original reports

Validation of the DNA Damage Immune Response Signature in Patients With Triple-Negative Breast Cancer From the SWOG 9313c Trial

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abstract

PURPOSE To independently validate two biomarkers, a 44-gene DNA damage immune response (DDIR) signature and stromal tumor-infiltrating lymphocytes (sTILs), as prognostic markers in patients with triple-negative breast cancer (TNBC) treated with adjuvant doxorubicin (A) and cyclophosphamide (C) in SWOG 9313.

METHODS Four hundred twenty-five centrally determined patient cases with TNBC from S9313 were identified. DDIR signature was performed on RNA isolated from formalin-fixed paraffin-embedded tumor tissue, and samples were classified as DDIR negative or positive using predefined cutoffs. Evaluation of sTILs was performed as described previously. Markers were tested for prognostic value for disease-free survival (DFS) and overall survival (OS) using Cox regression models adjusted for treatment assignment, nodal status, and tumor size.

RESULTS Among 425 patients with TNBC, 33% were node positive. DDIR was tested successfully in 90% of patients (381 of 425), 62% of which were DDIR signature positive. DDIR signature positivity was associated with improved DFS (hazard ratio [HR], 0.67; 95% CI, 0.48 to 0.92; $P = .015$) and OS (HR, 0.61; 95% CI, 0.43 to 0.89; $P = .010$). sTILs density assessment was available in 99% of patients and was associated with improved DFS (HR, 0.70; 95% CI, 0.51 to 0.96; $P = .026$ for sTILs density $\geq 20\%$ $v < 20\%$) and OS (HR, 0.59; 95% CI, 0.41 to 0.85; $P = .004$ for sTILs density $\geq 20\%$ $v < 20\%$). DDIR signature score and sTILs density were moderately correlated ($r = 0.60$), which precluded statistical significance for DFS in a joint model. Three-year DFS and OS in a subgroup of patients with DDIR positivity and T1c/T2N0 disease were 88% and 94%, respectively.

CONCLUSION The prognostic role of sTILs and DDIR in early-stage TNBC was confirmed. DDIR signature conferred improved prognosis in two thirds of patients with TNBC treated with adjuvant AC. DDIR signature has the potential to stratify outcome and to identify patients with less projected benefit after AC chemotherapy.

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ASSOCIATED CONTENT

Appendix

Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

Triple-negative breast cancer (TNBC) accounts for 15% to 20% of breast cancer and carries a poor prognosis. Despite receiving adjuvant anthracycline/taxane-based chemotherapy, approximately 20% to 40% of patients with early-stage TNBC develop metastatic disease.[1-3] Biomarkers that can prospectively select patients with TNBC with good outcomes after anthracycline-based adjuvant chemotherapy, or alternatively, that identify mechanisms of resistance to this treatment strategy, will optimize personalization of adjuvant chemotherapy for TNBC.

Although TNBC is rather uniformly treated in clinical practice, distinct biologic subgroups exist.[4] In particular, more than one half of TNBC tumors have molecular and genomic characteristics similar to *BRCA1/2*-mutant disease, described as BRCAness.[5,6] The Fanconi anemia/BRCA repair pathway is required for coordination of DNA repair mechanisms, including homologous recombination, which is essential for the repair of stalled DNA replication forks.[7] Loss of function of this pathway by mutation, promoter hypermethylation, or other epigenetic events results in genomic instability and DNA damage response deficiency, leading to reliance on less robust DNA repair mechanisms such as nonhomologous end joining.[8] BRCAness has also been reported to be associated with increased tumor lymphocytic infiltration and upregulation of immune gene expression.[6,9]

The DNA damage immune response (DDIR) signature (formerly the DNA damage repair deficient signature) is a 44-gene RNA-based signature developed to identify patients with immune activation as a result of DNA damage response deficiency. Importantly, this signature represents activation of the cyclic GMP–AMP synthase (cGAS)–stimulator of interferon genes (STING) immune pathway and is characterized by increased immune gene expression.[10] This functional approach allows the capture of multiple mechanisms of loss of DNA repair, resulting in a common gene expression signature. The 44-gene DDIR signature includes well-known immune checkpoint targets such as programmed death-ligand 1 and Indoleamine 2,3-dioxygenase 1, as well as several inflammatory cytokines. Constitutive activation of the cGAS-STING innate immune pathway in DDIR signature-positive cancer cells has been reported.[10] Tumor-specific immune activation via the STING pathway results in infiltration by T lymphocytes and upregulation of immune checkpoints, creating an inflammatory microenvironment.[11,12] In preliminary studies, when applied as a predefined binary cutoff, the DDIR signature has been shown to predict response to anthracycline-based treatment in both neoadjuvant and adjuvant settings, in hormone receptor-positive and receptor-negative breast cancer.[13] However, evaluation of the DDIR signature in a large, uniformly treated patient population with TNBC with long-term outcome data has not been performed previously.

We hypothesized that a subgroup of patients with TNBC identified using the DDIR signature would derive increased benefit from adjuvant doxorubicin plus cyclophosphamide (AC)–based DNA-damaging chemotherapy by virtue of decreased repair of the DNA damage induced by the treatment. We also sought to examine the association between stromal tumor-infiltrating lymphocytes (sTILs) and loss of DNA repair capacity as measured by the DDIR signature. To test these hypotheses, we used a cohort of 425 patients with early-stage TNBC treated with uniform adjuvant AC on the SWOG S9313 protocol.

METHODS

Patients

Patient selection, signature performance, and data analysis are reported according to Reporting Recommendations for Tumor Marker Prognostic Studies (REMARK) criteria.[14] Breast tumor sections from paraffin blocks collected prospectively from S9313 participants were used for this study. In S9313, patients with either high-risk (tumor size 1 cm or larger) node-negative or node-positive breast cancer were randomly assigned to one of two equivalent dose schedules of AC chemotherapy, given either sequentially or concurrently.[15] There was no significant difference in disease-free survival (DFS) or overall survival (OS) between arms.[15] Study population and treatment schedule details are provided in the Protocol. Investigators performed human investigations after approval by a local human investigations committee and in accord with an assurance filed with and approved by the Department of Health and Human Services. Informed consent from each participant or each participant's guardian was obtained. The current translational work was reviewed and approved by the National Cancer Institute Cancer Therapy Evaluation Program's Breast Cancer Steering Committee.

Estrogen receptor and progesterone receptor were determined locally and centrally (Allred scoring method; a score of 0 was considered negative). Human epidermal growth factor receptor 2 was determined centrally by immunohistochemistry and fluorescence in situ hybridization.[16] TNBC was defined as estrogen receptor and progesterone receptor negative (on both local and central review) and human epidermal growth factor receptor 2–negative in accordance with 2013 ASCO–College of American Pathologists testing guidelines.[17] Laboratories performing biomarker analyses were blinded to patient characteristics and outcomes. Selection of the 425 patients with TNBC has been described previously.[18]

Gene Expression Profiling

As described previously, microarray profiling was performed on total RNA extracted from pretreatment formalin-fixed paraffin-embedded breast tissue sections using the High Pure RNA Paraffin Kit (Roche Diagnostics, Mannheim, Germany) in a Clinical Laboratory Improvement Amendments–certified laboratory (Almac Diagnostics, Craigavon, UK).[13] Tumor macrodissection per standard operating procedure for the DDIR signature was not possible; therefore, RNA was extracted from the whole tissue section.[13] RNA was amplified using the WT-Ovation FFPE RNA Amplification System (NuGEN Technologies, San Carlos, CA) and hybridized to the Xcel Array (Protocol). Samples were randomly assigned to extraction and amplification batches on the basis of clinical and technical factors to ensure a balance of samples across the study while minimizing bias and batch effects.

Generation of DDIR Signature Scores

Microarray quality control analysis was performed to identify samples of suitably high quality before application of the DDIR signature, with appropriate analysis conducted to ensure no batch effects were observed. Each sample was independently corrected for background noise and normalized using a predefined quantile normalization model, and median summarization of probes to genes was calculated before applying the DDIR algorithm as described previously.[13] A potential limitation of the DDIR assay published in the original manuscript was the requirement for macrodissected tissue.[13] In clinical studies, such as the current one, tumor sections may have already been archived and may not be suitable for macrodissection. We therefore used an independent technical data set to identify a correction factor for non-macrodissected material (Protocol). Subsequently, DDIR scores from the S9313 cohort were adjusted for tumor percentage as defined by the central pathologist to account for non-macrodissected tissue samples and to control the proportion of tumor cells versus other cell types (Protocol). A previously published and predefined threshold of 0.3681 was used to define signature positivity.[13] Appendix Table A1 (online only) lists the 44 genes composing the DDIR signature.

Immunoregulatory Gene Expression and DDIR Status

Differential gene expression analysis was performed between DDIR signature-positive and DDIR signature-negative patients. Differentially expressed genes (DEGs) are defined on the basis of a fold change > 1.5 and an adjusted *P* value of .05 between DDIR signature-positive and DDIR signature-negative patients. Functional analysis of the resulting gene list allowed for the identification of genes and biologic processes linked to an immune-related function. Additional information is provided in the Protocol.

sTILs Assessment

Histopathologic determination of sTILs density was assessed using a single hematoxylin and eosin–stained invasive tumor section. Slide reviews were jointly performed by two independent breast histopathologists (S.B. and Y.G.-P.), who were blinded to outcome information, according to previously described criteria.[19,20] sTILs density is reported as a percentage estimate in increments of 10.

Statistical Analyses

DFS was defined as the time from registration to first invasive recurrence (local, regional, or distant), new primary invasive cancer in the contralateral breast, or death from any cause. OS was defined as the time from registration to death from any cause. Patients were censored on the date of last contact if an event had not been observed. Survival was assessed by the Kaplan-Meier method. Markers were tested for prognostic effect on DFS and OS using a Cox regression model and likelihood ratio tests adjusting for randomly assigned treatment, nodal status (positive/negative), and tumor size. The C-statistic, which is interpretable as the area under the curve in a receiver operating characteristic model and ranges from chance (0.50) to perfect (1.0), is reported. All reported *P* values and CIs are from two-sided tests. Statistical testing was performed in Stata version 15.1.

The estimated effect of DDIR status and sTILs density, both separately and together, was tested in a multivariable Cox model adjusted for nodal status, tumor size, and randomly assigned treatment. The Cox proportional hazards assumption was verified using a statistical test based on the Schoenfeld residuals. DDIR signature was also investigated as a continuous predictor of both DFS and OS (Protocol).

RESULTS

Identification of the Study Population

Selection of the 425 patients with TNBC from S9313 is provided in Figure 1. We have reported previously that DFS and OS were similar for participants of S9313 with and without archived tissue specimens.[21]

Patient Demographics

Demographic and clinical characteristics of the 425 patients with TNBC are described in Table 1. Median age at diagnosis was 46 years, and 33% of patients were node positive. At a median follow-up of 12.6 years, there were 166 DFS and 129 OS events.

Biomarker Result Availability

DDIR assessment was available for 89.6% (381 of 425 patients), and sTILs assessment was available for 99.5% (423 of 425 patients; reasons for biomarker unavailability are provided in the Protocol and Fig 1). Descriptive characteristics of DDIR scores and sTILs percentages are listed in Appendix Table A2 (online only) overall and by tumor characteristics. Baseline patient characteristics were similar between the full cohort (N = 425) and the DDIR-determined cohort (n = 381; Table 1). There was no difference in DFS or OS by DDIR status known or unknown (log-rank *P* = .84 for DFS and *P* = .95 for OS).

Association of DDIR Signature Status With Patient Outcomes

For the 381 patients with available DDIR signature results, 62% (238 of 381) were DDIR positive (on the basis of the predefined threshold of 0.3681). DDIR score was not associated with patient age, ethnicity, nodal status, tumor size, or randomly assigned treatment regimen. Five-year and 10-year DFS and OS estimates are listed in Table 2 by DDIR positivity and separately by sTILs percentage with a cutoff of 20%. When focusing on patients with T1c/T2 node-negative disease, 3- and 5-year DFS and OS estimates by DDIR status and sTILs percentage are listed in Appendix Table A3 (online only). Three and 5-year OS were 94% and 89%, respectively, for patients with T1c/T2 node-negative disease and DDIR positivity.

DDIR signature positivity was associated with improved DFS (hazard ratio [HR], 0.67; 95% CI, 0.48 to 0.92; *P* = .015) and OS (HR, 0.61; 95% CI, 0.43 to 0.89; *P* = .010), adjusting for treatment arm, nodal status, and tumor size (Table 3, model 1, Figs 2A and 2B). In addition, when modeled as a continuous variable, a higher DDIR score was associated with improved DFS (HR, 0.91; 95% CI, 0.86 to 0.97 for a 0.10 increase in score; *P* = .001) and improved OS (HR, 0.91; 95% CI, 0.85 to 0.97 for a 0.10 increase in score; *P* = .003; Table 3, model 2).

Association of sTILs With Patient Outcomes

For the 423 patients with available sTILs density results, 43% (184 of 423) demonstrated sTILs density ≥ 20%. sTILs density was not associated with patient age, ethnicity, T stage, nodal status, or randomly assigned treatment regimen. Increasing sTILs density was positively associated with better DFS and OS. When sTILs density was assessed as a binary variable (≥ 20% *v* < 20%), patients with sTILs density ≥ 20% exhibited significantly improved DFS and OS in comparison with patients with sTILs density less than 20% (HR, 0.70; 95% CI, 0.51 to 0.96; *P* = .026, and HR, 0.59; 95% CI, 0.41 to 0.85; *P* = .004, respectively; Table 3, model 3, Figs 2C and 2D). In addition, when assessed as a continuous variable, higher sTILs density was associated

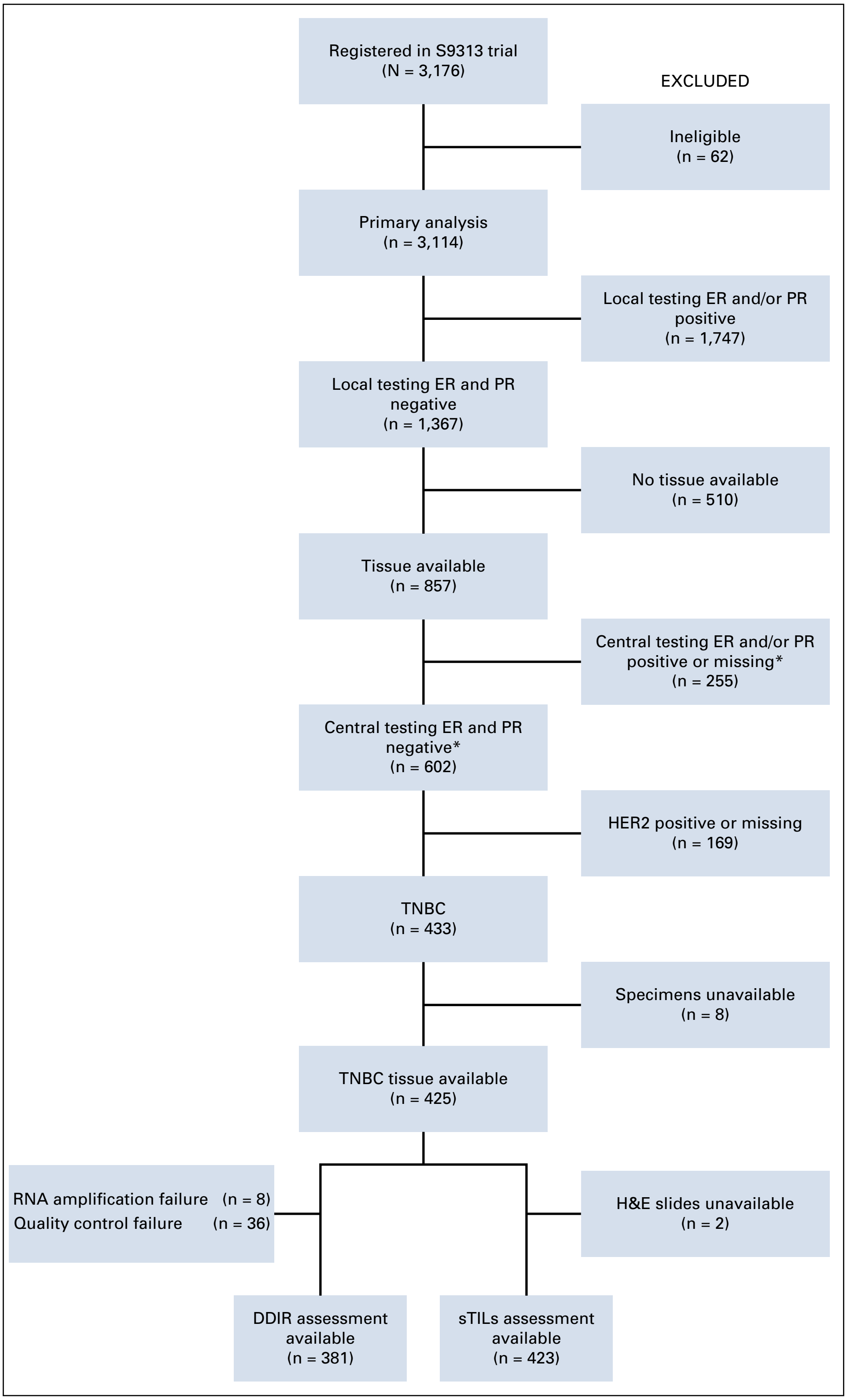

FIG 1. Reporting Recommendations for Tumor Marker Prognostic Studies (REMARK) diagram showing biomarker study subset of SWOG S9313 trial. (*) Central ER and PR testing were performed using the Allred scoring method. For the purpose of this biomarker study, ER and/or PR score > 0 was considered positive. DDIR, DNA damage immune response; ER, estrogen receptor; H&E, hematoxylin and eosin; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor; sTILs, stromal tumor-infiltrating lymphocytes; TNBC, triple-negative breast cancer.

with improved outcomes. For every 10% increase in sTILs density, there was improvement in DFS (HR, 0.86; 95% CI, 0.78 to 0.96; *P* = .005) and OS (HR, 0.82; 95% CI, 0.72 to 0.93; *P* = .001; Table 3, model 4).

Association of DDIR Scores With sTILs

DDIR signature score and sTILs density were moderately correlated, whereby higher DDIR scores were associated with increased sTILs density (Pearson $r = 0.60$; Fig 3),

TABLE 1. Demographic and Clinical Characteristics of the TNBC Study Cohort

Characteristic	All (N = 425)	DDIR Determined (n = 381)	DDIR Negative (n = 143)	DDIR Positive (n = 238)	P
Mean age, years (range)	45.6 (22-74)	45.6 (22-74)	46.4 (22-74)	45.1 (26-73)	.22
Nodal status, No. (%)					.65
Negative	285 (67.1)	262 (68.8)	96 (67.1)	166 (69.8)	
Positive	140 (32.9)	119 (31.2)	47 (32.9)	72 (30.2)	
Race/ethnicity, No. (%)					.58
White	364 (85.7)	324 (85.0)	125 (87.4)	199 (83.6)	
Black	54 (12.7)	51 (13.4)	16 (11.2)	35 (14.7)	
Asian	3 (0.7)	3 (0.8)	1 (0.7)	2 (0.8)	
Native American	1 (0.2)	1 (0.3)	0 (0.0)	1 (0.4)	
Unknown	3 (0.7)	2 (0.5)	1 (0.7)	1 (0.4)	
Randomly assigned treatment, No. (%)					1.00
Combined AC	220 (51.8)	198 (52.0)	74 (51.8)	124 (52.1)	
Sequential AC	205 (48.2)	183 (48.0)	69 (48.2)	114 (47.9)	
Tumor size, No. (%)					.27
T1c	133 (31.3)	111 (29.1)	37 (25.9)	74 (29.1)	
T2	262 (61.6)	244 (64.0)	93 (65.0)	151 (63.4)	
T3	30 (7.1)	26 (6.8)	13 (9.1)	23 (5.5)	

Abbreviations: AC, doxorubicin plus cyclophosphamide; DDIR, DNA damage immune response; TNBC, triple-negative breast cancer.

reflecting the correlation between the underpinning biology of the two biomarkers.

