B | 2 | 0 | 2 |
| TSSK3 | 2 | 0 | 2 |
| TTBK2 | 2 | 0 | 2 |
| TTC14 | 2 | 0 | 2 |
| TTC25 | 2 | 0 | 2 |
| TTC27 | 2 | 0 | 2 |
| TTC31 | 2 | 0 | 2 |

| | | | |
|---|---|---|---|
| TTC39C | 2 | 0 | 2 |
| TTC7B | 2 | 0 | 2 |
| TTLL13 | 2 | 0 | 2 |
| TUBGCP3 | 2 | 0 | 2 |
| TUBGCP4 | 2 | 0 | 2 |
| TUBGCP6 | 2 | 0 | 2 |
| TULP4 | 2 | 0 | 2 |
| TUSC3 | 2 | 0 | 2 |
| TXNDC11 | 2 | 0 | 2 |
| TYR | 2 | 0 | 2 |
| UACA | 2 | 0 | 2 |
| UBE2O | 2 | 0 | 2 |
| UBE2Q1 | 2 | 0 | 2 |
| UBE3B | 2 | 0 | 2 |
| UBE4A | 2 | 0 | 2 |
| UBL4B | 2 | 0 | 2 |
| UGGT1 | 2 | 0 | 2 |
| UGT1A5 | 2 | 0 | 2 |
| UGT2A3 | 2 | 0 | 2 |
| UGT2B7 | 2 | 0 | 2 |
| UHRF2 | 2 | 0 | 2 |
| UMOD | 2 | 0 | 2 |
| UPB1 | 2 | 0 | 2 |
| USF1 | 2 | 0 | 2 |
| USP13 | 2 | 0 | 2 |
| USP18 | 2 | 0 | 2 |
| USP22 | 2 | 0 | 2 |
| USP30 | 2 | 0 | 2 |
| USP48 | 2 | 0 | 2 |
| UTP6 | 2 | 0 | 2 |
| VDR | 2 | 0 | 2 |
| VLDLR | 2 | 0 | 2 |
| VPS33B | 2 | 0 | 2 |
| VPS39 | 2 | 0 | 2 |
| VTI1A | 2 | 0 | 2 |
| VTN | 2 | 0 | 2 |
| WAPAL | 2 | 0 | 2 |
| WAS | 2 | 0 | 2 |
| WBP1 | 2 | 0 | 2 |
| WDFY1 | 2 | 0 | 2 |
| WDR33 | 2 | 0 | 2 |

| | | | |
|---|---|---|---|
| WDR55 | 2 | 0 | 2 |
| WDR5B | 2 | 0 | 2 |
| WDR78 | 2 | 0 | 2 |
| WDR91 | 2 | 0 | 2 |
| WFDC10B | 2 | 0 | 2 |
| WIBG | 2 | 0 | 2 |
| WISP1 | 2 | 0 | 2 |
| WNT3 | 2 | 0 | 2 |
| WNT5A | 2 | 0 | 2 |
| WNT6 | 2 | 0 | 2 |
| WNT9A | 2 | 0 | 2 |
| XDH | 2 | 0 | 2 |
| XRCC6 | 2 | 0 | 2 |
| XRRA1 | 2 | 0 | 2 |
| YIF1A | 2 | 0 | 2 |
| YPEL2 | 2 | 0 | 2 |
| YTHDC2 | 2 | 0 | 2 |
| YWHAG | 2 | 0 | 2 |
| ZBED4 | 2 | 0 | 2 |
| ZBTB1 | 2 | 0 | 2 |
| ZBTB16 | 2 | 0 | 2 |
| ZBTB34 | 2 | 0 | 2 |
| ZBTB7C | 2 | 0 | 2 |
| ZCCHC10 | 2 | 0 | 2 |
| ZDHHC12 | 2 | 0 | 2 |
| ZGPAT | 2 | 0 | 2 |
| ZIC1 | 2 | 0 | 2 |
| ZMYND8 | 2 | 0 | 2 |
| ZNF180 | 2 | 0 | 2 |
| ZNF205 | 2 | 0 | 2 |
| ZNF207 | 2 | 0 | 2 |
| ZNF217 | 2 | 0 | 2 |
| ZNF238 | 2 | 0 | 2 |
| ZNF254 | 2 | 0 | 2 |
| ZNF257 | 2 | 0 | 2 |
| ZNF280C | 2 | 0 | 2 |
| ZNF295 | 2 | 0 | 2 |
| ZNF33A | 2 | 0 | 2 |
| ZNF416 | 2 | 0 | 2 |
| ZNF432 | 2 | 0 | 2 |
| ZNF434 | 2 | 0 | 2 |