Joint Association of DDIR Status and sTILs With Patient Outcomes

Table 3 lists Cox regression analysis of outcome by prognostic factor in a model also adjusting for randomly assigned treatment, nodal status, and tumor size. The *P* value is a likelihood ratio test of the model against clinical-pathologic variables only. When both continuous DDIR and sTILs are modeled jointly in the same model, the C-statistic shows no improvement over either variable alone, likely because of the strong correlation between the two (Table 3, model 5).

Association of Immune Gene Expression With DDIR Signature Status

Because the DDIR score was positively correlated with sTILs density, we explored the relationship between DEGs by DDIR status. In total, 860 probe sets were differentially expressed (777 upregulated and 83 downregulated in DDIR-positive patients). This equates to 422 unique genes with significant differential expression between DDIR-positive and DDIR-negative patients (Appendix Table A4, online only). Forty-nine percent of DEGS (206 of 422; mostly upregulated in DDIR-positive patients) were linked to immune response, suggesting this to be the most significant biologic process in this cohort (Appendix Table A5, online only). Other relevant biologic processes that were upregulated in DDIR-positive tumors were activation/regulation of immune response and cytokine-mediated signaling.

DISCUSSION

In this translational study, using a prespecified cutoff, we observed that 62% of patients with TNBC treated with adjuvant AC in S9313 had DDIR signature-positive

TABLE 2. Biomarkers and Outcome

Biomarker and Outcome	No. (%)	5-Year DFS, % (95% CI)	5-Year OS, % (95% CI)	10-Year DFS, % (95% CI)	10-Year OS, % (95% CI)
DDIR status (n = 381)					
Negative	143 (38)	66.4 (58.1 to 73.5)	77.6 (69.9 to 83.6)	58.4 (49.9 to 66.0)	66.7 (58.2 to 73.8)
Positive	238 (62)	79.3 (73.5 to 83.9)	86.4 (81.4 to 90.2)	71.3 (65.0 to 76.7)	79.0 (73.1 to 83.7)
sTILs (n = 423)					
< 20%	239 (56)	69.8 (63.5 to 75.2)	78.1 (72.3 to 82.9)	62.6 (56.1 to 68.5)	70.2 (63.9 to 75.6)
≥ 20%	184 (43)	80.4 (73.8 to 85.4)	89.1 (83.6 to 92.8)	71.3 (64.1 to 77.3)	79.5 (72.8 to 84.7)

Abbreviations: DDIR, DNA damage immune response; DFS, disease-free survival; OS, overall survival; sTILs, stromal tumor-infiltrating lymphocytes.

TABLE 3. Cox Regression Analysis of Outcome by Prognostic Factor in a Model Also Adjusting for Randomly Assigned Treatment, Nodal Status, and Tumor Size

		Disease-Free Survival				Overall Survival			
Model	**Prognostic Factor**	**HR**	**95% CI**	***P***	**C-Statistic**	**HR**	**95% CI**	***P***	**C-Statistic**
1	DDIR positive *v* negative	0.67	0.48 to 0.92	.015	0.602	0.61	0.43 to 0.89	.010	0.628
2	DDIR score 0.10 absolute change	0.91	0.86 to 0.97	.001	0.609	0.91	0.85 to 0.97	.003	0.632
3	sTILs ≥ 20% *v* < 20%	0.70	0.51 to 0.96	.026	0.596	0.59	0.41 to 0.85	.004	0.627
4	sTILs density 10% absolute change	0.86	0.78 to 0.96	.005	0.598	0.82	0.72 to 0.93	.001	0.625
5	DDRD score 0.10 absolute change	0.94	0.87 to 1.01	.009	0.607	0.94	0.87 to 1.02	.005	0.634
	sTILs density 10% absolute change	0.92	0.80 to 1.06			0.89	0.75 to 1.04		

NOTE. The *P* value is a likelihood ratio test of the addition of the biomarker to a model including the clinical variables only. The C-statistic is interpreted as the area under the receiver operating characteristic curve, with higher values indicating a better fit. Models 1 and 3 each test a single dichotomous factor, whereas models 2 and 4 each test a single continuous factor. Model 5 considers the joint effect of the DNA damage immune response (DDIR) and stromal tumor-infiltrating lymphocytes (sTILs) as continuous variables in the same model (*df* = 2) when added to a model with the clinical variables.

Abbreviations: DDRD, DNA damage repair deficient; HR, hazard ratio.

cancers. Importantly, in the context of adjuvant AC chemotherapy, DDIR positivity was strongly associated with improved DFS (HR, 0.67) and OS (HR, 0.61), independently of other clinicopathologic variables. Moreover, the presence of sTILs was associated with better outcomes, a finding consistent with several prior studies reporting a better prognosis in association with high levels of sTILs for patients with TNBC who receive adjuvant chemotherapy.[19,20,22,23] A recent pooled analysis of nine adjuvant clinical trials demonstrated the prognostic role of sTILs in patients with early-stage TNBC treated with adjuvant chemotherapy.[22] S9313 was not part of this pooled analysis and provides independent validation of these findings. Furthermore, in line with the immune response biology associated with the DDIR signature, a positive correlation between sTILs and DDIR score (r = 0.60) was observed, which masked detection of each variable's independent effect on DFS in a joint model.

Our results may have clinical implications. First, we hypothesized that DDIR positivity might result in better clinical outcomes in patients with TNBC, because chemotherapy would be expected to be more active against tumors with DNA repair deficiency. Indeed, suboptimal outcomes were observed in patients with DDIR signature negativity, with almost 35% suffering a DFS event by 5 years (5-year DFS, 66%). These patients may be better served by investigation of therapies alternative to or in addition to anthracycline-based chemotherapy within clinical trials (eg, antibody-drug conjugates, drugs targeting specific genomic aberrations). Molecular drivers of tumors with low DDIR scores should be investigated further to identify better treatment strategies for these patients, although it is possible that this group could represent a heterogeneous population with several underpinning biologies. Conversely, patients with DDIR positivity and lower clinical-pathologic risk (T1c/T2N0) experienced 3-year DFS of 88% and OS of 94% when treated with AC chemotherapy alone. Identification of such patients destined to have good outcomes may pave the way for de-escalation treatment trials (shorter chemotherapy regimens, nonanthracycline regimens).

Second, the apparent importance of immune regulation in the prognosis for these chemotherapy-treated patients suggests a few important hypotheses. It is known that the presence of sTILs is associated with neo/adjuvant chemotherapy response and good prognosis in TNBC.[19,20,23] Our data suggest that DDIR signature positivity may provide a more objective yet similar effect and may identify a larger proportion of patients with favorable prognosis. Sixty-two percent of patients had tumor DDIR signature positivity, compared with 43% of patients with sTILs ≥ 20 (36% of patients with sTILs ≥ 30%). Five-year DFS for patients with DDIR positivity and sTILs ≥ 20% were similar (79% and 80%, respectively) in the entire population and when evaluated in patients with node-negative T1c/T2 disease (83% and 85%, respectively). We also demonstrate that activation/regulation of immune response is the most significant biologic process in DDIR-positive tumors, suggesting that DDIR-positive tumors may represent a target population for immune checkpoint treatment.

Recently reported encouraging data support the efficacy of immune checkpoint inhibitors (ICIs) in patients with metastatic TNBC.[24,25] In many cancer types, several possible predictive factors have been associated with response and favorable outcomes after ICI therapies, including programmed death-ligand 1 expression in tumor cells and/or immune cells, sTILs density, tumor mutational burden, human leukocyte antigen status, and GI microbiome diversity.[25,26] DDIR signature might also serve as a predictive factor for this treatment class. Constitutive activation of the cGAS-STING innate immune pathway in DDIR-positive cancer cells has been identified previously.[10]

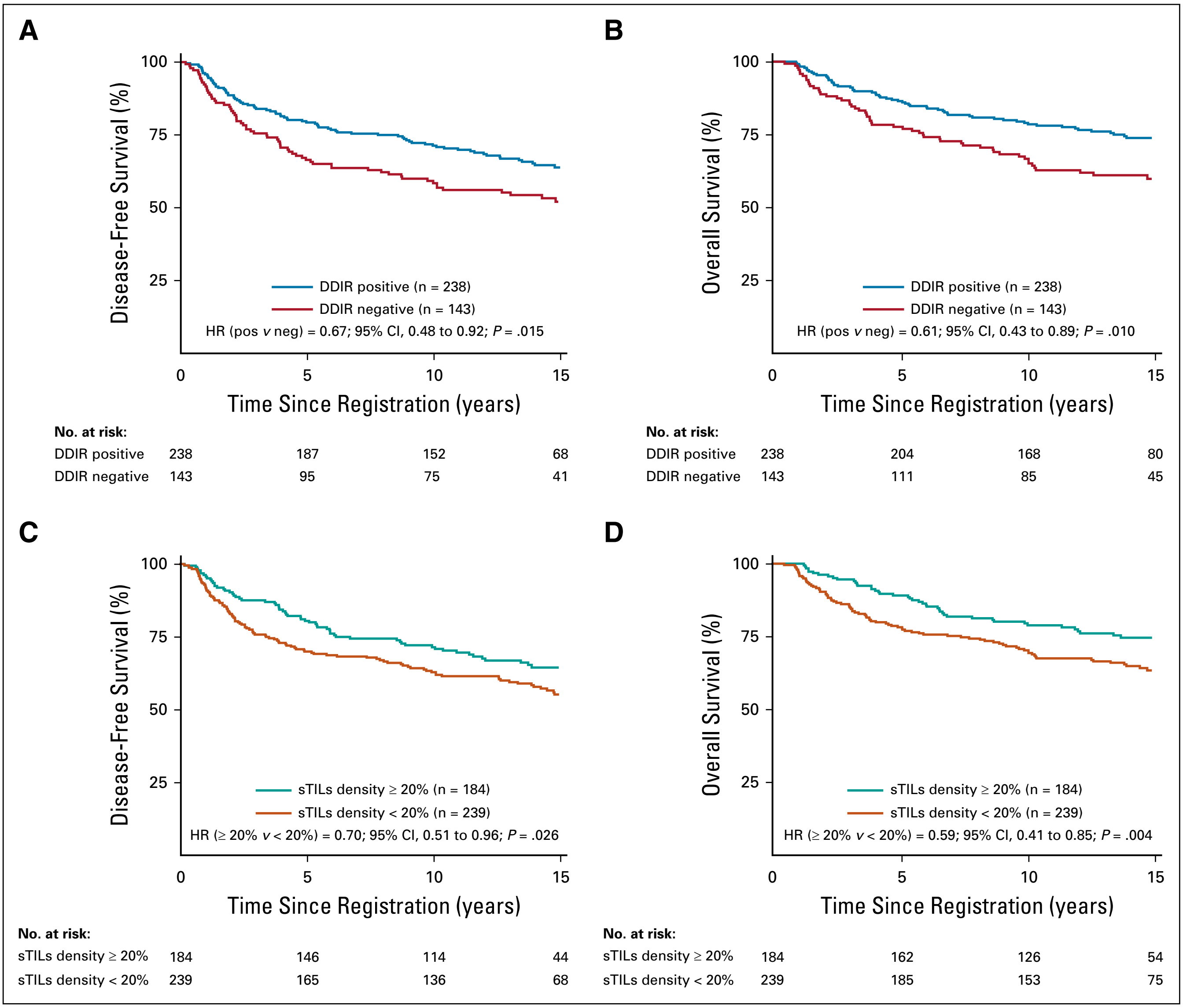

FIG 2. Kaplan-Meier survival analyses predicting (A) disease-free survival and (B) overall survival by DNA damage immune response (DDIR) signature status, and (C) disease-free survival and (D) overall survival by stromal tumor-infiltrating lymphocytes (sTILs) density. DDIR status is depicted as positive (pos) versus negative (neg) on the basis of the predefined cutoff of 0.3681. sTILs density is differentiated into ≥ 20% and < 20% subgroups. HR, hazard ratio.

Chronic STING activation as a result of ineffective DNA repair may promote an inflamed yet immunosuppressive microenvironment that could then potentially be targeted with ICIs.[11,12] Indeed, a DNA damage-sensing pathway signature was shown recently to be associated with response to neoadjuvant pembrolizumab in the I-SPY2 trial.[27] Poly-(ADP-ribose)polymerase (PARP) inhibitors have demonstrated clinical efficacy in *BRCA*-mutant metastatic breast cancer.[28,29] In *BRCA* wild-type tumors, the BRCAness phenotype may be associated with sensitivity to PARP inhibitor therapy, and biomarkers such as DDIR that can identify this phenotype have the potential to aid additional investigation of PARP inhibitors in *BRCA* wild-type cancers.[30,31]

Our study has certain limitations. All patients in the trial received adjuvant AC chemotherapy. It cannot be determined whether DDIR is prognostic in the absence of chemotherapy, or if it is predictive of benefit from AC chemotherapy. Previous retrospective studies have noted that DDIR signature is not prognostic in patients who did not receive neo/adjuvant chemotherapy.[13] These data suggest that our observed association of DDIR positivity with better outcomes is likely indicative of the predictive nature of this signature in the context of AC chemotherapy. Details on the nature of DFS events (distant, locoregional, contralateral breast cancer, and so forth) from S9313 are not readily available; therefore, we were unable to look at other end points such as distant DFS or invasive DFS. S9313 was

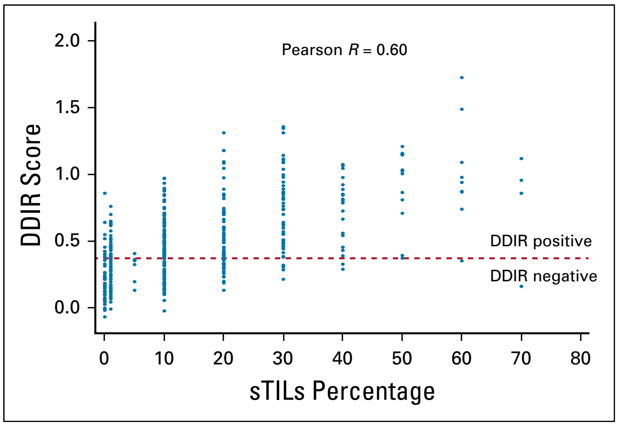

FIG 3. Scatterplot depicting the correlation of DNA damage immune response (DDIR) scores with stromal tumor-infiltrating lymphocytes (sTILs) density percentage in increments of 10 percentage points.

conducted before the demonstration of taxane activity in the adjuvant setting. Thus, we cannot speculate on the impact of DDIR status on taxane benefit, which is currently part of standard neo/adjuvant chemotherapy for TNBC.[32,33] Similarly, data regarding the association of DDIR signature with response to platinum agents in breast cancer are lacking. Although the prognosis of patients with DDIR positivity is superior to those with DDIR negativity, there are currently insufficient data to clinically modify the treatment of TNBC in the adjuvant setting on the basis of DDIR status.

In summary, we have identified the DDIR signature and sTILs as predictive of improved DFS and OS for TNBC in the context of adjuvant AC chemotherapy. There is a clear need to further explore the DDIR signature in prospective stratified studies to elucidate the assay's ability to predict response to DNA-damaging therapies, such as anthracycline, platinum agents, and PARP inhibitors, in breast cancer. Given the direct link with cGAS/STING biology, additional studies are also warranted to assess the ability of the DDIR signature to predict response to immune checkpoint-targeted therapies.

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Validation of the DNA Damage Immune Response Signature in Patients With Triple-Negative Breast Cancer From the SWOG 9313c Trial

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APPENDIX

Methods

S9313 trial details. In S9313, 3,125 women with early-stage breast cancer were recruited from April 1994 through May 1997. Patients were required to have one to three involved nodes or to have high-risk node-negative breast cancer, which was defined as a primary tumor $>$ 2 cm in size or $>$ 1 cm for tumors that were both estrogen and progesterone receptor negative. Patients were randomly assigned to receive either (arm I) doxorubicin and cyclophosphamide given in combination (AC; doxorubicin 54 mg/m^2 and cyclophosphamide 1.2 g/m^2 intravenously [IV] every 3 weeks for six cycles) or (arm II) AC in sequence (A3C; doxorubicin 40.5 mg/m^2 IV days 1 and 2 of a 21-day cycle for four cycles, followed by cyclophosphamide 2.4 g/m^2 IV every 2 weeks for three cycles). Granulocyte colony-stimulating factor was administered on day 3 after cyclophosphamide doses and continued until day 12 or until a postnadir count of 10,000 granulocytes.[15] There was no difference in disease-free survival or overall survival for patients treated on the two arms.[15]

Central human epidermal growth factor receptor 2 testing. Both human epidermal growth factor receptor 2 (HER2) fluorescence in situ hybridization and immunohistochemistry were performed using standard methodology, the details of which have already been published (Jansen MP, et al: J Clin Oncol 25:662-668, 2007).[16] *HER2* fluorescence in situ hybridization was performed using dual-color, direct-label fluorescent in situ hybridization using the *TOP2A*/*CEP17* probe set (Abbott Molecular/Vysis, Des Plaines, IL). HER2 immunohistochemistry procedures were performed on a Dako Autostainer (Dako, Carpinteria, CA). A polyclonal antibody to HER2 (A0485; Dako) was applied at a 1:200 dilution in phosphate-buffered saline to sections and was incubated for 40 minutes at room temperature. With intervening wash steps in phosphate-buffered saline, slides were incubated for 30 minutes at room temperature in a rabbit-specific, labeled polymer (EnVision[15]; Dako), which was followed by 10 minutes at 37°C in a solution that contained 3% hydrogen peroxide and 3,3-diaminobenzidine. Slides were counterstained with hematoxylin.

Immunostained slides were scored according to a modification of the scoring system approved by the US Food and Drug Administration (Gown AM, et al: Mod Path 21:1271-1277, 2008). Only invasive carcinoma was scored among the neoplastic cells. For tumor cells only, membrane staining intensity and pattern were evaluated by using the semiquantitative scale of 0 to $\geq$ 3.

Gene expression profiling. Hematoxylin and eosin (H&E)–stained sections from each patient case were centrally pathology-reviewed by a specialized breast clinical pathologist to quantify the proportion of tumor material and viable tumor cells within the specimen. Total RNA was extracted from formalin-fixed paraffin-embedded tissue curls using the High Pure RNA Paraffin Kit (Roche Diagnostics GmbH, Mannheim, Germany). RNA (required concentration, 12.5 ng/μL) was converted into complementary DNA (cDNA), amplified (required concentration, 140 ng/μL), and converted into a single-stranded form using the SPIA technology of the WT-Ovation FFPE RNA Amplification System (NuGEN Technologies, San Carlos, CA). The amplified cDNA was then fragmented, biotin labeled using the FL-Ovation cDNA Biotin Module (NuGEN Technologies), and hybridized to the Xcel. Arrays were scanned using the Affymetrix Genechip Scanner 7G (Affymetrix, Santa Clara, CA). Stratagene Universal Human Reference samples and ES-2 cell lines were used as process control measures, monitored using statistical process control charts. Quality control (QC) analysis was performed in each cohort.

- Microarray QC: Microarray QC analysis was performed to identify samples of suitably high quality before application of the DNA damage immune response (DDIR) assay. Samples were preprocessed using the robust multiarray average. QC assessment comprised a combination of the following metrics:
- Array image analysis: Array image analysis analyzes Affymetrix CEL files (containing raw intensity data) and assesses if large deviations in background values or unusual patterns in probe intensities exist that may indicate the presence of artifacts or problems with hybridization (such as leakage from the array or uneven washing).
- GeneChip QC: GeneChip QC examines a number of control parameters from the RPT files as supplied by Affymetrix. Full descriptions of these control parameters are available from the Affymetrix Statistical Algorithms Description Document. This assessment facilitates the monitoring of profile quality and allows for the evaluation of assay and hybridization performance. Affymetrix has specified absolute thresholds (lower limit, upper limit, or both limits) for a number of these parameters. In addition, it is expected that data should be comparable for the majority of studies; therefore, an assessment of overall profile similarity is performed using thresholds based on median absolute deviation. Any values outside median $\pm$ 3.5 sigma (sigma defined as 1.4826 times the median absolute deviation) for that metric will be flagged as potential QC outliers.
- Principal component analysis: Principal component analysis is used to detect outliers and (known or unknown) systematic structures using the robust multi-array average preprocessed expression data using the Hotelling T2 and residual Q method.
- Intensity distribution analysis: Histogram plots of normalized expression data are constructed to visualize the distribution patterns of the expression data. Distribution similarity is assessed using the Kolmogorov-Smirnov test. Clinical samples routinely fail data analysis QC assessment if they are flagged in two or more of the microarray QC metrics outlined previously in the text or if a sample had a percent present value below 20%.

DDIR signature scoring adjusted for tumor percentage. To use non–macro-dissected tumor material as input for the DDIR assay, a generalized linear model was developed within an independent technical cohort (n = 156 samples), in which tumor titration data using six ovarian samples were assessed at a number of titration points (0%, 25%, 50%, 75%, and 100%). This fitted model was subsequently applied to the DDIR scores of samples within the S9313 cohort to provide DDIR predictions, adjusted for the effects of tumor percentage resulting from non–macro-dissected sample material.

DDIR assessment as a continuous variable. DDIR assay scores were transformed to a representative continuous scale of 0 to 1 and evaluated against disease-free survival and overall survival end points using hazard ratios from Cox proportional hazards regression, Harrell's C-index, and the area under the receiver operating characteristic curve.

Tumor-infiltrating lymphocytes. Histopathologic analysis of stromal tumor-infiltrating lymphocytes (sTILs) percentages was performed on a single full-face H&E-stained tumor section using previously described criteria.[19,20,23] The density (%) of sTILs was recorded for stromal areas. sTIL density is defined as the percentage of tumor stroma containing infiltrating lymphocytes. Areas of in situ carcinoma and crush artifacts were not included. Histopathologic evaluation of sTILs was jointly performed by two breast pathologists (S.B. and P.P.), who were blinded to the clinical information, including treatment allocation and outcomes. All tumors were evaluated jointly, and the results were reported in increments of 10. A score of 0 was defined as 0% to 1%, all other estimates being rounded up to the next highest decile (ie, 11% to 20% represents a sTIL score of 20).

Differential expression analysis. Preprocessed data were filtered to remove all Affymetrix AFFX control probe sets and uninformative probe sets within the background region (background filtering). Background filtering was performed on the basis of a combination of the expression and the variance, selecting probe sets with an average expression above the threshold defined by σBg at a significance level of α. The variance selects probe sets with a variance above that of the background. A statistical *t* test was performed and corrected for multiple tests applied using the false discovery rate. Differentially expressed genes were defined by a fold change > 1.5 and an adjusted P value of .05. Functional enrichment analysis was performed on the resulting gene list to provide insight into the processed biologic associated with the genes in the list.

Results

DDIR assessment was not available for 44 of the 425 patients (RNA amplification failure, eight; data QC failure, 22; and bridging samples, 14). Assessment of sTILs was not available for two of the 425 patients because of unavailability of H&E slides.

TABLE A1. Genes Detected by the DDIR Assay

Rank	Gene Symbol	Weight	Gene Function
1	CXCL10	0.023	Immune response
2	MX1	0.0226	Immune response
3	IDO1	0.0221	Immune response
4	IFI44L	0.0191	Immune response
5	CD2	0.019	Immune response
6	GBP5	0.0181	Immune response
7	PRAME	0.0177	Cell proliferation, differentiation, and mitosis
8	ITGAL	0.0176	Immune response
9	LRP4	−0.0159	Cell adhesion and cell signaling
10	APOL3	0.0151	Lipid transport and localization
11	CDR1	−0.0149	Immune response
12	FYB	0.0149	Cell proliferation and adhesion
13	TSPAN7	−0.0148	Signal transduction, growth, and motility
14	RAC2	0.0148	Signal transduction, growth, and motility
15	KLHDC7B	0.014	Protein binding
16	GRB14	0.0137	Signal transduction, growth, and motility
17	AC138128.1	−0.0136	Unreported
18	KIF26A	−0.0136	Transport and signaling
19	CD274	0.0133	Immune response
20	CD109	−0.0129	Immune response
21	ETV7	0.0124	Transcriptional regulation
22	MFAP5	−0.0121	Extracellular matrix remodeling
23	OLFM4	−0.0117	Mediation of cell adhesion
24	PI15	−0.0115	Proteolysis
25	FOSB	−0.0111	Immune response
26	FAM19A5	−0.011	Immune response
27	NLRC5	0.0101	Immune response
28	PRICKLE1	−0.0089	Nuclear trafficking
29	EGR1	−0.0086	Transcriptional regulation
30	CLDN10	−0.0086	Cell adhesion
31	ADAMTS4	−0.0085	Proteolysis
32	SP140L	0.0084	DNA, protein, and metal ion binding
33	ANXA1	−0.0082	Immune response
34	RSAD2	0.0081	Immune response
35	ESR1	0.0079	Transcriptional regulation
36	IKZF3	0.0073	Immune response

(continued on following page)

TABLE A1. Genes Detected by the DDIR Assay (continued)

Rank	Gene Symbol	Weight	Gene Function
37	OR2I1P	0.007	Olfactory receptor activity
38	EGFR	−0.0066	Proliferation and apoptosis
39	NAT1	0.0065	Metabolism
40	LATS2	−0.0063	Proliferation and mitosis
41	CYP2B6	0.0061	Metabolism
42	PTPRC	0.0051	Proliferation, differentiation, and mitosis
43	PPP1R1A	−0.0041	Potentiation and meiosis
44	AL137218.1	−0.0017	Unreported

NOTE. Rank, gene symbol, weight, and gene function of the genes detected in the DNA damage immune response (DDIR) signature. Positive weight values are additive to the DDIR signature score. Negative weight values are subtractive from the DDIR signature score.

TABLE A2. Distributions of DDIR Score and sTILs Density

	DDIR Score						sTILs Density					
	All	Node Negative	Node Positive	T1c	T2	T3	All	Node Negative	Node Positive	T1c	T2	T3
No.	381	262	119	111	244	26	423	285	138	133	260	30
Mean	0.50	0.49	0.43	0.55	0.48	0.40	17.10	15.90	19.60	17.10	17.60	12.90
SD	0.31	0.30	0.33	0.34	0.30	0.26	16.30	14.80	18.90	17.50	16.20	11.80
Quartile 1	0.27	0.27	0.25	0.28	0.26	0.21	1.00	1.00	1.00	1.00	1.00	1.00
Quartile 2	0.43	0.43	0.43	0.49	0.42	0.36	10.00	10.00	10.00	10.00	10.00	10.00
Quartile 3	0.70	0.69	0.70	0.81	0.64	0.55	30.00	20.00	30.00	30.00	30.00	20.00

Abbreviations: DDIR, DNA damage immune response; sTILs, stromal tumor-infiltrating lymphocytes.

TABLE A3. Survival Among Patients With T1c/T2 and Node-Negative Disease

Biomarker	3-Year DFS, % (95% CI)	3-Year OS, % (95% CI)	5-Year DFS, % (95% CI)	5-Year OS, % (95% CI)
DDIR status				
Negative	84 (74 to 90)	92 (85 to 96)	72 (61 to 80)	85 (76 to 91)
Positive	88 (82 to 92)	94 (89 to 97)	83 (76 to 88)	89 (83 to 93)
sTILs				
< 20%	82 (75 to 87)	91 (86 to 95)	74 (66 to 80)	84 (77 to 89)
≥ 20%	92 (85 to 96)	97 (92 to 99)	85 (77 to 90)	92 (85 to 96)

Abbreviations: DDIR, DNA damage immune response; DFS, disease-free survival; OS, overall survival; sTILs, stromal tumor-infiltrating lymphocytes.