| | | | |
|---|---|---|---|
| ZNF441 | 2 | 0 | 2 |
| ZNF471 | 2 | 0 | 2 |
| ZNF491 | 2 | 0 | 2 |
| ZNF513 | 2 | 0 | 2 |
| ZNF540 | 2 | 0 | 2 |
| ZNF546 | 2 | 0 | 2 |
| ZNF563 | 2 | 0 | 2 |
| ZNF564 | 2 | 0 | 2 |
| ZNF568 | 2 | 0 | 2 |
| ZNF584 | 2 | 0 | 2 |
| ZNF597 | 2 | 0 | 2 |
| ZNF610 | 2 | 0 | 2 |
| ZNF619 | 2 | 0 | 2 |
| ZNF620 | 2 | 0 | 2 |
| ZNF622 | 2 | 0 | 2 |
| ZNF680 | 2 | 0 | 2 |
| ZNF687 | 2 | 0 | 2 |
| ZNF701 | 2 | 0 | 2 |
| ZNF71 | 2 | 0 | 2 |
| ZNF800 | 2 | 0 | 2 |
| ZNF804B | 2 | 0 | 2 |
| ZNF813 | 2 | 0 | 2 |
| ZNF823 | 2 | 0 | 2 |
| ZNF862 | 2 | 0 | 2 |
| ZP2 | 2 | 0 | 2 |
| ZPBP | 2 | 0 | 2 |
| ZRANB1 | 2 | 0 | 2 |
| ZRANB3 | 2 | 0 | 2 |
| ZSCAN21 | 2 | 0 | 2 |
| ZSCAN29 | 2 | 0 | 2 |
| ZWINT | 2 | 0 | 2 |

**eTable 5. Most frequently mutated genes identified to be associated with chemosensitivity in the TCGA discovery cohort.**

| Gene Symbol* | No. (%) of patients harboring mutations | Gene size (Kb) | P value (passenger probability)† |
|---|---|---|---|
| *ADAMTS16* | 9 (4.3) | 4.97 | $9.90 \times 10^{-5}$ |
| *BRCA2* | 9 (4.3) | 11.39 | $2.33 \times 10^{-2}$ |
| *MAGEC1* | 8 (3.8) | 4.34 | $2.09 \times 10^{-4}$ |
| *VPS11* | 8 (3.8) | 3.28 | $3.10 \times 10^{-5}$ |
| *ZNFX1* | 8 (3.8) | 7.37 | $5.70 \times 10^{-3}$ |

* Genes mutated in chemosensitive samples but not in any chemoresistant cases. Included are the five most frequently mutated genes.

† We estimated P values on the basis of the number of patients harboring mutations in each gene, the gene size and the background mutation rate (approximately $1.7x10^{-06}$) reported in the TCGA OvCa sample cohort [Nature 2011;474:609-615].

**eTable 6. Chemotherapy response status and clinicopathologic characteristics of OvCa patients with different ADAMTS statuses in the TCGA discovery cohort.***

| | **Discovery cohort** (n=210) | **ADAMTS wild-type** (n=187) | **ADAMTS mutation** (n=23) | ***P*†** |
|---|---|---|---|---|
| **Chemotherapy Response‡** | | | | |
| Resistance | 69 (33) | 69 (37) | 0 (0) | |
| Sensitive | 141 (67) | 118 (63) | 23 (100) | <0.001¶ |
| **BRCA status** | | | | |
| Wild-type | 168 (80) | 152 (81) | 16 (70) | |
| Mutant | 42 (20) | 35 (19) | 7 (30) | 0.26¶ |
| **Age** | | | | |
| Mean, years [SD] | 60.3 [11.3] | 60.3 [11.3] | 60.4 [11.8] | |
| Range | 30.5-87.5 | 30.5 – 87.5 | 40.0 – 78.1 | 0.84** |
| **FIGO Stage§** | | | | |
| II | 7 (3) | 7 (4) | 0 (0) | |
| III / IV | 203 (97) | 180 (96) | 23 (100) | 1.00¶ |
| **WHO Grade** | | | | |
| 2 | 16 (8) | 15 (8) | 1 (5) | |
| 3 | 189 (92) | 168 (92) | 21 (95) | 1.00¶ |
| Unknown | 5 | 4 | 1 | |
| **Residual tumor size, mm‖** | | | | |
| 0 | 42 (22) | 37 (22) | 5 (24) | |
| 1 - 20 | 113 (60) | 99 (59) | 14 (67) | |
| > 20 | 34 (18) | 32 (19) | 2 (9) | 0.79¶# |
| Unknown | 21 | 19 | 2 | |

Abbreviations: TCGA, The Cancer Genome Atlas; SD, standard deviation; FIGO, the International Federation of Gynecology and Obstetrics; WHO, World Health Organization.