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.20415.C1-a_s_at	ENSG00000131203 OTTHUMG00000164057	3620	*IDO1*	Indoleamine 2,3-dioxygenase 1	3.49155	6.43991	−7.71872	0	0
ADXEC.2464.C1_at	ENSG00000138755 OTTHUMG00000160889	4283	*CXCL9*	Chemokine (C-X-C motif) ligand 9	5.33225	7.68033	−5.09146	9.99^{E-32}	3.53^{E-28}
ADXEC.6891.C2_at	ENSG0002700154451 OTTHUMG00000010006	115362	*GBP5*	Guanylate- binding protein 5	2.20512	4.49763	−4.89908	2.61^{E-38}	4.85^{E-34}
ADXECAD.17552_s_at	ENSG00000211660	—	*IGLV2-23*	Immunoglobulin lambda variable 2-23	4.82631	6.86998	−4.12293	8.41^{E-14}	1.58^{E-11}
ADXEC.21261.C1_s_at	ENSG00000204681 ENSG00000206466 ENSG00000206468 ENSG00000206511 ENSG00000206513 ENSG00000213886 ENSG00000224654 ENSG00000226898 ENSG00000228913 ENSG00000231968 ENSG00000232569 ENSG00000232632 ENSG00000237051 ENSG00000237112 OTTHUMG00000004871 OTTHUMG00000004874 OTTHUMG00000031095 OTTHUMG00000031289 OTTHUMG00000031365 OTTHUMG00000031587 OTTHUMG00000148761 OTTHUMG00000148765 OTTHUMG00000148971 OTTHUMG00000148975 OTTHUMG00000149256 OTTHUMG00000149260 OTTHUMG00000149486 OTTHUMG00000149490	2550 10537	*GABBR1* *UBD*	GABA B receptor, 1 Ubiquitin D	4.29811	6.30879	−4.02971	2.10^{E-36}	1.94^{E-32}
ADXECEMUTR.5280_s_at	—	3514	*IGKC*	Immunoglobulin kappa constant	5.60275	7.59854	−3.98836	3.58^{E-16}	9.91^{E-14}
ADXEC.6891.C2_s_at	ENSG00000154451 OTTHUMG00000010006	115362	*GBP5*	Guanylate binding protein 5	5.87049	7.86447	−3.98335	3.36^{E-44}	8.31^{E-40}
ADXECEMUTR.1431_s_at	ENSG00000211666 ENSG00000211671 OTTHUMG00000151235 OTTHUMG00000151240	—	*IGLV2-14* *IGLV2-14* *IGLV2-8* *IGLV2-8*	Immunoglobulin lambda variable 2-14 NULL Immunoglobulin lambda variable 2-8 NULL	5.84984	7.81516	−3.90498	3.40^{E-16}	9.54^{E-14}
ADXECAD.10522_s_at	ENSG00000211899 OTTHUMG00000152452	3507	*IGHM*	Immunoglobulin heavy constant mu	7.09846	8.98583	−3.6996	1.09^{E-19}	6.01^{E-17}
ADXEC.20299.C1_at	ENSG00000156234 OTTHUMG00000130201	10563	*CXCL13*	Chemokine (C-X-C motif) ligand 13	3.44487	5.32918	−3.69177	7.85^{E-26}	1.12^{E-22}
ADXEC.11676.C1_at	ENSG00000169245 OTTHUMG00000160887	3627	*CXCL10*	Chemokine (C-X-C motif) ligand 10	2.53699	4.38835	−3.60841	1.40^{E-44}	5.20^{E-40}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.21261.C2_s_at	ENSG00000204681 ENSG00000206466 ENSG00000206468 ENSG00000206511 ENSG00000206513 ENSG00000213886 ENSG00000224654 ENSG00000226898 ENSG00000228913 ENSG00000231968 ENSG00000232569 ENSG00000232632 ENSG00000237051 ENSG00000237112 OTTHUMG00000004871 OTTHUMG00000004874 OTTHUMG00000031095 OTTHUMG00000031289 OTTHUMG00000031365 OTTHUMG00000031587 OTTHUMG00000148761 OTTHUMG00000148765 OTTHUMG00000148971 OTTHUMG00000148975 OTTHUMG00000149256 OTTHUMG00000149260 OTTHUMG00000149486 OTTHUMG00000149490	2550 10537	*GABBR1* *UBD*	GABA B receptor, 1 Ubiquitin D	4.07237	5.89372	−3.53411	1.14^{E-33}	6.03^{E-30}
ADXEC.11938.C5_at	—	—	—	—	3.98744	5.77275	−3.44693	5.24^{E-14}	1.01^{E-11}
ADXEC.18512.C1_at	ENSG00000127951 OTTHUMG00000130681	10875	*FGL2*	Fibrinogen-like 2	7.34208	8.9947	−3.14404	1.87^{E-27}	3.14^{E-24}
ADXECNTDJ.2312_s_at	ENSG00000211892 ENSG00000211896 ENSG00000211897 OTTHUMG00000152481 OTTHUMG00000152495 OTTHUMG00000152539	3500 3502 3503 3507 28396	*IGHG1* *IGHG3* *IGHG4* *IGHM* *IGHV4-31*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant gamma 3 (G3m marker) Immunoglobulin heavy constant gamma 4 (G4m marker) Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	8.06328	9.66083	−3.02629	1.94^{E-13}	3.51^{E-11}
ADXECEMUTR.6415_at	—	3514	*IGKC*	Immunoglobulin kappa constant	3.22777	4.8108	−2.99598	1.62^{E-11}	2.16^{E-09}
ADXECADA.21030_at	—	6373	*CXCL11*	Chemokine (C-X-C motif) ligand 11	4.0256	5.60187	−2.98196	2.05^{E-31}	6.34^{E-28}
ADXECEMUTR.1413_s_at	ENSG00000211660 OTTHUMG00000151234	—	*IGLV2-23* *IGLV2-23*	Immunoglobulin lambda variable 2-23 NULL	3.07738	4.62791	−2.92924	2.81^{E-11}	3.61^{E-09}
ADXEC.522.CB2_s_at	ENSG00000230463 OTTHUMG00000148818	3125 3126	*HLA-DRB3* *HLA-DRB4*	Major histocompatibility complex, class II, DR beta 3 Major histocompatibility complex, class II, DR beta 4	6.58255	8.11696	−2.89669	3.00^{E-09}	2.83^{E-07}
ADXEC.11938.C5_x_at	—	—	—	—	4.83419	6.36296	−2.88541	1.83^{E-14}	3.89^{E-12}
ADXECAD.17088_s_at	ENSG00000239951	—	*IGKV3-20*	Immunoglobulin kappa variable 3-20	6.9432	8.47191	−2.88526	5.06^{E-14}	9.83^{E-12}
ADXECADA.52_at	ENSG00000081237 ENSG00000262418 OTTHUMG00000035702 OTTHUMG00000175273	5788	*PTPRC*	Protein tyrosine phosphatase, receptor type, C	4.25872	5.7863	−2.88302	2.61^{E-22}	1.98^{E-19}
ADXECEMUTR.6415_s_at	—	3514	*IGKC*	Immunoglobulin kappa constant	4.02779	5.54022	−2.85289	6.74^{E-14}	1.28^{E-11}
ADXEC.29879.C1_s_at	ENSG00000004468 OTTHUMG00000048206	952	*CD38*	CD38 molecule	2.89588	4.3846	−2.80641	3.50^{E-30}	9.27^{E-27}
ADXEC.3225.C1-a_s_at	ENSG00000125347 OTTHUMG00000059497	3659	*IRF1*	Interferon regulatory factor 1	4.44889	5.93458	−2.80051	1.18^{E-24}	1.39^{E-21}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.20355.C1_s_at	ENSG00000211772 ENSG00000260881 OTTHUMG00000158912 OTTHUMG00000174781	—	*TRBC2* *TRBC2*	T-cell receptor beta constant 2 NULL	7.82604	9.26998	−2.72061	1.19^{E-22}	9.95^{E-20}
ADXEC.6072.C2-a_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	6.27962	7.71751	−2.70925	3.01^{E-29}	6.77^{E-26}
ADXEC.14394.C1_s_at	ENSG00000239713 OTTHUMG00000151081	60489	*APOBEC3G*	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G	4.74497	6.18107	−2.70589	9.53^{E-21}	5.79^{E-18}
ADXECNTDJ.4752_at	ENSG00000026751 OTTHUMG00000024008	57823	*SLAMF7*	SLAM family member 7	3.16012	4.59049	−2.69515	4.78^{E-24}	5.21^{E-21}
ADXEC.21236.C1_s_at	ENSG00000181617 OTTHUMG00000129393	260436	*FDCSP*	Follicular dendritic cell secreted protein	6.10901	7.53662	−2.69001	0.000344968	0.00765838
ADXEC.14394.C2_x_at	ENSG00000128383 OTTHUMG00000151004	200315 100913187	*APOBEC3A* *APOBEC3A_B*	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3A APOBEC3A and APOBEC3B deletion hybrid	2.58524	4.00864	−2.68217	1.77^{E-19}	9.37^{E-17}
ADXEC.11453.C1_at	ENSG00000188404 OTTHUMG00000034809	6402	*SELL*	Selectin L	3.64657	5.06894	−2.68027	1.83^{E-25}	2.38^{E-22}
ADXEC.9036.C1_s_at	ENSG00000147168 OTTHUMG00000021787	3561	*IL2RG*	Interleukin 2 receptor, gamma	7.14268	8.55525	−2.66212	1.42^{E-24}	1.65^{E-21}
ADXEC.2957.C2_s_at	ENSG00000168394 ENSG00000206297 ENSG00000224212 ENSG00000224748 ENSG00000226173 ENSG00000227816 ENSG00000230705 ENSG00000232367 OTTHUMG00000012640 OTTHUMG00000031067 OTTHUMG00000031337 OTTHUMG00000140128 OTTHUMG00000148832 OTTHUMG00000149101 OTTHUMG00000149358 OTTHUMG00000149619	6890	*TAP1*	Transporter 1, ATP-binding cassette, subfamily B (MDR/TAP)	6.47722	7.88574	−2.65465	2.07^{E-30}	5.91^{E-27}
ADXEC.3032.C2_at	—	2633	*GBP1*	Guanylate binding protein 1, interferon-inducible	5.67658	7.08437	−2.6533	3.98^{E-26}	5.90^{E-23}
ADXEC.15996.C1_at	ENSG00000108700 OTTHUMG00000132883	6355	*CCL8*	Chemokine (C-C motif) ligand 8	4.18692	5.59299	−2.65014	2.57^{E-17}	9.11^{E-15}
ADXEC.1903.C1_s_at	ENSG00000132465 OTTHUMG00000129909	3512	*IGJ*	Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	5.79005	7.19561	−2.64921	2.25^{E-13}	4.04^{E-11}
ADXEC.830.C8_s_at	ENSG00000119917 OTTHUMG00000018708	3437	*IFIT3*	Interferon-induced protein with tetratricopeptide repeats 3	3.67353	5.07483	−2.64139	8.59E-22	6.07^{E-19}
ADXEC.119.C3_s_at	ENSG00000137403 ENSG00000204642 ENSG00000206509 ENSG00000229698 ENSG00000235220 ENSG00000237508 OTTHUMG00000004783 OTTHUMG00000031156 OTTHUMG00000031438 OTTHUMG00000041181 OTTHUMG00000148884 OTTHUMG00000149164	3134	*HLA-F*	Major histocompatibility complex, class I, F	9.10266	10.5026	−2.63897	4.15^{E-32}	1.62^{E-28}
ADXEC.6681.C1_at	ENSG00000115267 OTTHUMG00000132055	64135	*IFIH1*	Interferon induced with helicase C domain 1	3.74073	5.1233	−2.60731	3.30^{E-15}	7.89^{E-13}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECRS.21496_s_at	ENSG00000111335 OTTHUMG00000169802	4939	*OAS2*	2′-5′-Oligoadenylate synthetase 2, 69/71 kDa	5.76494	7.1395	−2.59289	4.88^{E-16}	1.32^{E-13}
ADXECAD.25710_s_at	ENSG00000121858 OTTHUMG00000156917	8743	*TNFSF10*	Tumor necrosis factor (ligand) superfamily, member 10	6.29476	7.66481	−2.5848	3.45^{E-14}	6.99^{E-12}
ADXECAD.9742_at	ENSG00000177409 OTTHUMG00000155807	219285	*SAMD9L*	Sterile alpha motif domain containing 9-like	5.5574	6.91652	−2.56529	3.32^{E-31}	9.84^{E-28}
ADXEC.23233.C1_at	ENSG00000162654 OTTHUMG00000010663	115361	*GBP4*	Guanylate binding protein 4	7.22905	8.58763	−2.56433	1.42^{E-26}	2.20^{E-23}
ADXEC.30159.C1_at	—	10964	*IFI44L*	Interferon-induced protein 44-like	5.39292	6.7457	−2.55403	2.19^{E-18}	9.86^{E-16}
ADXEC.8915.C1_at	ENSG00000081237	5788	*PTPRC*	Protein tyrosine phosphatase, receptor type, C	6.02686	7.37536	−2.54647	9.18^{E-32}	3.41^{E-28}
ADXOCEC.12110.C2_s_at	ENSG00000137959 OTTHUMG00000009724	10964	*IFI44L*	Interferon-induced protein 44-like	6.21706	7.56043	−2.53743	6.76^{E-21}	4.25^{E-18}
ADXEC.6079.C1_x_at	ENSG00000137959 OTTHUMG00000009724	10964	*IFI44L*	Interferon-induced protein 44-like	3.23779	4.5572	−2.49564	1.57^{E-25}	2.12^{E-22}
ADXEC.25108.C1_at	—	—	—	—	2.43289	3.74809	−2.48837	1.39^{E-14}	2.99^{E-12}
ADXEC.6681.C1_x_at	ENSG00000115267 OTTHUMG00000132055	64135	*IFIH1*	Interferon induced with helicase C domain 1	3.18326	4.49549	−2.48325	5.61^{E-18}	2.21^{E-15}
ADXECADA.11554_at	—	64135	*IFIH1*	Interferon induced with helicase C domain 1	3.81146	5.11924	−2.47561	3.16^{E-23}	2.96^{E-20}
ADXEC.20258.C1_s_at	ENSG00000177409 OTTHUMG00000155807	219285	*SAMD9L*	Sterile alpha motif domain containing 9-like	5.78852	7.09197	−2.46819	1.89^{E-31}	6.10^{E-28}
ADXEC.14394.C2_at	ENSG00000128383 OTTHUMG00000151004	200315 100913187	*APOBEC3A* *APOBEC3A_B*	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3A APOBEC3A and APOBEC3B deletion hybrid	2.62996	3.92149	−2.44787	1.49^{E-17}	5.48^{E-15}
ADXEC.31983.C1_at	—	—	—	—	7.13675	8.42223	−2.43764	$9.38E^{-30}$	$2.32E^{-26}$
ADXECEMUTR.3815_at	ENSG00000173193 OTTHUMG00000159552	54625	*PARP14*	Poly (ADP-ribose) polymerase family, member 14	4.76144	6.04678	−2.4374	6.13^{E-24}	6.59^{E-21}
ADXEC.6996.C1_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	7.94025	9.21648	−2.42205	8.64^{E-36}	6.41^{E-32}
ADXEC.15369.C1_s_at	ENSG00000128340 ENSG00000255594 OTTHUMG00000150540	5880	*RAC2*	Ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	6.2244	7.49657	−2.41524	5.17^{E-26}	7.51^{E-23}
ADXEC.1189.C27_x_at	ENSG00000211675 ENSG00000254709 OTTHUMG00000151218 OTTHUMG00000165670	100423062	*IGLL5*	Immunoglobulin lambda-like polypeptide 5	9.82726	11.0963	−2.40998	2.95^{E-13}	5.18^{E-11}
ADXEC.6079.C1_at	ENSG00000137959 OTTHUMG00000009724	10964	*IFI44L*	Interferon-induced protein 44-like	2.20162	3.46871	−2.40676	1.08^{E-20}	6.48^{E-18}
ADXEC.6683.C1_s_at	ENSG00000157601 OTTHUMG00000086755	4599	*MX1*	Myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 (mouse)	7.38851	8.64409	−2.38763	2.43^{E-17}	8.72^{E-15}
ADXEC.3561.C1_s_at	ENSG00000111331 OTTHUMG00000169795	4940	*OAS3*	2′-5′-Oligoadenylate synthetase 3, 100 kDa	7.04131	8.29673	−2.38737	2.20^{E-22}	1.70^{E-19}
ADXEC.541.C2_x_at	ENSG00000211896 OTTHUMG00000152495	3500 3507 28396	*IGHG1* *IGHM* *IGHV4-31*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	7.8503	9.10497	−2.38613	2.53^{E-09}	2.43^{E-07}
ADXEC.22975.C1_s_at	ENSG00000115956 OTTHUMG00000129562	5341	*PLEK*	Pleckstrin	4.87621	6.1304	−2.38534	1.33^{E-35}	8.97^{E-32}
ADXECEMUTR.3438_at	ENSG00000173193 OTTHUMG00000159552	54625	*PARP14*	Poly (ADP-ribose) polymerase family, member 14	4.90106	6.15465	−2.38435	1.11^{E-18}	5.08^{E-16}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECEMUTR.1412_x_at	ENSG00000242534 ENSG00000244116 OTTHUMG00000151616 OTTHUMG00000151652	3514	*IGKC*	Immunoglobulin kappa constant	3.30674	4.55484	−2.37528	1.78^{E-11}	2.36^{E-09}
ADXEC.21004.C1_s_at	ENSG00000228278 ENSG00000229314 OTTHUMG00000021012 OTTHUMG00000021014	5004 5005	*ORM1* *ORM2*	Orosomucoid 1 Orosomucoid 2	5.11867	6.36492	−2.37224	5.62^{E-05}	0.00178058
ADXEC.2372.C2_s_at	ENSG00000090382 OTTHUMG00000169342	4069	*LYZ*	Lysozyme	4.83778	6.08285	−2.3703	3.85^{E-15}	9.10^{E-13}
ADXECNTDJ.85_at	ENSG00000156219	419	*ART3*	ADP-ribosyltransferase 3	4.43707	5.68168	−2.36956	1.53^{E-20}	9.02^{E-18}
ADXEC.22889.C1_s_at	ENSG00000168685 OTTHUMG00000090791	3575	*IL7R*	Interleukin 7 receptor	4.10389	5.34366	−2.36161	5.11^{E-15}	1.18^{E-12}
ADXEC.1189.C3_x_at	—	3500 3537	*IGHG1* *IGLC1*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin lambda constant 1 (Mcg marker)	10.4205	11.6562	−2.35489	3.66^{E-12}	5.28^{E-10}
ADXEC.20355.C1_x_at	ENSG00000211772 ENSG00000260881 OTTHUMG00000158912 OTTHUMG00000174781	—	*TRBC2* *TRBC2*	T-cell receptor beta constant 2 NULL	7.14565	8.38035	−2.35332	3.59^{E-23}	3.28^{E-20}
ADXECAD.1735_at	ENSG00000161570 OTTHUMG00000132949	6352	*CCL5*	Chemokine (C-C motif) ligand 5	6.08653	7.3207	−2.35246	4.07^{E-18}	1.69^{E-15}
ADXEC.30429.C1_s_at	ENSG00000132530 OTTHUMG00000177908	54739	*XAF1*	XIAP associated factor 1	7.46971	8.70271	−2.35056	6.80^{E-24}	7.21^{E-21}
ADXEC.5349.C1_s_at	ENSG00000173193 OTTHUMG00000159552	54625	*PARP14*	Poly (ADP-ribose) polymerase family, member 14	6.61849	7.84516	−2.34027	5.88^{E-23}	5.13^{E-20}
ADXPCEC.13209.C1_s_at	—	80830	*APOL6*	Apolipoprotein L, 6	3.50534	4.72887	−2.33516	2.76^{E-14}	5.71^{E-12}
ADXEC.2372.C3_s_at	ENSG00000090382 OTTHUMG00000169342	4069	*LYZ*	Lysozyme	4.30917	5.53024	−2.3312	1.80^{E-13}	3.26^{E-11}
ADXEC.224.C28_s_at	ENSG00000206305 ENSG00000257473 OTTHUMG00000012723	3117 100509457	*HLA-DQA1* *LOC100509457*	Major histocompatibility complex, class II, DQ alpha 1 HLA class II histocompatibility antigen, DQ alpha 1 chain-like	4.96966	6.18975	−2.32962	0.00168743	0.0244355
ADXEC.7221.C1_at	ENSG00000156587 OTTHUMG00000167047	9246	*UBE2L6*	Ubiquitin-conjugating enzyme E2L 6	6.6738	7.89189	−2.32638	5.43^{E-37}	5.76^{E-33}
ADXEC.1189.CB3_x_at	ENSG00000211677 ENSG00000211679 ENSG00000211685 OTTHUMG00000151017 OTTHUMG00000151214 OTTHUMG00000151217	28823	*IGLV1-44*	Immunoglobulin lambda variable 1-44	9.77682	10.9878	−2.31499	2.65^{E-13}	4.68^{E-11}
ADXECNTDJ.8067_s_at	ENSG00000132530 OTTHUMG00000177908	54739	*XAF1*	XIAP associated factor 1	5.06782	6.27283	−2.30539	4.48^{E-15}	1.04^{E-12}
ADXEC.22509.C1_at	ENSG00000111335 OTTHUMG00000169802	4939	*OAS2*	2′-5′-Oligoadenylate synthetase 2, 69/71 kDa	3.31109	4.51346	−2.30118	3.05^{E-18}	1.31^{E-15}
ADXECAD.8153_at	—	567	*B2M*	Beta-2-microglobulin	6.36333	7.56315	−2.2971	1.06^{E-23}	1.09^{E-20}
ADXEC.20230.C1-a_s_at	ENSG00000115165 OTTHUMG00000154551	9595	*CYTIP*	Cytohesin 1 interacting protein	3.9139	5.11131	−2.29326	1.07^{E-17}	3.98^{E-15}
ADXEC.7259.C1_s_at	ENSG00000137965 OTTHUMG00000009723	10561	*IFI44*	Interferon-induced protein 44	5.70286	6.89984	−2.2926	2.83^{E-21}	1.92^{E-18}
ADXECEMUTR.1285_s_at	ENSG00000229164 OTTHUMG00000028683	28663 28738 28755	*TRAC* *TRAJ17* *TRAV20*	T-cell receptor alpha constant T cell receptor alpha joining 17 T cell receptor alpha variable 20	3.75086	4.94597	−2.28963	2.14^{E-14}	4.55^{E-12}
ADXECADA.420_s_at	ENSG00000035720 OTTHUMG00000129304	26228	*STAP1*	Signal transducing adaptor family member 1	3.80542	4.99935	−2.28776	8.35^{E-14}	1.57^{E-11}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.23233.C1_x_at	ENSG00000162654 OTTHUMG00000010663	115361	*GBP4*	Guanylate binding protein 4	6.23062	7.42447	−2.28764	2.66^{E-26}	4.02^{E-23}
ADXECADA.13828_at	—	—	—	—	2.90485	4.09801	−2.28653	3.99^{E-16}	1.10^{E-13}
ADXEC.20343.C1_at	ENSG00000239457 ENSG00000241106 ENSG00000241386 ENSG00000241910 ENSG00000243496 ENSG00000243612 OTTHUMG00000031213 OTTHUMG00000031513 OTTHUMG00000140121 OTTHUMG00000148824 OTTHUMG00000149075 OTTHUMG00000149590	3112	*HLA-DOB*	Major histocompatibility complex, class II, DO beta	4.47646	5.66962	−2.28653	6.87^{E-16}	1.80^{E-13}
ADXEC.6902.C1_s_at	ENSG00000026751 OTTHUMG00000024008	57823	*SLAMF7*	SLAM family member 7	5.26608	6.45804	−2.28463	2.39^{E-18}	1.07^{E-15}
ADXECRS.21496_at	ENSG00000111335 OTTHUMG00000169802	4939	*OAS2*	2′-5′-Oligoadenylate synthetase 2, 69/71 kDa	5.16066	6.35209	−2.28379	5.23^{E-11}	6.46^{E-09}
AFFX-HUMISGF3A/M97935_5_at	—	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	5.6987	6.88813	−2.28062	1.62^{E-37}	2.00^{E-33}
ADXECAD.12596_at	ENSG00000156738 OTTHUMG00000167614	931	*MS4A1*	Membrane-spanning 4-domains, subfamily A, member 1	2.64181	3.83088	−2.28006	1.28^{E-12}	2.02^{E-10}
ADXECEMUTR.669_at	ENSG00000143297 OTTHUMG00000017481	83416	*FCRL5*	Fc receptor-like 5	2.79311	3.98051	−2.27742	5.75^{E-15}	1.32^{E-12}
ADXEC.8308.C1-a_s_at	ENSG00000134321 OTTHUMG00000090352	91543	*RSAD2*	Radical *S*-adenosyl methionine domain containing 2	3.64213	4.82685	−2.27319	8.80^{E-16}	2.27^{E-13}
ADXECNTDJ.1058_x_at	—	54900	*LAX1*	Lymphocyte transmembrane adaptor 1	3.81822	5.00291	−2.27315	6.56^{E-16}	1.73^{E-13}
Adx-Hs-ISGF3A-600-5_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	4.41172	5.59625	−2.2729	1.08^{E-20}	6.48^{E-18}
ADXEC.224.C4_s_at	ENSG00000206305 ENSG00000257473 OTTHUMG00000012723	3117 100509457	*HLA-DQA1* *LOC100509457*	Major histocompatibility complex, class II, DQ alpha 1 HLA class II histocompatibility antigen, DQ alpha 1 chain-like	5.2581	6.44226	−2.27231	0.00179297	0.0254715
ADXEC.6072.C2_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	4.70466	5.87784	−2.25508	5.58^{E-17}	1.90^{E-14}
ADXEC.1022.CB2_s_at	ENSG00000211592 ENSG00000231486 OTTHUMG00000151684 OTTHUMG00000151686	3514 50802	*IGK* *IGKC*	Immunoglobulin kappa locus Immunoglobulin kappa constant	10.4595	11.6305	−2.25172	9.85^{E-11}	1.18^{E-08}
ADXEC.224.C28-a_s_at	ENSG00000206305 ENSG00000257473 OTTHUMG00000012723	3117 100509457	*HLA-DQA1* *LOC100509457*	Major histocompatibility complex, class II, DQ alpha 1 HLA class II histocompatibility antigen, DQ alpha 1 chain-like	3.98741	5.15752	−2.25028	0.00144219	0.0217961
ADXEC.1189.CB1_x_at	ENSG00000211677 ENSG00000211679 OTTHUMG00000151214 OTTHUMG00000151217	3537 28823 100290481	*CYAT1* *IGLC1* *IGLV1-44*	Immunoglobulin lambda light chain-like Immunoglobulin lambda constant 1 (Mcg marker) Immunoglobulin lambda variable 1-44	10.1528	11.3217	−2.24835	7.78^{E-13}	1.28^{E-10}
ADXEC.1189.CB4_x_at	ENSG00000211677 ENSG00000211679 OTTHUMG00000151214 OTTHUMG00000151217	—	*IGLC2* *IGLC2* *IGLC3* *IGLC3*	Immunoglobulin lambda constant 2 (Kern-Oz-marker) NULL Immunoglobulin lambda constant 3 (Kern-Oz+ marker) NULL	10.4268	11.5917	−2.24219	1.86^{E-12}	2.82^{E-10}