* Values are reported as No. (%). Missing values are excluded from the percentage calculation and statistical test.

† Statistical test (*P* value) between ADAMTS carriers and ADAMTS non-carriers.

‡ Platinum status was defined as resistant if the platinum-free interval was less than 6 months and the patient had experienced progression or recurrence. Platinum status was defined as sensitive if the platinum-free interval was 6 months or more, there was no evidence of progression or recurrence, and the follow-up interval was at least 6 months from the date of the last primary platinum treatment.

§ Cases were staged according to the 1988 FIGO staging system.

‖ Residual tumor size was defined as the size of residual disease at the conclusion of the primary surgical procedure. Patients with no macroscopic disease were labeled as 0 mm. Patients were divided into three groups on the basis of this parameter, patients with no macroscopic disease (0 mm), patients with residual tumor size between 1 and 20 mm (1 – 20), and patients with residual tumor size of greater than 20 mm (> 20).

¶ Fisher's exact test.

# tumors with no macroscopic disease versus tumors with macroscopic disease.

** Mann-Whitney test.

**eTable 7. Chemotherapy response status and clinicopathologic characteristics of OvCa patients with different ADAMTS statuses in the TCGA validation cohort.[*]**

| | **Validation cohort** (n=302) | **ADAMTS wild-type** (n=272) | **ADAMTS mutation** (n=30) | ***P*†** |
|---|---|---|---|---|
| **Chemotherapy Response‡** | | | | |
| Resistance | 15 (28) | 15 (32) | 0 (0) | |
| Sensitive | 38 (72) | 32 (68) | 6 (100) | 0.17¶ |
| Unknown | 249 | 225 | 24 | |
| **BRCA status** | | | | |
| Wild-type | 264 (87) | 240 (88) | 24 (80) | |
| mutant | 38 (13) | 32 (12) | 6 (20) | 0.24¶ |
| **Age** | | | | |
| Mean, years [SD] | 59.8 [11.6] | 59.8 [11.7] | 59.3 [11.0] | |
| Range | 27.2-84.7 | 27.2 – 84.7 | 40.4 – 81.7 | 0.82** |
| **FIGO Stage§** | | | | |
| II | 15 (6) | 9 (4) | 6 (23) | |
| III / IV | 219 (94) | 199 (96) | 20 (77) | 0.0027¶ |
| Unknown | 68 | 64 | 4 | |
| **WHO Grade** | | | | |
| 2 | 34 (15) | 31 (15) | 3 (12) | |
| 3 | 196 (85) | 173 (85) | 23 (88) | 0.78¶ |
| Unknown | 72 | 68 | 4 | |
| **Residual tumor size, mm‖** | | | | |
| 0 | 40 (20) | 38 (21) | 2 (9) | |
| 1 - 20 | 118 (58) | 106 (59) | 12 (55) | |
| > 20 | 45 (22) | 37 (20) | 8 (36) | 0.26¶# |
| Unknown | 99 | 91 | 8 | |

Abbreviations: TCGA, The Cancer Genome Atlas; SD, standard deviation; FIGO, the International Federation of Gynecology and Obstetrics; WHO, World Health Organization.

* Values are reported as No. (%). Missing values are excluded from the percentage calculation and statistical test.

† Statistical test (*P* value) between ADAMTS carriers and ADAMTS non-carriers.

‡ Platinum status was defined as resistant if the platinum-free interval was less than 6 months and the patient had experienced progression or recurrence. Platinum status was defined as sensitive if the platinum-free interval was 6 months or more, there was no evidence of progression or recurrence, and the follow-up interval was at least 6 months from the date of the last primary platinum treatment.

§ Cases were staged according to the 1988 FIGO staging system.

‖ Residual tumor size was defined as the size of residual disease at the conclusion of the primary surgical procedure. Patients with no macroscopic disease were labeled as 0 mm. Patients were divided into three groups on the basis of this parameter, patients with no macroscopic disease (0 mm), patients with residual tumor size between 1 and 20 mm (1 – 20), and patients with residual tumor size of greater than 20 mm (> 20).

¶ Fisher's exact test.