ADXECADA.9938_at	ENSG00000103351 OTTHUMG00000177581	23059	*CLUAP1*	Clusterin associated protein 1	3.33281	4.49558	−2.23887	6.48^{E-16}	1.72^{E-13}
ADXEC.23345.C1_at	ENSG00000132274 OTTHUMG00000066904	10346	*TRIM22*	Tripartite motif containing 22	6.29911	7.46145	−2.2382	4.36^{E-21}	2.86^{E-18}
ADXEC.11639.C1_at	—	—	—	—	3.21611	4.37496	−2.2328	5.66^{E-14}	1.08^{E-11}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECAD.1735_x_at	ENSG00000161570 OTTHUMG00000132949	6352	*CCL5*	Chemokine (C-C motif) ligand 5	5.84976	7.00732	−2.23079	4.54^{E-18}	1.86^{E-15}
ADXEC.7218.C1_s_at	ENSG00000012223 OTTHUMG00000156325	4057	*LTF*	Lactotransferrin	7.88753	9.04341	−2.22821	4.74^{E-06}	0.000211081
ADXEC.5349.C4-a_s_at	ENSG00000173193 OTTHUMG00000159552	54625	*PARP14*	Poly (ADP-ribose) polymerase family, member 14	7.38494	8.54074	−2.22807	2.43^{E-24}	2.69^{E-21}
ADXEC.22969.C1_s_at	ENSG00000132274 OTTHUMG00000066904	10346	*TRIM22*	Tripartite motif containing 22	4.25785	5.41293	−2.22697	2.79^{E-25}	3.51^{E-22}
ADXEC.31506.C1_at	—	4261	*CIITA*	Class II, major histocompatibility complex, transactivator	5.44674	6.59947	−2.22333	3.90^{E-19}	1.92^{E-16}
ADXEC.1477.C1_s_at	ENSG00000111801 ENSG00000186470 OTTHUMG00000014450 OTTHUMG00000014451	10384 11118	*BTN3A2* *BTN3A3*	Butyrophilin, subfamily 3, member A2 Butyrophilin, subfamily 3, member A3	5.68195	6.83305	−2.22083	1.24^{E-16}	3.91^{E-14}
ADXEC.3496.C1_s_at	ENSG00000006074 OTTHUMG00000133001	6362 101060271	*CCL18* *LOC101060271*	Chemokine (C-C motif) ligand 18 (pulmonary and activation-regulated) c-C motif chemokine 18-like	3.45776	4.60797	−2.21946	5.23^{E-09}	4.69^{E-07}
ADXEC.2579.C1_at	ENSG00000185745 OTTHUMG00000018712	3434	*IFIT1*	Interferon-induced protein with tetratricopeptide repeats 1	6.0444	7.19206	−2.21553	2.41^{E-13}	4.28^{E-11}
ADXECNTDJ.7500_s_at	ENSG00000183508 OTTHUMG00000013703	54855	*FAM46C*	Family with sequence similarity 46, member C	4.45451	5.6004	−2.21281	3.23^{E-09}	3.04^{E-07}
ADXECADA.8176_s_at	ENSG00000143297 OTTHUMG00000017481	83416	*FCRL5*	Fc receptor-like 5	2.68437	3.82785	−2.20913	5.30^{E-12}	7.53^{E-10}
ADXECAD.3333_s_at	ENSG00000172578 OTTHUMG00000148673	89857	*KLHL6*	Kelch-like family member 6	5.65926	6.80124	−2.20684	5.45^{E-10}	5.85^{E-08}
ADXEC.5316.C1_at	ENSG00000091490 OTTHUMG00000160331	23231	*SEL1L3*	Sel-1 suppressor of lin-12-like 3 (*Caenorhabditis elegans*)	4.82771	5.96955	−2.20663	2.66^{E-11}	3.43^{E-09}
ADXEC.10461.C2_s_at	ENSG00000093072 OTTHUMG00000030726	51816	*CECR1*	Cat eye syndrome chromosome region, candidate 1	7.51241	8.65084	−2.20141	2.27^{E-24}	2.55^{E-21}
ADXECEMUTR.1465_x_at	ENSG00000211644 OTTHUMG00000151035	96610	*LOC96610*	BMS1 homolog, ribosome assembly protein (yeast) pseudogene	3.62654	4.76068	−2.19487	6.50^{E-12}	9.11^{E-10}
ADXECADA.11548_at	ENSG00000117091 OTTHUMG00000024009	962	*CD48*	CD48 molecule	3.50369	4.6368	−2.19332	9.80^{E-15}	2.16^{E-12}
ADXEC.2957.C3_s_at	ENSG00000204261 ENSG00000206232 ENSG00000206296 ENSG00000231591 ENSG00000233089 ENSG00000233140 ENSG00000234365 ENSG00000235540 OTTHUMG00000140123 OTTHUMG00000140124 OTTHUMG00000140125 OTTHUMG00000140126 OTTHUMG00000148828 OTTHUMG00000149081 OTTHUMG00000149347 OTTHUMG00000149596	100507463	*LOC100507463*	Uncharacterized LOC100507463	3.16851	4.30043	−2.19149	7.96^{E-18}	3.00^{E-15}
ADXEC.20447.C1-a_s_at	ENSG00000023445 OTTHUMG00000167324	330	*BIRC3*	Baculoviral IAP repeat containing 3	3.40406	4.53581	−2.19125	2.54^{E-14}	5.30^{E-12}
ADXEC.23036.C1_at	ENSG00000100368 OTTHUMG00000150546	1439	*CSF2RB*	Colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	2.69091	3.82035	−2.18774	6.52^{E-19}	3.06^{E-16}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXLCEC.0.CB22_x_at	ENSG00000211677 ENSG00000211679 OTTHUMG00000151214 OTTHUMG00000151217	3537 28823 100290481	*CYAT1* *IGLC1* *IGLV1-44*	Immunoglobulin lambda light chain-like Immunoglobulin lambda constant 1 (Mcg marker) Immunoglobulin lambda variable 1-44	11.2062	12.335	−2.18683	2.04^{E-12}	3.05^{E-10}
ADXOCEC.12150.C1_s_at	—	10964	*IFI44L*	Interferon-induced protein 44-like	5.06796	6.19457	−2.18345	5.23^{E-19}	2.52^{E-16}
ADXLCEC.10308.C1_at	ENSG00000137478	9873	*FCHSD2*	FCH and double SH3 domains 2	3.81617	4.94217	−2.18252	5.95^{E-08}	4.29^{E-06}
ADXEC.3768.C1_s_at	ENSG00000140379 OTTHUMG00000144173	597	*BCL2A1*	BCL2-related protein A1	2.5889	3.71381	−2.18088	2.11^{E-12}	3.15^{E-10}
ADXEC.1189.C23_x_at	ENSG00000211677 ENSG00000211679 OTTHUMG00000151214 OTTHUMG00000151217	—	*IGLC2* *IGLC2* *IGLC3* *IGLC3*	Immunoglobulin lambda constant 2 (Kern-Oz- marker) NULL Immunoglobulin lambda constant 3 (Kern-Oz+ marker) NULL	11.0423	12.167	−2.18061	1.80^{E-12}	2.74^{E-10}
ADXPCEC.10702.C1_at	—	—	—	—	3.6222	4.74672	−2.18029	1.79^{E-19}	9.41^{E-17}
ADXEC.19216.C2_s_at	—	3126	*HLA-DRB4*	Major histocompatibility complex, class II, DR beta 4	5.69655	6.82106	−2.18028	2.20^{E-06}	0.000107268
ADXECADA.23380_s_at	—	6373	*CXCL11*	Chemokine (C-X-C motif) ligand 11	2.03576	3.15945	−2.17904	4.54^{E-21}	2.95^{E-18}
ADXEC.30953.C1_at	ENSG00000102524 OTTHUMG00000017329	10673	*TNFSF13B*	Tumor necrosis factor (ligand) superfamily, member 13b	5.62904	6.74879	−2.17309	4.43^{E-22}	3.29^{E-19}
ADXECADA.1300_s_at	—	80830	*APOL6*	Apolipoprotein L, 6	5.35421	6.47237	−2.1707	2.08^{E-22}	1.62^{E-19}
ADXECNTDJ.36_s_at	ENSG00000211899 OTTHUMG00000152452	3507	*IGHM*	Immunoglobulin heavy constant mu	4.73354	5.85014	−2.16835	3.14^{E-12}	4.55^{E-10}
ADXEC.541.CB2_x_at	ENSG00000211896 ENSG00000211897 ENSG00000253755 OTTHUMG00000152493 OTTHUMG00000152495 OTTHUMG00000152539	3500 3502 3507 28396	*IGHG1* *IGHG3* *IGHM* *IGHV4-31*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant gamma 3 (G3m marker) Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	8.87316	9.9897	−2.16827	9.52^{E-12}	1.29^{E-09}
ADXECADA.20991_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	7.45179	8.5681	−2.16792	4.07^{E-38}	6.03^{E-34}
ADXEC.31757.C1_at	—	—	—	—	4.29584	5.41019	−2.16498	3.53^{E-18}	1.49^{E-15}
Adx-Hs-ISGF3A-300-3_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	8.15647	9.27056	−2.16459	4.25^{E-34}	2.43^{E-30}
ADXECAD.1724_s_at	ENSG00000090382 OTTHUMG00000169342	4069	*LYZ*	Lysozyme	5.3106	6.42111	−2.15923	4.31^{E-14}	8.53^{E-12}
ADXEC.583.C1_s_at	—	713	*C1QB*	Complement component 1, q subcomponent, B chain	6.5435	7.65048	−2.15394	9.94^{E-20}	5.54^{E-17}
ADXEC.1644.C1-a_s_at	ENSG00000140105 OTTHUMG00000171572	7453	*WARS*	Tryptophanyl-tRNA synthetase	5.25167	6.35776	−2.15261	1.89^{E-23}	1.84^{E-20}
ADXEC.8759.C1_at	ENSG00000133106 OTTHUMG00000016814	94240	*EPSTI1*	Epithelial stromal interaction 1 (breast)	4.24474	5.34976	−2.15102	2.23^{E-22}	1.70^{E-19}
ADXEC.1189.CB2_x_at	—	3537	*IGLC1*	Immunoglobulin lambda constant 1 (Mcg marker)	10.0388	11.1418	−2.1481	5.98^{E-13}	9.99^{E-11}
ADXEC.20355.C2_s_at	ENSG00000262134 OTTHUMG00000178100	28639	*TRBC1*	T-cell receptor beta constant 1	3.7555	4.85684	−2.14554	6.35^{E-17}	2.13^{E-14}
ADXECEMUTR.3438_x_at	ENSG00000173193 OTTHUMG00000159552	54625	*PARP14*	Poly (ADP-ribose) polymerase family, member 14	2.83488	3.93135	−2.13831	5.80^{E-20}	3.33^{E-17}
AFFX-HUMISGF3A/M97935_MB_at	—	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	6.34689	7.4397	−2.13289	2.54^{E-32}	1.05^{E-28}
ADXEC.29003.C1-a_s_at	—	80830	*APOL6*	Apolipoprotein L, 6	7.6421	8.7343	−2.13199	4.64^{E-23}	4.20^{E-20}
ADXECEMUTR.2334_s_at	ENSG00000115419 OTTHUMG00000132701	2744	*GLS*	Glutaminase	7.14074	8.23291	−2.13195	1.12^{E-26}	1.77^{E-23}
ADXEC.6035.C1_s_at	ENSG00000133106 OTTHUMG00000016814	94240	*EPSTI1*	Epithelial stromal interaction 1 (breast)	3.74571	4.83634	−2.12968	5.55^{E-18}	2.21^{E-15}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXOCEC.7134.C2_at	ENSG00000135899 OTTHUMG00000133204	3431	*SP110*	SP110 nuclear body protein	3.11184	4.2007	−2.12706	5.05^{E-11}	6.30^{E-09}
ADXEC.2862.C1_s_at	ENSG00000130208 OTTHUMG00000180844	341	*APOC1*	Apolipoprotein C-I	5.86174	6.94731	−2.12222	8.12^{E-13}	1.32^{E-10}
ADXECAD.7838_s_at	ENSG00000117228 OTTHUMG00000010614	2633	*GBP1*	Guanylate binding protein 1, interferon-inducible	4.0349	5.11936	−2.12059	6.33^{E-23}	5.46^{E-20}
ADXEC.23904.C1-a_s_at	ENSG00000043462 OTTHUMG00000163121	3937	*LCP2*	Lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76 kDa)	5.9184	7.00262	−2.12023	1.63^{E-19}	8.83^{E-17}
ADXEC.1189.C19_x_at	ENSG00000211677 ENSG00000211679 ENSG00000211685 OTTHUMG00000151017 OTTHUMG00000151214 OTTHUMG00000151217	28823	*IGLV1-44*	Immunoglobulin lambda variable 1-44	9.07779	10.1582	−2.1147	4.73^{E-12}	6.79^{E-10}
Adx-Hs-ISGF3A-400-3_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	8.20415	9.28303	−2.11238	4.84^{E-36}	3.99^{E-32}
ADXEC.15732.C1_x_at	ENSG00000156219 OTTHUMG00000130110	419	*ART3*	ADP-ribosyltransferase 3	2.56034	3.63707	−2.10926	7.42^{E-07}	4.12^{E-05}
ADXEC.2450.C1-a_s_at	ENSG00000002549 OTTHUMG00000048214	51056	*LAP3*	Leucine aminopeptidase 3	3.83898	4.91353	−2.10606	2.74^{E-18}	1.19^{E-15}
ADXEC.30483.C1_s_at	ENSG00000075884	55843	*ARHGAP15*	Rho GTPase activating protein 15	3.83529	4.90887	−2.10465	4.44^{E-15}	1.04^{E-12}
ADXEC.119.C51_x_at	ENSG00000137403 ENSG00000204642 ENSG00000206509 ENSG00000229698 ENSG00000235220 ENSG00000237508 OTTHUMG00000004783 OTTHUMG00000031156 OTTHUMG00000031438 OTTHUMG00000041181 OTTHUMG00000148884 OTTHUMG00000149164	3134	*HLA-F*	Major histocompatibility complex, class I, F	4.1243	5.19787	−2.10464	2.72^{E-09}	2.60^{E-07}
ADXEC.25108.C1_x_at	—	—	—	—	2.92115	3.99222	−2.10099	1.74^{E-14}	3.71^{E-12}
ADXECAD.8178_at	—	—	—	—	8.2885	9.35821	−2.09902	1.18^{E-27}	2.09^{E-24}
ADXECNTDJ.1535_s_at	ENSG00000110777 OTTHUMG00000166659	5450	*POU2AF1*	POU class 2 associating factor 1	5.20316	6.26877	−2.09306	9.88^{E-07}	5.30^{E-05}
ADXEC.21778.C1_s_at	ENSG00000102524 OTTHUMG00000017329	10673	*TNFSF13B*	Tumor necrosis factor (ligand) superfamily, member 13b	7.26037	8.32465	−2.09113	1.62^{E-22}	1.31^{E-19}
ADXECRS.42251_s_at	ENSG00000115419 OTTHUMG00000132701	2744	*GLS*	Glutaminase	6.64437	7.70659	−2.08814	1.12^{E-26}	1.77^{E-23}
AFFX-HUMISGF3A/M97935_3_at	ENSG00000115415	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	5.09163	6.15122	−2.08433	5.88^{E-30}	1.50^{E-26}
ADXECADA.20256_s_at	ENSG00000206337 ENSG00000227429 ENSG00000230389 ENSG00000237105 OTTHUMG00000031282 OTTHUMG00000031580 OTTHUMG00000037036 OTTHUMG00000149480	10866	*HCP5*	HLA complex P5 (nonprotein coding)	5.51305	6.57186	−2.08322	1.91^{E-19}	9.95^{E-17}
ADXEC.11833.C1_at	ENSG00000130487	113730	*KLHDC7B*	Kelch domain containing 7B	6.27113	7.32699	−2.07897	4.72^{E-14}	9.28^{E-12}
ADXECNTDJ.8070_at	ENSG00000132530 OTTHUMG00000177908	54739	*XAF1*	XIAP associated factor 1	4.78528	5.83886	−2.07567	2.31^{E-19}	1.17^{E-16}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.4833.C1_at	ENSG00000168421 OTTHUMG00000099373	399	*RHOH*	Ras homolog family member H	3.05072	4.10067	−2.07046	5.97^{E-13}	9.99^{E-11}
ADXEC.6372.C1_at	ENSG00000188820 OTTHUMG00000015438	441168	*FAM26F*	Family with sequence similarity 26, member F	3.63479	4.68217	−2.06678	4.20^{E-16}	1.15^{E-13}
ADXEC.8794.C1_at	ENSG00000143119 OTTHUMG00000048020	963	*CD53*	CD53 molecule	4.38497	5.43159	−2.06568	5.17^{E-16}	1.40^{E-13}
ADXEC.11066.C1_s_at	ENSG00000117215 OTTHUMG00000002701	26279	*PLA2G2D*	Phospholipase A2, group IID	4.50062	5.54596	−2.06385	1.29^{E-22}	1.07^{E-19}
ADXEC.6133.C8_s_at	ENSG00000186818 ENSG00000262397 ENSG00000263061 ENSG00000263108 OTTHUMG00000065879	11006	*LILRB4*	Leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 4	6.82192	7.8624	−2.05692	3.41^{E-23}	3.16^{E-20}
ADXECNTDJ.7501_at	ENSG00000183508 OTTHUMG00000013703	54855	*FAM46C*	Family with sequence similarity 46, member C	4.19588	5.23636	−2.0569	3.08^{E-11}	3.94^{E-09}
ADXECADA.19485_at	ENSG00000269215	2533	*FYB*	FYN binding protein	4.80313	5.841	−2.05318	1.22^{E-27}	2.10^{E-24}
ADXEC.541.C5_x_at	ENSG00000211893 ENSG00000211896 ENSG00000253755 OTTHUMG00000152482 OTTHUMG00000152493 OTTHUMG00000152495	3500 3501 3507 28396	*IGHG1* *IGHG2* *IGHM* *IGHV4-31*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant gamma 2 (G2m marker) Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	5.62387	6.66084	−2.05191	1.47^{E-12}	2.28^{E-10}
ADXEC.8794.C1_x_at	ENSG00000143119 OTTHUMG00000048020	963	*CD53*	CD53 molecule	4.17601	5.21112	−2.04927	1.49^{E-15}	3.72^{E-13}
ADXEC.11578.C1_at	ENSG00000086300 OTTHUMG00000023650	29887	*SNX10*	Sorting nexin 10	4.65828	5.69142	−2.04648	6.49^{E-18}	2.48^{E-15}
ADXEC.15732.C1_at	ENSG00000156219 OTTHUMG00000130110	419	*ART3*	ADP-ribosyltransferase 3	2.70328	3.73454	−2.04381	1.39^{E-06}	7.23^{E-05}
ADXEC.19339.C1_at	ENSG00000106560 OTTHUMG00000157488	26157	*GIMAP2*	GTPase, IMAP family member 2	4.28574	5.3153	−2.0414	3.89^{E-18}	1.62^{E-15}
ADXEC.3103.C1_s_at	ENSG00000162645 OTTHUMG00000010662	2634	*GBP2*	Guanylate binding protein 2, interferon-inducible	4.65938	5.68258	−2.03243	2.09^{E-15}	5.11^{E-13}
Adx-Hs-ISGF3A-600-3_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	6.83342	7.85255	−2.0267	2.78^{E-30}	7.65^{E-27}
ADXECNTDJ.1455_x_at	—	4069	*LYZ*	Lysozyme	4.96057	5.97843	−2.02492	2.04^{E-16}	5.95^{E-14}
ADXEC.5570.C2-a_s_at	ENSG00000188313 OTTHUMG00000159427	5359	*PLSCR1*	phospholipid scramblase 1	4.86584	5.88307	−2.02404	1.03^{E-10}	1.23^{E-08}
ADXECAD.2658_s_at	ENSG00000153064 OTTHUMG00000160958	55024	*BANK1*	B-cell scaffold protein with ankyrin repeats 1	2.97519	3.99225	−2.0238	6.46^{E-13}	1.07^{E-10}
ADXECADA.22193_s_at	ENSG00000183508 OTTHUMG00000013703	54855	*FAM46C*	Family with sequence similarity 46, member C	4.54856	5.56483	−2.02268	6.63^{E-12}	9.27^{E-10}
ADXEC.14394.C3_x_at	ENSG00000179750 ENSG00000262156 OTTHUMG00000151085 OTTHUMG00000175305	9582 200315 100913187	*APOBEC3A* *APOBEC3A_B* *APOBEC3B*	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3A APOBEC3A and APOBEC3B deletion hybrid Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3B	4.27318	5.28785	−2.02044	1.66^{E-07}	1.08^{E-05}
ADXEC.20389.C1_s_at	ENSG00000101347 OTTHUMG00000032402	25939	*SAMHD1*	SAM domain and HD domain 1	6.06735	7.08152	−2.01973	2.06^{E-22}	1.62^{E-19}
ADXEC.6156.C1_s_at	ENSG00000163131 OTTHUMG00000035010	1520	*CTSS*	Cathepsin S	7.96887	8.98165	−2.0178	1.51^{E-25}	2.08^{E-22}
ADXEC.5795.C1_s_at	ENSG00000100365 OTTHUMG00000150548	4689	*NCF4*	Neutrophil cytosolic factor 4, 40 kDa	5.92178	6.93332	−2.01607	6.84^{E-15}	1.55^{E-12}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.119.C51_at	ENSG00000137403 ENSG00000204642 ENSG00000206509 ENSG00000229698 ENSG00000235220 ENSG00000237508 OTTHUMG00000004783 OTTHUMG00000031156 OTTHUMG00000031438 OTTHUMG00000041181 OTTHUMG00000148884 OTTHUMG00000149164	3134	*HLA-F*	Major histocompatibility complex, class I, F	3.37679	4.38739	−2.01476	$2.13^{\text{E-06}}$	0.000104487
ADXEC.31313.C1_at	ENSG00000165168 ENSG00000268765 OTTHUMG00000033175	1536	*CYBB*	Cytochrome b-245, beta polypeptide	5.99847	7.00346	−2.00693	$8.74^{\text{E-16}}$	$2.27^{\text{E-13}}$
ADXEC.12744.C1_at	ENSG00000133321 OTTHUMG00000167850	5920	*RARRES3*	Retinoic acid receptor responder (tazarotene induced) 3	5.9758	6.98021	−2.00612	$5.15^{\text{E-18}}$	$2.09^{\text{E-15}}$
ADXOCEC.9547.C1_at	ENSG00000137959	10964	*IFI44L*	Interferon-induced protein 44-like	2.11351	3.11667	−2.00438	$4.94^{\text{E-22}}$	$3.59^{\text{E-19}}$
ADXEC.16385.C1_at	ENSG00000183508 OTTHUMG00000013703	54855	*FAM46C*	Family with sequence similarity 46, member C	4.76232	5.76384	−2.0021	$1.68^{\text{E-11}}$	$2.23^{\text{E-09}}$
ADXEC.1189.CB7_x_at	—	28823	*IGLV1-44*	Immunoglobulin lambda variable 1-44	11.2452	12.2464	−2.00168	$2.17^{\text{E-11}}$	$2.83^{\text{E-09}}$
ADXEC.1366.C1_s_at	—	2634	*GBP2*	Guanylate binding protein 2, interferon-inducible	2.72719	3.72838	−2.00165	$4.06^{\text{E-13}}$	$7.03^{\text{E-11}}$
AFFX-HUMISGF3A/M97935_MA_at	—	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	5.77671	6.77741	−2.00096	$5.80^{\text{E-25}}$	$6.94^{\text{E-22}}$
ADXEC.22969.C1_at	ENSG00000132274 OTTHUMG00000066904	10346	*TRIM22*	Tripartite motif containing 22	5.78822	6.78695	−1.99825	$7.64^{\text{E-10}}$	$8.05^{\text{E-08}}$
ADXECAD.9691_at	ENSG00000162654 OTTHUMG00000010663	115361	*GBP4*	Guanylate binding protein 4	1.77173	2.77034	−1.99808	$1.29^{\text{E-23}}$	$1.32^{\text{E-20}}$
ADXECADA.7172_at	ENSG00000234883 OTTHUMG00000078367	114614 406947	*MIR155* *MIR155HG*	MicroRNA 155 MIR155 host gene (nonprotein coding)	3.22787	4.22545	−1.99665	$1.53^{\text{E-13}}$	$2.79^{\text{E-11}}$
ADXEC.21884.C1_s_at	ENSG00000237988	—	*OR2I1P*	Olfactory receptor, family 2, subfamily I, member 1 pseudogene	3.15508	4.15086	−1.99417	$7.81^{\text{E-18}}$	$2.96^{\text{E-15}}$
ADXEC.20447.C1_at	ENSG00000023445 OTTHUMG00000167324	330	*BIRC3*	Baculoviral IAP repeat containing 3	6.24381	7.23896	−1.99328	$3.36^{\text{E-14}}$	$6.85^{\text{E-12}}$
ADXEC.1022.C5_x_at	—	3514	*IGKC*	Immunoglobulin kappa constant	11.5101	12.5026	−1.98961	$1.36^{\text{E-13}}$	$2.50^{\text{E-11}}$
ADXEC.11858.C1_at	ENSG00000115419 OTTHUMG00000132701	2744	*GLS*	Glutaminase	5.78789	6.78018	−1.98933	$5.99^{\text{E-18}}$	$2.35^{\text{E-15}}$
Adx-Hs-ISGF3A-400-5_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	5.53875	6.53059	−1.98872	$1.01^{\text{E-15}}$	$2.58^{\text{E-13}}$
ADXEC.29969.C1_at	ENSG00000161570 OTTHUMG00000132949	6352	*CCL5*	Chemokine (C-C motif) ligand 5	6.05079	7.04037	−1.9856	$6.36^{\text{E-29}}$	$1.31^{\text{E-25}}$
ADXEC.17347.C1_at	ENSG00000169403 OTTHUMG00000003953	5724	*PTAFR*	Platelet-activating factor receptor	6.35869	7.34639	−1.98303	$5.60^{\text{E-18}}$	$2.21^{\text{E-15}}$
ADXEC.18072.C1_at	ENSG00000105369 OTTHUMG00000182678	973	*CD79A*	CD79a molecule, immunoglobulin-associated alpha	5.90346	6.8906	−1.98224	$2.15^{\text{E-17}}$	$7.79^{\text{E-15}}$
ADXECNTDJ.199_s_at	ENSG00000263303	3903	*LAIR1*	Leukocyte-associated immunoglobulin-like receptor 1	6.55886	7.54492	−1.98077	$2.74^{\text{E-19}}$	$1.37^{\text{E-16}}$
ADXEC.13342.C1_x_at	ENSG00000173821 OTTHUMG00000161415	57674	*RNF213*	Ring finger protein 213	4.95659	5.942	−1.97987	$6.63^{\text{E-17}}$	$2.21^{\text{E-14}}$
ADXECAD.20607_s_at	ENSG00000122862 OTTHUMG00000018369	5552	*SRGN*	Serglycin	4.6923	5.67651	−1.97823	$6.18^{\text{E-08}}$	$4.44^{\text{E-06}}$
ADXECNTDJ.4796_s_at	ENSG00000163840 OTTHUMG00000159524	151636	*DTX3L*	Deltex 3-like (*Drosophila*)	4.4377	5.42031	−1.97604	$1.77^{\text{E-16}}$	$5.31^{\text{E-14}}$

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.11420.C1_at	ENSG00000133574 OTTHUMG00000157475	55303	*GIMAP4*	GTPase, IMAP family member 4	7.18136	8.16348	−1.97537	1.31^{E-18}	5.97^{E-16}
ADXEC.26389.C1_at	ENSG00000205413 OTTHUMG00000155809	54809	*SAMD9*	Sterile alpha motif domain containing 9	3.47663	4.45837	−1.97485	9.00^{E-15}	2.01^{E-12}
ADXPCEC.12489.C2_s_at	—	—	—	—	3.8722	4.8528	−1.97329	5.15^{E-08}	3.76^{E-06}
ADXEC.14394.C3_at	ENSG00000179750 ENSG00000262156 OTTHUMG00000151085 OTTHUMG00000175305	9582 200315 100913187	*APOBEC3A* *APOBEC3A_B* *APOBEC3B*	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3A APOBEC3A and APOBEC3B deletion hybrid Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3B	4.16574	5.14607	−1.97292	1.47^{E-07}	9.77^{E-06}
ADXECEMUTR.1457_x_at	ENSG00000242534 ENSG00000244116 OTTHUMG00000151616 OTTHUMG00000151652	3514	*IGKC*	Immunoglobulin kappa constant	4.25937	5.23819	−1.97085	4.96^{E-11}	6.19^{E-09}
ADXEC.2450.C1_x_at	ENSG00000002549 OTTHUMG00000048214	51056	*LAP3*	Leucine aminopeptidase 3	8.48908	9.46772	−1.97061	2.57^{E-29}	5.97^{E-26}
ADXECRS.20430_s_at	ENSG00000078081 OTTHUMG00000158387	27074	*LAMP3*	Lysosomal-associated membrane protein 3	3.06374	4.04108	−1.96883	1.83^{E-14}	3.89^{E-12}
ADXEC.21063.C1_at	ENSG00000138646 OTTHUMG00000130953	51191	*HERC5*	HECT and RLD domain containing E3 ubiquitin protein ligase 5	4.05122	5.02846	−1.96869	4.00^{E-15}	9.36^{E-13}
ADXECRS.2823_s_at	ENSG00000245164 OTTHUMG00000165025	100130231	*LINC00861*	Long intergenic nonprotein coding RNA 861	4.77971	5.75671	−1.96837	2.05^{E-11}	2.68^{E-09}
ADXEC.1477.C4_x_at	ENSG00000111801 OTTHUMG00000014451	10384	*BTN3A3*	Butyrophilin, subfamily 3, member A3	5.22694	6.20287	−1.9669	1.67^{E-19}	8.88^{E-17}
ADXECRS.31890_s_at	ENSG00000163568 OTTHUMG00000037183	9447	*AIM2*	Absent in melanoma 2	2.50387	3.47943	−1.9664	3.44^{E-16}	9.63^{E-14}
ADXEC.2833.C1_at	—	712	*C1QA*	Complement component 1, q subcomponent, A chain	3.73388	4.70939	−1.96634	5.55^{E-14}	1.06^{E-11}
Adx-Hs-ISGF3A-300-5_s_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	5.48701	6.45773	−1.95981	7.15^{E-17}	2.37^{E-14}
ADXECAD.2691_x_at	—	—	—	—	3.97774	4.94794	−1.95911	5.50^{E-16}	1.47^{E-13}
ADXECNTDJ.4447_at	ENSG00000101342 OTTHUMG00000032400	140711	*TLDC2*	TBC/LysM-associated domain containing 2	5.75767	6.72696	−1.95788	4.65^{E-22}	3.42^{E-19}
ADXEC.1601.C1_at	—	—	—	—	5.09814	6.06604	−1.95599	7.39^{E-17}	2.42^{E-14}
ADXECNTDJ.1455_at	—	4069	*LYZ*	Lysozyme	4.94589	5.91312	−1.95508	1.28^{E-16}	4.00^{E-14}
ADXEC.9663.C1_at	ENSG00000162692 OTTHUMG00000010982	7412	*VCAM1*	Vascular cell adhesion molecule 1	3.70716	4.67313	−1.95337	1.83^{E-11}	2.42^{E-09}
ADXEC.491.C4_at	ENSG00000105193 ENSG00000178715 OTTHUMG00000003169 OTTHUMG00000182972	6217	*RPS16*	Ribosomal protein S16	6.18983	7.15443	−1.95152	2.53^{E-17}	9.04^{E-15}
ADXECAD.20132_s_at	ENSG00000140105 OTTHUMG00000171572	7453	*WARS*	Tryptophanyl-tRNA synthetase	4.34256	5.30585	−1.94975	6.27^{E-17}	2.11^{E-14}
ADXECADA.10514_s_at	ENSG00000101347 OTTHUMG00000032402	25939	*SAMHD1*	SAM domain and HD domain 1	7.37239	8.33516	−1.94904	5.50^{E-16}	1.47^{E-13}
ADXEC.442.C10_x_at	ENSG00000197249 OTTHUMG00000150355	5265	*SERPINA1*	Serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1	5.39938	6.35786	−1.94327	1.09^{E-09}	1.12^{E-07}
ADXECADA.24441_x_at	ENSG00000163131 OTTHUMG00000035010	1520	*CTSS*	Cathepsin S	3.93734	4.89444	−1.94141	1.25^{E-34}	7.70^{E-31}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.21173.C1_at	ENSG00000160326 ENSG00000261768 OTTHUMG00000020874 OTTHUMG00000174705	11182	*SLC2A6*	Solute carrier family 2 (facilitated glucose transporter), member 6	5.49106	6.44757	−1.9406	7.13^{E-10}	7.56^{E-08}
ADXEC.20029.C1_s_at	ENSG00000121858 OTTHUMG00000156917	8743	*TNFSF10*	Tumor necrosis factor (ligand) superfamily, member 10	3.98266	4.93882	−1.94014	3.90^{E-08}	2.92^{E-06}
ADXEC.24.C2_s_at	ENSG00000173221 OTTHUMG00000121167	2745	*GLRX*	Glutaredoxin (thioltransferase)	6.25789	7.21178	−1.9371	2.37^{E-13}	4.23^{E-11}
ADXEC.119.C32_x_at	ENSG00000206435 ENSG00000206452 ENSG00000228299 ENSG00000237022 OTTHUMG00000037240 OTTHUMG00000148965 OTTHUMG00000149248 OTTHUMG00000149943	3107	*HLA-C*	Major histocompatibility complex, class I, C	7.76696	8.7127	−1.92617	1.52^{E-05}	0.000582559
ADXECEMUTR.6000_at	ENSG00000242472 OTTHUMG00000152461	3492 3493 3494 3500 3501 3502 3507 28396	*IGH* *IGHA1* *IGHA2* *IGHG1* *IGHG2* *IGHG3* *IGHM* *IGHV4-31*	Immunoglobulin heavy locus Immunoglobulin heavy constant alpha 1 Immunoglobulin heavy constant alpha 2 (A2m marker) Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant gamma 2 (G2m marker) Immunoglobulin heavy constant gamma 3 (G3m marker) Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	5.22548	6.17118	−1.92612	3.25^{E-14}	6.66^{E-12}
ADXECRS.28008_at	ENSG00000269404 OTTHUMG00000183039	6689	*SPIB*	Spi-B transcription factor (Spi-1/PU.1 related)	3.71992	4.66557	−1.92606	8.64^{E-10}	9.01^{E-08}
ADXEC.11171.C1_s_at	ENSG00000128284 OTTHUMG00000150632	80833	*APOL3*	Apolipoprotein L, 3	3.52894	4.47392	−1.92516	5.20^{E-23}	4.59^{E-20}
ADXECAD.26628_x_at	ENSG00000223532 ENSG00000234745 OTTHUMG00000031153 OTTHUMG00000031435	3106	*HLA-B*	Major histocompatibility complex, class I, B	7.22469	8.16834	−1.92339	4.62^{E-16}	1.26^{E-13}
ADXEC.11171.C2_s_at	ENSG00000100342 OTTHUMG00000030427	8542	*APOL1*	Apolipoprotein L, 1	6.08461	7.02758	−1.92248	3.63^{E-21}	2.43^{E-18}
ADXEC.1399.C10_s_at	ENSG00000067066 OTTHUMG00000133203	6672	*SP100*	SP100 nuclear antigen	5.1586	6.09961	−1.91987	4.49^{E-18}	1.85^{E-15}
ADXEC.18072.C1_x_at	ENSG00000105369 OTTHUMG00000182678	973	*CD79A*	CD79a molecule, immunoglobulin-associated alpha	5.78645	6.72733	−1.91971	1.53^{E-16}	4.73^{E-14}
ADXEC.23005.C1_s_at	ENSG00000140749 OTTHUMG00000090709	10261	*IGSF6*	Immunoglobulin superfamily, member 6	4.85054	5.78927	−1.91684	6.79^{E-16}	1.78^{E-13}
ADXECEMUTR.1034_s_at	ENSG00000019582 OTTHUMG00000163559	972	*CD74*	CD74 molecule, major histocompatibility complex, class II invariant chain	7.21932	8.15771	−1.91639	4.91^{E-18}	2.00^{E-15}
ADXEC.2450.C1_at	ENSG00000002549 OTTHUMG00000048214	51056	*LAP3*	Leucine aminopeptidase 3	8.88245	9.8206	−1.91606	5.97^{E-33}	2.76^{E-29}
ADXEC.21884.C2_s_at	ENSG00000237988	—	*OR2I1P*	Olfactory receptor, family 2, subfamily I, member 1 pseudogene	3.52434	4.46026	−1.9131	2.42^{E-16}	6.92^{E-14}
ADXEC.442.CB1_s_at	ENSG00000197249 OTTHUMG00000150355	5265	*SERPINA1*	Serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1	7.18407	8.11831	−1.91089	4.21^{E-11}	5.30^{E-09}
ADXEC.23121.C1_at	ENSG00000096996 OTTHUMG00000183417	3594	*IL12RB1*	Interleukin 12 receptor, beta 1	4.3219	5.25573	−1.91035	4.91^{E-13}	8.36^{E-11}
ADXECAD.24300_s_at	ENSG00000082074 OTTHUMG00000162071	2533	*FYB*	FYN binding protein	4.73156	5.66522	−1.91011	9.98^{E-17}	3.23^{E-14}
ADXEC.19547.C1_at	ENSG00000118308 OTTHUMG00000170192	4033	*LRMP*	Lymphoid-restricted membrane protein	3.23827	4.17037	−1.90804	1.99^{E-06}	9.85^{E-05}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.1056.C7_s_at	ENSG00000112096 OTTHUMG00000015940	6648 100129518	*LOC100129518* *SOD2*	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	4.27528	5.20693	−1.90745	4.74^{E-10}	5.13^{E-08}
ADXEC.3406.C1_s_at	—	28755	*TRAC*	T-cell receptor alpha constant	10.6687	11.5992	−1.90596	6.19^{E-27}	1.02^{E-23}
ADXEC.4039.C1_x_at	ENSG00000168961 OTTHUMG00000179831	3965	*LGALS9*	Lectin, galactoside-binding, soluble, 9	7.04399	7.9738	−1.90503	6.33^{E-33}	2.76^{E-29}
ADXEC.6996.C1_x_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	4.3467	5.27633	−1.90479	7.27^{E-28}	1.33^{E-24}
ADXECADA.1441_at	—	—	—	—	7.08276	8.01069	−1.90254	2.09^{E-19}	1.07^{E-16}
ADXEC.3314.C2_s_at	ENSG00000211899 OTTHUMG00000152452	3507	*IGHM*	Immunoglobulin heavy constant mu	6.14428	7.07132	−1.90136	1.93^{E-12}	2.91^{E-10}
ADXEC.541.C13_x_at	ENSG00000211896 OTTHUMG00000152495	3500 3501	*IGHG1* *IGHG2*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant gamma 2 (G2m marker)	9.54713	10.474	−1.9012	6.47^{E-12}	9.09^{E-10}
ADXEC.1189.C34_x_at	ENSG00000211677 ENSG00000211679 OTTHUMG00000151214 OTTHUMG00000151217	3537 28823 100290481	*CYAT1* *IGLC1* *IGLV1-44*	Immunoglobulin lambda light chain-like Immunoglobulin lambda constant 1 (Mcg marker) Immunoglobulin lambda variable 1-44	10.2689	11.1942	−1.89902	2.83^{E-12}	4.12^{E-10}
ADXECRS.25652_x_at	—	3126	*HLA-DRB4*	Major histocompatibility complex, class II, DR beta 4	3.64057	4.56574	−1.89891	2.24^{E-08}	1.78^{E-06}
ADXEC.1255.C3_s_at	ENSG00000179604 OTTHUMG00000178419	23580	*CDC42EP4*	CDC42 effector protein (Rho GTPase binding) 4	6.28595	7.21075	−1.89842	1.72^{E-06}	8.72^{E-05}
ADXEC.1946.C1_at	ENSG00000185507 OTTHUMG00000132019	3665	*IRF7*	Interferon regulatory factor 7	7.47335	8.39771	−1.89785	5.82^{E-21}	3.72^{E-18}
ADXECNTDJ.2849_at	ENSG00000156234 OTTHUMG00000130201	10563	*CXCL13*	Chemokine (C-X-C motif) ligand 13	2.67528	3.59922	−1.89729	1.28^{E-13}	2.35^{E-11}
ADXEC.2989.C6_at	—	—	—	—	7.37413	8.29266	−1.89019	7.47^{E-19}	3.46^{E-16}
ADXEC.4829.C1_at	ENSG00000134326 OTTHUMG00000151629	129607	*CMPK2*	Cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial	3.70994	4.62847	−1.89019	6.08^{E-16}	1.62^{E-13}
ADXEC.32772.C1_x_at	—	567	*B2M*	Beta-2-microglobulin	7.22223	8.13872	−1.88751	1.74^{E-21}	1.21^{E-18}
ADXEC.6996.C1_at	ENSG00000115415 OTTHUMG00000132699	6772	*STAT1*	Signal transducer and activator of transcription 1, 91 kDa	4.51019	5.42557	−1.88606	2.70^{E-22}	2.02^{E-19}
ADXEC.3160.C1_s_at	ENSG00000159189 OTTHUMG00000002891	714	*C1QC*	Complement component 1, q subcomponent, C chain	7.47719	8.38887	−1.88123	5.76^{E-13}	9.67^{E-11}
ADXEC.1644.C1_at	ENSG00000140105 OTTHUMG00000171572	7453	*WARS*	Tryptophanyl-tRNA synthetase	5.66183	6.57072	−1.8776	2.93^{E-25}	3.63^{E-22}
ADXEC.6664.C1_at	ENSG00000111335 OTTHUMG00000169802	4939	*OAS2*	2′-5′-Oligoadenylate synthetase 2, 69/71 kDa	6.30073	7.20879	−1.87652	2.38^{E-16}	6.88^{E-14}
ADXEC.8819.C1_s_at	ENSG00000182179 OTTHUMG00000158267	7318 100847079	*MIR5193* *UBA7*	MicroRNA 5193 Ubiquitin-like modifier activating enzyme 7	8.38601	9.29254	−1.87453	6.16^{E-18}	2.38^{E-15}
ADXEC.4610.C1_at	ENSG00000130775 OTTHUMG00000003735	9473	*THEMIS2*	Thymocyte selection associated family member 2	6.00382	6.90893	−1.87269	1.52^{E-11}	2.03^{E-09}
ADXEC.5068.C1_at	ENSG00000140853 OTTHUMG00000133470	84166	*NLRC5*	NLR family, CARD domain containing 5	6.32653	7.23065	−1.8714	8.35^{E-24}	8.72^{E-21}
ADXEC.16064.C1_s_at	ENSG00000158714 OTTHUMG00000035433	56833	*SLAMF8*	SLAM family member 8	5.47736	6.3812	−1.87104	3.33^{E-15}	7.93^{E-13}
ADXEC.6133.C7_x_at	ENSG00000131042 ENSG00000263222 OTTHUMG00000064896	10288	*LILRB2*	Leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 2	5.75261	6.65237	−1.86576	1.53^{E-16}	4.73^{E-14}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.119.C44_x_at	ENSG00000206503 ENSG00000224320 ENSG00000227715 ENSG00000229215 ENSG00000235657 ENSG00000265434 OTTHUMG00000031434 OTTHUMG00000130501 OTTHUMG00000148721 OTTHUMG00000148897 OTTHUMG00000149428	3105	*HLA-A*	Major histocompatibility complex, class I, A	9.71936	10.619	−1.86554	3.74^{E-14}	7.52^{E-12}
ADXEC.2268.C2_s_at	ENSG00000089127 OTTHUMG00000169792	4938	*OAS1*	2′-5′-Oligoadenylate synthetase 1, 40/46 kDa	4.78577	5.6848	−1.86481	2.79^{E-09}	2.66^{E-07}
ADXEC.4124.C1_at	—	—	—	—	4.14319	5.04177	−1.86423	5.37^{E-05}	0.00172007
ADXECEMUTR.868_at	ENSG00000153283 OTTHUMG00000159275	10225	*CD96*	CD96 molecule	3.45049	4.34858	−1.86361	7.99^{E-11}	9.66^{E-09}
ADXEC.20410.C1_s_at	ENSG00000136250 OTTHUMG00000023566	313	*AOAH*	Acyloxyacyl hydrolase (neutrophil)	4.19376	5.09018	−1.86145	5.85^{E-17}	1.98^{E-14}
ADXEC.29811.C1_at	ENSG00000177409 OTTHUMG00000155807	219285	*SAMD9L*	Sterile alpha motif domain containing 9-like	5.19945	6.09458	−1.85978	6.28^{E-20}	3.59^{E-17}
ADXEC.23424.C1_at	ENSG00000167984	197358	*NLRC3*	NLR family, CARD domain containing 3	3.94205	4.8354	−1.85749	1.92^{E-16}	5.68^{E-14}
ADXPCEC.424.CB2_at	—	—	—	—	9.99479	10.8875	−1.85668	2.92^{E-33}	1.45^{E-29}
ADXEC.23076.C1_at	ENSG00000110324 OTTHUMG00000166523	3587	*IL10RA*	Interleukin 10 receptor, alpha	4.26567	5.15825	−1.85649	2.61^{E-12}	3.83^{E-10}
ADXEC.7250.C1-a_s_at	ENSG00000185862 OTTHUMG00000132869	2124	*EVI2B*	Ecotropic viral integration site 2B	6.82529	7.71771	−1.8563	4.80^{E-15}	1.11^{E-12}
ADXEC.6891.C7_s_at	ENSG00000162645 OTTHUMG00000010662	2634	*GBP2*	Guanylate binding protein 2, interferon-inducible	6.18324	7.07492	−1.85533	2.53^{E-15}	6.14^{E-13}