# tumors with no macroscopic disease versus tumors with macroscopic disease.

** Mann-Whitney test.

**eTable 8. Median follow-ups of OvCa patients in different cohorts**

| | Median Follow-up, months (patients included)* | | | Ratio of Median Follow-up† | |
|---|---|---|---|---|---|
| **Cohorts** | **Discovery [n = 210]** | **Validation [n = 302]** | **Combined [n = 512]** | **Validation cohort** | **Combined cohort** |
| OS | 37.8 (209) | 16.8 (232) | 29.8 (441) | 0.44 | 0.79 |
| PFS | 14.7 (210) | 9.8 (156) | 13.5 (366) | 0.67 | 0.92 |
| PFI | 9.6 (204) | 5.4 (83) | 8.5 (287) | 0.56 | 0.88 |

Abbreviations: OS, overall survival; PFS, progression-free survival; PFI, platinum-free interval; NA, not applicable.

* Some cases were excluded from these analyses because of missing or incomplete data or a negative platinum-free survival duration (Nature 2011;474:609-615). The numbers in the parenthesis indicated the number of patients that was used in the analyses.

† denotes median follow-up ratio of other OvCa cohorts versus TCGA Discovery cohort.

**eTable 9. Chemotherapy response status and clinicopathologic characteristics of OvCa patients with different ADAMTS statuses in the TCGA combined cohort.[*]**

| | **Combined cohort** (n=512) | **ADAMTS wild-type** (n=459) | **ADAMTS mutation** (n=53) | ***P*†** |
|---|---|---|---|---|
| **Chemotherapy Response‡** | | | | |
| Resistance | 84 (32) | 84 (36) | 0 (0) | |
| Sensitive | 179 (68) | 150 (64) | 29 (100) | <0.001¶ |
| Unknown | 249 | 225 | 24 | |
| **BRCA status** | | | | |
| Wild-type | 432 (84) | 392 (85) | 40 (75) | |
| mutant | 80 (16) | 67 (15) | 13 (25) | 0.07¶ |
| **Age** | | | | |
| Mean, years [SD] | 60.0 [11.5] | 60.0 [11.5] | 59.8 [11.3] | |
| Range | 27.2-87.5 | 27.2 – 87.5 | 40.0 – 81.7 | 0.97** |
| **FIGO Stage§** | | | | |
| II | 22 (5) | 16 (4) | 6 (12) | |
| III / IV | 422 (95) | 379 (96) | 43 (88) | 0.025¶ |
| Unknown | 68 | 64 | 4 | |
| **WHO Grade** | | | | |
| 2 | 50 (11) | 46 (12) | 4 (8) | |
| 3 | 385 (89) | 341 (88) | 44 (92) | 0.63¶ |
| Unknown | 77 | 72 | 5 | |
| **Residual tumor size, mm‖** | | | | |
| 0 | 82 (21) | 75 (21) | 7 (16) | |
| 1 - 20 | 231 (59) | 205 (59) | 26 (61) | |
| > 20 | 79 (20) | 69 (20) | 10 (23) | 0.55¶# |
| Unknown | 120 | 110 | 10 | |

Abbreviations: TCGA, The Cancer Genome Atlas; SD, standard deviation; FIGO, the International Federation of Gynecology and Obstetrics; WHO, World Health Organization.

* Values are reported as No. (%). Missing values are excluded from the percentage calculation and statistical test.

† Statistical test (*P* value) between ADAMTS carriers and ADAMTS non-carriers.

‡ Platinum status was defined as resistant if the platinum-free interval was less than 6 months and the patient had experienced progression or recurrence. Platinum status was defined as sensitive if the platinum-free interval was 6 months or more, there was no evidence of progression or recurrence, and the follow-up interval was at least 6 months from the date of the last primary platinum treatment.

§ Cases were staged according to the 1988 FIGO staging system.

‖ Residual tumor size was defined as the size of residual disease at the conclusion of the primary surgical procedure. Patients with no macroscopic disease were labeled as 0 mm. Patients were divided into three groups on the basis of this parameter, patients with no macroscopic disease (0 mm), patients with residual tumor size between 1 and 20 mm (1 – 20), and patients with residual tumor size of greater than 20 mm (> 20).

¶ Fisher's exact test.

# tumors with no macroscopic disease versus tumors with macroscopic disease.

** Mann-Whitney test.

**eTable 10. Univariate and multivariate Cox proportional hazards model analyses for overall survival, progression-free survival and platinum-free survival in women with ovarian cancer in the TCGA combined cohort***

| | | Univariate Analysis | | | Multivariate Analysis‡ | |
|---|---|---|---|---|---|---|
| | **Variable** | HR (95%CI)† | P value§ | | HR (95%CI)† | P value§ |
| **Overall Survival** | ADAMTS status | | | | | |
| | Wild-type | 1 [Ref] | | | 1 [Ref] | |
| | mutation | 0.54(0.34– 0.87) | 0.011 | | 0.53(0.32-0.87) | 0.012 |
| | BRCA status | | | | | |
| | Wild-type | 1 [Ref] | | | 1 [Ref] | |
| | mutation | 0.43(0.28–0.66) | <0.001 | | 0.44(0.28-0.69) | <0.001 |
| | Tumor Stage | | | | | |
| | II | 1 [Ref] | | | 1 [Ref] | |
| | III and IV | 2.95(1.22–7.18) | 0.017 | | 3.33(1.06-10.49) | 0.040 |
| | Residual tumor size, mm | | | | | |
| | 0‖ | 1[Ref] | | | 1 [Ref] | |
| | 1 - 20 | 2.10(1.33-3.29) | 0.001 | | 1.85(1.18-2.92) | 0.008 |
| | > 20 | 2.50(1.49-4.21) | 0.001 | | 2.05(1.21-3.46) | 0.007 |
| | Age at diagnosis, yr | 1.02(1.01-1.04) | <0.001 | | 1.02(1.01-1.04) | 0.001 |
| **Progression-free Survival** | ADAMTS status | | | | | |
| | Wild-type | 1 [Ref] | | | 1 [Ref] | |
| | mutation | 0.42(0.28-0.64) | <0.001 | | 0.40(0.25-0.62) | <0.001 |
| | BRCA status | | | | | |
| | Wild-type | 1 [Ref] | | | 1 [Ref] | |
| | mutation | 0.60(0.43-0.85) | 0.004 | | 0.63(0.44-0.91) | 0.014 |
| | Tumor Stage | | | | | |
| | II | 1 [Ref] | | | 1 [Ref] | |
| | III and IV | 2.44(1.29-4.59) | 0.006 | | 2.46(1.14-5.29) | 0.022 |
| | Residual tumor size, mm | | | | | |
| | 0‖ | 1 [Ref] | | | 1 [Ref] | |
| | 1 - 20 | 1.81(1.27-2.57) | 0.001 | | 1.80(1.26-2.58) | 0.001 |
| | > 20 | 1.78(1.16-2.74) | 0.008 | | 1.59(1.02-2.47) | 0.040 |
| | Age at diagnosis, yr | 1.00(0.99-1.01) | 0.889 | | 1.00(0.99-1.01) | 0.819 |
| **Platinum-free Survival** | ADAMTS status | | | | | |
| | Wild-type | 1 [Ref] | | | 1 [Ref] | |
| | mutation | 0.48(0.30– 0.76) | 0.002 | | 0.45(0.28-0.73) | 0.001 |
| | BRCA status | | | | | |
| | Wild-type | 1 [Ref] | | | 1 [Ref] | |
| | mutation | 0.62(0.43–0.90) | 0.011 | | 0.62(0.42-0.92) | 0.018 |
| | Tumor Stage | | | | | |
| | II | 1 [Ref] | | | 1 [Ref] | |
| | III and IV | 2.12(1.04–4.30) | 0.038 | | 1.89(0.83-4.29) | 0.130 |
| | Residual tumor size, mm | | | | | |
| | 0‖ | 1[Ref] | | | 1 [Ref] | |
| | 1 - 20 | 1.63(1.13-2.35) | 0.009 | | 1.63(1.12-2.36) | 0.010 |
| | > 20 | 1.60(1.02-2.50) | 0.040 | | 1.50(0.95-2.37) | 0.083 |
| | Age at diagnosis, yr | 1.00(0.99-1.02) | 0.443 | | 1.01(0.99-1.02) | 0.372 |

* Included are data from the TCGA combined cohort including total 512 OvCa patients. Patient characteristics was detailed in Supplementary Table 1. BRCA mutations include somatic and germline mutations of *BRCA1* and *BRCA2*. Both *ADAMTS* and *BRCA1/2* mutations are depicted in eFigure 24 in the Supplement.

† HR, hazard ratio; CI, confidence interval.

‡ Based on a multivariate Cox proportional hazards model, including all variables in the table.

§ Wald's test, *P* values.

‖ Patients with no macroscopic disease are labeled as 0 mm.

**eReferences**


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