ADXEC.23400.C1_x_at	ENSG00000165168 ENSG00000268765 OTTHUMG00000033175	1536	*CYBB*	Cytochrome b-245, beta polypeptide	8.02986	8.92038	−1.85384	2.52^{E-29}	5.97^{E-26}
ADXEC.32125.C1_s_at	ENSG00000179583 OTTHUMG00000129753	4261	*CIITA*	Class II, major histocompatibility complex, transactivator	5.81095	6.70097	−1.8532	2.71^{E-18}	1.18^{E-15}
ADXEC.1022.C20_x_at	ENSG00000211592 ENSG00000211597 ENSG00000231486 OTTHUMG00000151679 OTTHUMG00000151684 OTTHUMG00000151686	3514 50802	*IGK* *IGKC*	Immunoglobulin kappa locus Immunoglobulin kappa constant	11.1112	11.9999	−1.85154	5.18^{E-13}	8.78^{E-11}
ADXECAD.23435_s_at	ENSG00000204287 ENSG00000206308 ENSG00000226260 ENSG00000227993 ENSG00000228987 ENSG00000230726 ENSG00000234794 OTTHUMG00000012742 OTTHUMG00000031269 OTTHUMG00000031567 OTTHUMG00000138993 OTTHUMG00000149060 OTTHUMG00000149327 OTTHUMG00000149575	3117 3122	*HLA-DQA1* *HLA-DRA*	Major histocompatibility complex, class II, DQ alpha 1 Major histocompatibility complex, class II, DR alpha	3.92377	4.8098	−1.84808	1.80E-11	2.37^{E-09}
ADXEC.29978.C1_at	ENSG00000135074	8728	*ADAM19*	ADAM metallopeptidase domain 19	4.25382	5.13983	−1.84806	2.57^{E-10}	2.89^{E-08}
ADXEC.18098.C1_at	ENSG00000181381 OTTHUMG00000161412	91351	*DDX60L*	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60-like	5.96336	6.84699	−1.84502	5.73^{E-22}	4.09^{E-19}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECADA.23590_at	ENSG00000107201 OTTHUMG00000019746	23586	*DDX58*	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58	4.97749	5.86071	−1.84448	1.34^{E-12}	2.11^{E-10}
ADXEC.111.CB14_s_at	ENSG00000019582 OTTHUMG00000163559	972	*CD74*	CD74 molecule, major histocompatibility complex, class II invariant chain	8.69838	9.57868	−1.84076	7.27^{E-17}	2.40^{E-14}
ADXEC.21503.C1_at	—	643977	*FLJ32255*	Uncharacterized LOC643977	5.91144	6.78986	−1.83836	1.87^{E-06}	9.32^{E-05}
ADXEC.3369.C1_at	ENSG00000180353 OTTHUMG00000159409	3059	*HCLS1*	Hematopoietic cell-specific Lyn substrate 1	5.75531	6.63314	−1.8376	1.35^{E-18}	6.11^{E-16}
ADXEC.13342.C1_at	ENSG00000173821 OTTHUMG00000161415	57674	*RNF213*	Ring finger protein 213	4.89181	5.76874	−1.83647	1.70^{E-15}	4.24^{E-13}
ADXEC.522.C10_s_at	ENSG00000230708 OTTHUMG00000031346	3115	*HLA-DPB1*	Major histocompatibility complex, class II, DP beta 1	5.22953	6.10432	−1.83374	2.36^{E-12}	3.49^{E-10}
ADXECEMUTR.3751_at	ENSG00000074621 OTTHUMG00000167960	9187	*SLC24A1*	Solute carrier family 24 (sodium/potassium/calcium exchanger), member 1	5.72588	6.60049	−1.83352	7.91^{E-09}	6.89^{E-07}
ADXECRS.22704_s_at	—	5698	*PSMB9*	Proteasome (prosome, macropain) subunit, beta type, 9	3.57617	4.44935	−1.83169	7.10^{E-23}	6.05^{E-20}
ADXEC.20850.C1_at	ENSG00000096996 OTTHUMG00000183417	3594	*IL12RB1*	Interleukin 12 receptor, beta 1	4.31818	5.19112	−1.8314	7.11^{E-29}	1.39^{E-25}
ADXEC.22978.C1_at	ENSG00000104951 OTTHUMG00000183377	259307	*IL4I1*	Interleukin 4 induced 1	7.53672	8.40808	−1.82939	1.14^{E-25}	1.59^{E-22}
ADXEC.23126.C1_at	ENSG00000197471 OTTHUMG00000097765	6693	*SPN*	Sialophorin	4.04033	4.91072	−1.82816	8.59^{E-21}	5.26^{E-18}
ADXEC.614.C1_s_at	ENSG00000185215 OTTHUMG00000171890	7127	*TNFAIP2*	Tumor necrosis factor, alpha-induced protein 2	6.31803	7.18561	−1.82461	3.84^{E-18}	1.61^{E-15}
ADXEC.28662.C1-a_s_at	ENSG00000100219 OTTHUMG00000151094	7494	*XBP1*	X-box binding protein 1	6.33766	7.2045	−1.82367	2.06^{E-10}	2.34^{E-08}
ADXEC.12905.C1_at	ENSG00000101017 OTTHUMG00000033053	958	*CD40*	CD40 molecule, TNF receptor superfamily member 5	4.51541	5.37919	−1.8198	6.44^{E-18}	2.48^{E-15}
ADXEC.30763.C1_at	ENSG00000196533 ENSG00000263961 OTTHUMG00000036122	440712	*C1orf186*	Chromosome 1 open reading frame 186	2.9401	3.80215	−1.81762	1.10^{E-05}	0.000440588
ADXEC.7199.C2_s_at	ENSG00000122862 OTTHUMG00000018369	5552	*SRGN*	Serglycin	6.441	7.30301	−1.81758	8.27^{E-20}	4.68^{E-17}
ADXEC.6543.C1_at	ENSG00000172724 OTTHUMG00000019833	6363	*CCL19*	Chemokine (C-C motif) ligand 19	9.53124	10.3927	−1.81692	2.15^{E-12}	3.20^{E-10}
ADXEC.24209.C1_at	—	91526	*ANKRD44*	Ankyrin repeat domain 44	3.78144	4.64259	−1.81648	4.51^{E-09}	4.08^{E-07}
ADXEC.4610.C1_x_at	ENSG00000130775 OTTHUMG00000003735	9473	*THEMIS2*	Thymocyte selection associated family member 2	6.13146	6.99197	−1.81569	4.17^{E-14}	8.29^{E-12}
ADXEC.23258.C1_s_at	ENSG00000123329 OTTHUMG00000150147	64333	*ARHGAP9*	Rho GTPase activating protein 9	5.66483	6.52534	−1.81568	1.09E^{-20}	6.48^{E-18}
ADXEC.119.C6_x_at	ENSG00000204525 ENSG00000233841 OTTHUMG00000031154 OTTHUMG00000031436	3107	*HLA-C*	Major histocompatibility complex, class I, C	3.83277	4.68936	−1.81076	0.000169184	0.00436472
ADXEC.12456.C1_at	ENSG00000167208 OTTHUMG00000133173	124460	*SNX20*	Sorting nexin 20	4.86056	5.71707	−1.81065	1.53^{E-22}	1.24^{E-19}
ADXOCEC.7134.C2_x_at	ENSG00000135899 OTTHUMG00000133204	3431	*SP110*	SP110 nuclear body protein	3.56998	4.42589	−1.80991	4.22^{E-13}	7.25^{E-11}
ADXECEMUTR.4413_at	—	4297	*KMT2A*	Lysine (K)-specific methyltransferase 2A	4.74173	5.59339	−1.80458	4.05^{E-10}	4.46^{E-08}
ADXEC.138.CB2-a_s_at	ENSG00000166710 OTTHUMG00000131247	567	*B2M*	Beta-2-microglobulin	9.1405	9.99155	−1.80381	1.82^{E-21}	1.25^{E-18}
ADXECAD.17266_at	—	50615	*IL21R*	Interleukin 21 receptor	4.30745	5.15488	−1.7993	5.41^{E-22}	3.90^{E-19}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.14799.C1_at	ENSG00000132109 OTTHUMG00000165701	6737	*TRIM21*	Tripartite motif containing 21	5.59049	6.4379	−1.79927	2.88^{E-15}	6.93^{E-13}
ADXECAD.19551_x_at	ENSG00000164308 OTTHUMG00000128718	64167	*ERAP2*	Endoplasmic reticulum aminopeptidase 2	3.05316	3.89998	−1.79854	3.90^{E-09}	3.59^{E-07}
ADXEC.2833.C1_x_at	—	712	*C1QA*	Complement component 1, q subcomponent, A chain	6.23437	7.081	−1.79829	7.78^{E-23}	6.56^{E-20}
ADXEC.23126.C1_x_at	ENSG00000197471 OTTHUMG00000097765	6693	*SPN*	Sialophorin	4.064	4.91002	−1.79753	1.90^{E-22}	1.52^{E-19}
ADXECADA.22526_s_at	ENSG00000128335 OTTHUMG00000150634	23780	*APOL2*	Apolipoprotein L, 2	7.1849	8.03055	−1.79707	4.91^{E-12}	7.04^{E-10}
ADXEC.26496.C1_at	ENSG00000204359 ENSG00000239754 ENSG00000241253 ENSG00000241534 ENSG00000242335 ENSG00000243570 ENSG00000243649 OTTHUMG00000004992 OTTHUMG00000031198 OTTHUMG00000031499 OTTHUMG00000137485 OTTHUMG00000149098 OTTHUMG00000149355 OTTHUMG00000149616	629	*CFB*	Complement factor B	3.58233	4.42709	−1.79597	3.06^{E-05}	0.001063
ADXEC.14860.C1_at	ENSG00000117091 OTTHUMG00000024009	962	*CD48*	CD48 molecule	4.4973	5.34157	−1.79535	2.43^{E-19}	1.23^{E-16}
ADXEC.25003.C1_x_at	ENSG00000163565 OTTHUMG00000037108	3428	*IFI16*	Interferon, gamma-inducible protein 16	5.31042	6.15418	−1.79471	2.25^{E-14}	4.75^{E-12}
ADXEC.16763.C1_at	ENSG00000169442 OTTHUMG00000003491	1043	*CD52*	CD52 molecule	6.7482	7.59189	−1.79463	1.02^{E-18}	4.71^{E-16}
ADXEC.3092.C1_s_at	ENSG00000141574 OTTHUMG00000178668	6398	*SECTM1*	Secreted and transmembrane 1	6.99145	7.83433	−1.79363	1.15^{E-12}	1.83^{E-10}
ADXECNTDJ.2864_at	ENSG00000156587 OTTHUMG00000167047	9246	*UBE2L6*	Ubiquitin-conjugating enzyme E2L 6	4.62271	5.46538	−1.79337	2.01^{E-08}	1.62^{E-06}
ADXEC.22834.C1-a_s_at	ENSG00000135899 OTTHUMG00000133204	3431	*SP110*	SP110 nuclear body protein	6.75412	7.59472	−1.7908	1.54^{E-23}	1.54^{E-20}
ADXEC.20342.C1_at	ENSG00000203747 OTTHUMG00000034466	2214	*FCGR3A*	Fc fragment of IgG, low affinity IIIa, receptor (CD16a)	5.76635	6.60635	−1.79005	5.29^{E-14}	1.02^{E-11}
ADXECAD.14444_at	ENSG00000143119 OTTHUMG00000048020	963	*CD53*	CD53 molecule	6.28922	7.12866	−1.78935	9.59^{E-16}	2.45^{E-13}
ADXEC.4039.C1_at	ENSG00000168961 OTTHUMG00000179831	3965	*LGALS9*	Lectin, galactoside-binding, soluble, 9	7.14925	7.98822	−1.78877	5.97^{E-29}	1.26^{E-25}
ADXECNTDJ.5195_at	ENSG00000205413 OTTHUMG00000155809	54809	*SAMD9*	Sterile alpha motif domain containing 9	4.1157	4.95436	−1.78839	3.25^{E-08}	2.49^{E-06}
ADXEC.8192.C1_at	ENSG00000158869 OTTHUMG00000034343	2207	*FCER1G*	Fc fragment of IgE, high affinity I, receptor for; gamma polypeptide	6.96523	7.80355	−1.78797	4.96^{E-17}	1.71^{E-14}
ADXOCEC.9547.C1_x_at	ENSG00000137959	10964	*IFI44L*	Interferon-induced protein 44-like	2.1474	2.98491	−1.78696	2.64^{E-18}	1.16^{E-15}
ADXEC.491.C4_x_at	ENSG00000105193 ENSG00000178715 OTTHUMG00000003169 OTTHUMG00000182972	6217	*RPS16*	Ribosomal protein S16	4.59747	5.43387	−1.78558	3.27^{E-18}	1.39^{E-15}
ADXECADA.729_at	ENSG00000115267 OTTHUMG00000132055	64135	*IFIH1*	Interferon induced with helicase C domain 1	3.81135	4.64767	−1.78549	1.72^{E-16}	5.22^{E-14}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.6543.C1_x_at	ENSG00000172724 OTTHUMG00000019833	6363	*CCL19*	Chemokine (C-C motif) ligand 19	8.20563	9.04171	−1.7852	1.39^{E-12}	2.17^{E-10}
ADXECAD.24530_s_at	ENSG00000111331 OTTHUMG00000169795	4940	*OAS3*	2′-5′-Oligoadenylate synthetase 3, 100 kDa	4.01416	4.84966	−1.78448	8.30^{E-11}	1.00^{E-08}
ADXECRS.658_s_at	ENSG00000161405 OTTHUMG00000133250	22806	*IKZF3*	IKAROS family zinc finger 3 (Aiolos)	4.35629	5.19154	−1.78418	4.96^{E-14}	9.65^{E-12}
ADXEC.7824.C1_at	—	—	—	—	5.08317	5.91814	−1.78383	8.65^{E-10}	9.01^{E-08}
ADXEC.1201.C2_s_at	ENSG00000067066 OTTHUMG00000133203	6672	*SP100*	SP100 nuclear antigen	4.81948	5.65431	−1.78364	7.59^{E-15}	1.71^{E-12}
ADXEC.5437.C3_x_at	ENSG00000025434 OTTHUMG00000150628	10062	*NR1H3*	Nuclear receptor subfamily 1, group H, member 3	9.59495	10.4292	−1.78299	3.16^{E-14}	6.50^{E-12}
ADXECEMUTR.3658_at	ENSG00000179583 OTTHUMG00000129753	4261	*CIITA*	Class II, major histocompatibility complex, transactivator	5.37491	6.20887	−1.78257	1.89^{E-16}	5.64^{E-14}
ADXEC.18.C1_s_at	ENSG00000185201 ENSG00000185885 OTTHUMG00000165357 OTTHUMG00000165359	8519 10581	*IFITM1* *IFITM2*	Interferon induced transmembrane protein 1 Interferon induced transmembrane protein 2	4.44194	5.27298	−1.77897	1.88^{E-05}	0.000704483
ADXEC.23400.C1_at	ENSG00000165168 ENSG00000268765 OTTHUMG00000033175	1536	*CYBB*	Cytochrome b-245, beta polypeptide	6.27862	7.10952	−1.7788	1.89^{E-24}	2.15^{E-21}
ADXECADA.11632_x_at	—	—	—	—	6.98307	7.81184	−1.77617	1.13^{E-14}	2.46^{E-12}
ADXEC.9349.C1_s_at	ENSG00000239836 ENSG00000240065 ENSG00000240118 ENSG00000240508 ENSG00000242711 ENSG00000243067 ENSG00000243594 ENSG00000243958 OTTHUMG00000012781 OTTHUMG00000031287 OTTHUMG00000031585 OTTHUMG00000140189 OTTHUMG00000148833 OTTHUMG00000149102 OTTHUMG00000149359 OTTHUMG00000149620	5698	*PSMB9*	Proteasome (prosome, macropain) subunit, beta type, 9	4.22869	5.05714	−1.77578	2.45^{E-28}	4.65^{E-25}
ADXEC.11295.C2_s_at	ENSG00000226264 ENSG00000234154 ENSG00000239329 ENSG00000241296 ENSG00000241674 ENSG00000242092 ENSG00000242386 ENSG00000242574 OTTHUMG00000012587 OTTHUMG00000031176 OTTHUMG00000031467 OTTHUMG00000140192 OTTHUMG00000148834 OTTHUMG00000149103 OTTHUMG00000149360 OTTHUMG00000149621	3109	*HLA-DMB*	Major histocompatibility complex, class II, DM beta	5.12108	5.94912	−1.77527	2.59^{E-20}	1.50^{E-17}
ADXECRS.39931_s_at	ENSG00000101347 OTTHUMG00000032402	25939	*SAMHD1*	SAM domain and HD domain 1	7.34884	8.17568	−1.7738	4.56^{E-19}	2.21^{E-16}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECEMUTR.2840_x_at	ENSG00000211697 ENSG00000211699 ENSG00000211701 ENSG00000228668 OTTHUMG00000155095 OTTHUMG00000155097 OTTHUMG00000155101 OTTHUMG00000155102	445347	*TARP*	TCR gamma alternate reading frame protein	2.81003	3.63662	−1.77349	7.96^{E-13}	1.30^{E-10}
ADXEC.9016.C1_at	ENSG00000163823 OTTHUMG00000133451	1230	*CCR1*	Chemokine (C-C motif) receptor 1	7.00396	7.82817	−1.77056	5.59^{E-19}	2.66^{E-16}
ADXEC.814.C1_at	ENSG00000163840 OTTHUMG00000159524	151636	*DTX3L*	Deltex 3-like (*Drosophila*)	7.24319	8.06684	−1.76988	2.66^{E-15}	6.43^{E-13}
ADXPCEC.106.C30_s_at	ENSG00000019582 OTTHUMG00000163559	972	*CD74*	CD74 molecule, major histocompatibility complex, class II invariant chain	9.07606	9.89907	−1.76909	3.15^{E-21}	$2.12^{E-1}8$
ADXECRS.31462_at	—	80830	*APOL6*	Apolipoprotein L, 6	6.71464	7.53749	−1.7689	6.08^{E-18}	2.37^{E-15}
ADXECAD.21101_s_at	ENSG00000163131 OTTHUMG00000035010	1520	*CTSS*	Cathepsin S	2.44801	3.27022	−1.76811	3.97^{E-14}	7.94^{E-12}
ADXEC.2862.C3_x_at	ENSG00000130208 OTTHUMG00000180844	341	*APOC1*	Apolipoprotein C-I	7.04481	7.86552	−1.76627	2.95^{E-17}	1.04^{E-14}
ADXECRS.31462_x_at	—	80830	*APOL6*	Apolipoprotein L, 6	6.84801	7.66806	−1.76546	7.03^{E-19}	3.28^{E-16}
ADXEC.9748.C1_at	ENSG00000118849 OTTHUMG00000158834	5918	*RARRES1*	Retinoic acid receptor responder (tazarotene induced) 1	5.07118	5.88794	−1.76145	0.000759497	0.0137901
ADXECNTDJ.37_s_at	ENSG00000211899 OTTHUMG00000152452	3507	*IGHM*	Immunoglobulin heavy constant mu	6.0843	6.90051	−1.76077	5.63^{E-12}	7.97^{E-10}
ADXEC.32309.C1_at	ENSG00000179583 OTTHUMG00000129753	4261	*CIITA*	Class II, major histocompatibility complex, transactivator	5.12128	5.93527	−1.75807	3.56^{E-16}	9.90^{E-14}
ADXEC.6543.C1_s_at	ENSG00000172724 OTTHUMG00000019833	6363	*CCL19*	Chemokine (C-C motif) ligand 19	5.6098	6.42377	−1.75804	7.28^{E-08}	5.16^{E-06}
ADXECNTDJ.7597_s_at	ENSG00000094755 OTTHUMG00000130443	2568	*GABRP*	GABA A receptor, pi	5.66244	6.47615	−1.75772	5.42^{E-05}	0.00173231
ADXEC.6806.C1_at	ENSG00000026751 OTTHUMG00000024008	57823	*SLAMF7*	SLAM family member 7	4.09631	4.90839	−1.75574	1.26^{E-15}	3.18^{E-13}
ADXEC.138.CB1_x_at	ENSG00000166710 OTTHUMG00000131247	567	*B2M*	Beta-2-microglobulin	9.88478	10.6962	−1.75493	6.68^{E-29}	1.34^{E-25}
ADXEC.31841.C1_x_at	ENSG00000229754 OTTHUMG00000155244	3580	*CXCR2P1*	Chemokine (C-X-C motif) receptor 2 pseudogene 1	2.11029	2.92029	−1.75321	9.75^{E-20}	5.48^{E-17}
ADXECNTDJ.8069_at	ENSG00000132530 OTTHUMG00000177908	54739	*XAF1*	XIAP associated factor 1	4.10298	4.9119	−1.7519	1.54^{E-16}	4.73^{E-14}
ADXEC.15017.C1-a_s_at	ENSG00000185880 OTTHUMG00000131246	140691	*TRIM69*	Tripartite motif containing 69	4.94644	5.75336	−1.74948	1.66^{E-10}	1.91^{E-08}
ADXECAD.23434_s_at	ENSG00000136167 OTTHUMG00000016864	3936	*LCP1*	Lymphocyte cytosolic protein 1 (L-plastin)	6.75131	7.55742	−1.7485	6.45^{E-07}	3.64^{E-05}
ADXEC.138.C10_x_at	ENSG00000166710 OTTHUMG00000131247	567	*B2M*	Beta-2-microglobulin	9.72991	10.5354	−1.7478	1.29^{E-31}	4.37^{E-28}
ADXEC.16910.C1_s_at	ENSG00000105122 OTTHUMG00000182450	64926	*RASAL3*	RAS protein activator like 3	6.50352	7.30808	−1.74661	2.64^{E-18}	1.16^{E-15}
ADXEC.21347.C1_at	ENSG00000135077 OTTHUMG00000130249	84868	*HAVCR2*	Hepatitis A virus cellular receptor 2	3.6652	4.469	−1.74569	1.15^{E-12}	1.82^{E-10}
ADXEC.5349.C2_at	—	—	—	—	3.86482	4.66736	−1.74417	1.73^{E-16}	5.23^{E-14}
ADXECNTDJ.5191_at	ENSG00000134321 OTTHUMG00000090352	91543	*RSAD2*	Radical *S*-adenosyl methionine domain containing 2	3.0207	3.8231	−1.744	3.56^{E-13}	6.21^{E-11}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.1022.C6_x_at	ENSG00000211632 ENSG00000224041 ENSG00000244437 OTTHUMG00000151563 OTTHUMG00000151568 OTTHUMG00000151653	50802	*IGK*	Immunoglobulin kappa locus	9.33937	10.1414	−1.74362	5.11^{E-12}	7.29^{E-10}
ADXECADA.2653_at	ENSG00000254838 OTTHUMG00000165506	387751	*GVINP1*	GTPase, very large interferon inducible pseudogene 1	3.14214	3.94362	−1.74289	1.47^{E-12}	2.28^{E-10}
ADXECADA.23711_s_at	ENSG00000136514 OTTHUMG00000156459	64108	*RTP4*	Receptor (chemosensory) transporter protein 4	3.28222	4.0832	−1.74229	4.89^{E-13}	8.35^{E-11}
ADXEC.20449.C1_at	ENSG00000100453 OTTHUMG00000029369	3002	*GZMB*	Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	3.32901	4.12983	−1.74209	2.14^{E-15}	5.23^{E-13}
ADXEC.2268.C3_s_at	ENSG00000089127 OTTHUMG00000169792	4938	*OAS1*	2′-5′-Oligoadenylate synthetase 1, 40/46 kDa	4.8887	5.6889	−1.74133	3.37^{E-10}	3.74^{E-08}
ADXEC.11420.C1-a_s_at	ENSG00000133574 OTTHUMG00000157475	55303	*GIMAP4*	GTPase, IMAP family member 4	4.86265	5.66213	−1.74047	6.71^{E-14}	1.28^{E-11}
ADXEC.23016.C1_at	ENSG00000056558 OTTHUMG00000020578	7185	*TRAF1*	TNF receptor-associated factor 1	6.38931	7.18694	−1.73824	3.02^{E-13}	5.29^{E-11}
ADXEC.60.C3_at	ENSG00000116701 OTTHUMG00000035329	4688	*NCF2*	Neutrophil cytosolic factor 2	4.24989	5.04734	−1.73803	1.05^{E-08}	9.03^{E-07}
ADXEC.3331.C1_s_at	ENSG00000077420 OTTHUMG00000017841	54518	*APBB1IP*	Amyloid beta (A4) precursor protein-binding, family B, member 1 interacting protein	4.537	5.33418	−1.7377	6.75^{E-14}	1.28^{E-11}
ADXEC.119.C55_x_at	ENSG00000204525 ENSG00000206435 ENSG00000206450 ENSG00000206452 ENSG00000224608 ENSG00000225691 ENSG00000228299 ENSG00000228964 ENSG00000232126 ENSG00000233841 ENSG00000237022 OTTHUMG00000031154 OTTHUMG00000031436 OTTHUMG00000036662 OTTHUMG00000037240 OTTHUMG00000148965 OTTHUMG00000149247 OTTHUMG00000149248 OTTHUMG00000149478 OTTHUMG00000149479 OTTHUMG00000149943 OTTHUMG00000149955	3106 3107	*HLA-B* *HLA-C*	Major histocompatibility complex, class I, B Major histocompatibility complex, class I, C	4.95006	5.74562	−1.73576	8.00^{E-05}	0.00237795
ADXEC.11578.C1-a_s_at	ENSG00000086300 OTTHUMG00000023650	29887	*SNX10*	Sorting nexin 10	3.69216	4.486	−1.73368	1.66^{E-13}	3.02^{E-11}
ADXEC.6664.C1-a_s_at	ENSG00000111335 OTTHUMG00000169802	4939	*OAS2*	2′-5′-Oligoadenylate synthetase 2, 69/71 kDa	6.01398	6.807	−1.7327	3.55^{E-15}	8.41^{E-13}
ADXEC.13126.C1_at	ENSG00000107742 OTTHUMG00000018430	9806	*SPOCK2*	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2	6.20663	6.99955	−1.73259	1.37^{E-10}	1.61^{E-08}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.481.C10_x_at	ENSG00000204287 ENSG00000206308 ENSG00000226260 ENSG00000227993 ENSG00000228987 ENSG00000230726 ENSG00000234794 OTTHUMG00000012742 OTTHUMG00000031269 OTTHUMG00000031567 OTTHUMG00000138993 OTTHUMG00000149060 OTTHUMG00000149327 OTTHUMG00000149575	3122	*HLA-DRA*	Major histocompatibility complex, class II, DR alpha	3.23936	4.02826	−1.72776	4.48^{E-07}	2.63^{E-05}
ADXEC.23215.C1_at	ENSG00000168384 ENSG00000206291 ENSG00000224103 ENSG00000228163 ENSG00000229685 ENSG00000231389 ENSG00000235844 ENSG00000236177 OTTHUMG00000012625 OTTHUMG00000031058 OTTHUMG00000031328 OTTHUMG00000140241 OTTHUMG00000148836 OTTHUMG00000149106 OTTHUMG00000149363 OTTHUMG00000149624	3113	*HLA-DPA1*	Major histocompatibility complex, class II, DP alpha 1	5.27933	6.06704	−1.72633	1.42^{E-12}	2.21^{E-10}
ADXEC.11619.C1_at	ENSG00000205744 OTTHUMG00000180853	79958	*DENND1C*	DENN/MADD domain containing 1C	5.76573	6.5534	−1.72628	3.17^{E-17}	1.11^{E-14}
ADXECADA.4972_s_at	ENSG00000096060 OTTHUMG00000014576	2289	*FKBP5*	FK506 binding protein 5	5.19855	5.98618	−1.72624	7.47^{E-09}	6.56^{E-07}
ADXECAD.18269_s_at	ENSG00000163644 OTTHUMG00000130952	152926	*PPM1K*	Protein phosphatase, Mg2+/Mn2+ dependent, 1K	5.53487	6.32132	−1.72482	4.53^{E-14}	8.93^{E-12}
ADXECAD.19551_at	ENSG00000164308 OTTHUMG00000128718	64167	*ERAP2*	Endoplasmic reticulum aminopeptidase 2	2.77361	3.55941	−1.72405	6.93^{E-07}	3.88^{E-05}
ADXEC.119.C45_x_at	ENSG00000206435 ENSG00000206452 ENSG00000228299 ENSG00000237022 OTTHUMG00000037240 OTTHUMG00000148965 OTTHUMG00000149248 OTTHUMG00000149943	3107	*HLA-C*	Major histocompatibility complex, class I, C	8.85475	9.63905	−1.72225	4.54^{E-19}	2.21^{E-16}
ADXEC.25003.C1_at	ENSG00000163565 OTTHUMG00000037108	3428	*IFI16*	Interferon, gamma-inducible protein 16	6.05229	6.83562	−1.7211	2.67^{E-13}	4.71^{E-11}
ADXEC.6133.C1_s_at	ENSG00000104972	10859	*LILRB1*	Leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 1	6.13779	6.92059	−1.72047	3.71^{E-19}	1.84^{E-16}
ADXEC.22822.C1_at	—	—	—	—	3.0604	3.84193	−1.71895	1.01^{E-12}	1.62^{E-10}
ADXLCEC.5698.C1_s_at	—	441108	*C5orf56*	Chromosome 5 open reading frame 56	2.07313	2.85451	−1.71877	1.32^{E-14}	2.85^{E-12}
ADXEC.12823.C1_at	ENSG00000125354 OTTHUMG00000022280	23157	09/06	Septin 6	6.87795	7.65908	−1.71847	2.09^{E-09}	2.03^{E-07}
ADXEC.119.CB1_x_at	ENSG00000223532 ENSG00000234745 OTTHUMG00000031153 OTTHUMG00000031435	3106	*HLA-B*	Major histocompatibility complex, class I, B	10.6643	11.4452	−1.71822	1.88^{E-15}	4.63^{E-13}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECRS.23469_s_at	ENSG00000187912 OTTHUMG00000169312	388512	*CLEC17A*	C-type lectin domain family 17, member A	2.83234	3.61306	−1.71799	1.11^{E-08}	9.54^{E-07}
ADXEC.224.C14_x_at	ENSG00000225890 ENSG00000228284 ENSG00000236418 OTTHUMG00000149069 OTTHUMG00000149336 OTTHUMG00000149584	3117 100509457	*HLA-DQA1* *LOC100509457*	Major histocompatibility complex, class II, DQ alpha 1 HLA class II histocompatibility antigen, DQ alpha 1 chain-like	4.60605	5.3858	−1.71684	9.18^{E-06}	0.000376935
ADXEC.20449.C1_x_at	ENSG00000100453 OTTHUMG00000029369	3002	*GZMB*	Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	3.50229	4.28101	−1.71561	1.29^{E-16}	4.01^{E-14}
ADXECRS.7275_at	ENSG00000263304 OTTHUMG00000179762	284021	*MILR1*	Mast cell immunoglobulin-like receptor 1	4.42634	5.20419	−1.71458	7.10^{E-07}	3.95^{E-05}
ADXEC.29145.C1_s_at	ENSG00000173821 OTTHUMG00000161415	57674	*RNF213*	Ring finger protein 213	6.24023	7.01767	−1.71408	9.72^{E-18}	3.62^{E-15}
ADXEC.31791.C1_at	ENSG00000115085	7535	*ZAP70*	Zeta-chain (TCR) associated protein kinase 70 kDa	2.15729	2.93396	−1.71317	6.65^{E-13}	1.10^{E-10}
ADXPCEC.1278.C1_s_at	ENSG00000160255 OTTHUMG00000090257	3689	*ITGB2*	Integrin, beta 2 (complement component 3 receptor 3 and 4 subunit)	6.41817	7.19411	−1.71231	6.20^{E-19}	2.93^{E-16}
ADXECNTDJ.8224_at	—	—	—	—	6.843	7.61693	−1.70993	2.25^{E-07}	1.43^{E-05}
ADXPCEC.10579.C1_at	ENSG00000197536 OTTHUMG00000059493	441108	*C5orf56*	Chromosome 5 open reading frame 56	3.83537	4.60709	−1.7073	5.32^{E-19}	2.54^{E-16}
ADXEC.24212.C1_at	ENSG00000267349 OTTHUMG00000179901	—	*OTTHUMG00000179901* *RP11-686D22.9*	NULL NULL	3.32581	4.09584	−1.7053	4.73^{E-14}	9.29^{E-12}
ADXEC.541.C10_x_at	ENSG00000253755 OTTHUMG00000152493	3500 3507	*IGHG1* *IGHM*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant mu	9.22239	9.99212	−1.70494	1.29^{E-13}	2.38^{E-11}
ADXEC.2602.C1_s_at	ENSG00000130489 OTTHUMG00000150251	9997	*SCO2*	SCO2 cytochrome c oxidase assembly protein	5.29079	6.05941	−1.70364	1.01^{E-16}	3.27^{E-14}
ADXEC.20525.C1_s_at	ENSG00000204482 ENSG00000206433 ENSG00000223465 ENSG00000226182 ENSG00000230791 ENSG00000231048 ENSG00000234514 ENSG00000235915 OTTHUMG00000031264 OTTHUMG00000031562 OTTHUMG00000040404 OTTHUMG00000148785 OTTHUMG00000148999 OTTHUMG00000149282 OTTHUMG00000149513 OTTHUMG00000149937	7940	*LST1*	Leukocyte-specific transcript 1	6.65738	7.42487	−1.70231	9.25^{E-11}	1.11^{E-08}
ADXEC.3295.C1_s_at	ENSG00000162892 OTTHUMG00000036459	11009	*IL24*	Interleukin 24	2.80988	3.57697	−1.70183	2.26^{E-09}	2.19^{E-07}
ADXEC.32733.C1_s_at	—	100129399	*LOC100129399*	Uncharacterized LOC100129399	7.06652	7.83359	−1.70181	1.45^{E-07}	9.64^{E-06}
ADXECAD.12399_at	—	3500	*IGHG1*	Immunoglobulin heavy constant gamma 1 (G1m marker)	5.2617	6.02849	−1.70147	1.22^{E-10}	1.45^{E-08}
ADXEC.22939.C1_s_at	ENSG00000056558 OTTHUMG00000020578	7185	*TRAF1*	TNF receptor-associated factor 1	5.2202	5.98677	−1.70122	9.39^{E-15}	2.08^{E-12}
ADXECNTDJ.82_s_at	ENSG00000082074 OTTHUMG00000162071	2533	*FYB*	FYN binding protein	4.66331	5.42955	−1.70082	2.56^{E-18}	1.14^{E-15}
ADXEC.8090.C1-a_s_at	ENSG00000127951 OTTHUMG00000130681	10875	*FGL2*	Fibrinogen-like 2	2.66694	3.43259	−1.70014	6.38^{E-10}	6.81^{E-08}
ADXEC.3276.C1_at	ENSG00000109861 OTTHUMG00000167290	1075	*CTSC*	Cathepsin C	5.67629	6.44172	−1.69988	1.10^{E-12}	1.76^{E-10}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECADA.20312_at	ENSG00000105851 OTTHUMG00000157641	5294	*PIK3CG*	Phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit gamma	4.87968	5.64451	−1.69917	8.58^{E-08}	5.99^{E-06}
ADXEC.15017.C1_at	ENSG00000185880 OTTHUMG00000131246	140691	*TRIM69*	Tripartite motif containing 69	6.13944	6.90401	−1.69887	3.18^{E-18}	1.37^{E-15}
ADXEC.10021.C3_s_at	ENSG00000105185 ENSG00000255909 OTTHUMG00000168907 OTTHUMG00000180224	9141	*PDCD5*	Programmed cell death 5	6.43487	7.19883	−1.69815	5.86^{E-05}	0.00183997
ADXEC.22688.C1_at	ENSG00000264198 OTTHUMG00000179517	22806	*IKZF3*	IKAROS family zinc finger 3 (Aiolos)	4.68827	5.44988	−1.69538	1.66^{E-19}	8.88^{E-17}
ADXEC.29271.C1_s_at	ENSG00000069493 OTTHUMG00000168369	29121	*CLEC2D*	C-type lectin domain family 2, member D	4.54394	5.30506	−1.6948	3.54^{E-11}	4.50^{E-09}
ADXEC.11760.C1_at	ENSG00000153563 OTTHUMG00000130265	925	*CD8A*	CD8a molecule	4.57498	5.3352	−1.69375	3.96^{E-15}	9.32^{E-13}
ADXEC.31359.C1_s_at	ENSG00000111335 OTTHUMG00000169802	4939	*OAS2*	2′-5′-Oligoadenylate synthetase 2, 69/71 kDa	5.30529	6.06499	−1.69313	2.43^{E-12}	3.58^{E-10}
ADXECEMUTR.1432_x_at	ENSG00000242534 ENSG00000244116 OTTHUMG00000151616 OTTHUMG00000151652	3514	*IGKC*	Immunoglobulin kappa constant	2.8024	3.56167	−1.69263	2.09^{E-09}	2.03^{E-07}
ADXECNTDJ.10067_s_at	—	—	—	—	5.44549	6.20457	−1.6924	2.39^{E-13}	4.24^{E-11}
ADXECNTDJ.6430_at	ENSG00000153563 OTTHUMG00000130265	925	*CD8A*	CD8a molecule	4.73213	5.48974	−1.69069	8.34^{E-15}	1.87^{E-12}
ADXEC.23683.C1_x_at	ENSG00000169508 OTTHUMG00000017263	1880	*GPR183*	G protein-coupled receptor 183	4.41737	5.17368	−1.68917	1.18^{E-11}	1.59^{E-09}
ADXECNTDJ.774_s_at	ENSG00000172243 OTTHUMG00000133597	64581	*CLEC7A*	C-type lectin domain family 7, member A	5.27231	6.02841	−1.68892	1.85^{E-10}	2.11^{E-08}
ADXECNTDJ.1435_s_at	ENSG00000108679 OTTHUMG00000177572	3959	*LGALS3BP*	Lectin, galactoside-binding, soluble, 3 binding protein	7.59942	8.35544	−1.68883	4.16^{E-09}	3.80^{E-07}
ADXECADA.16046_at	ENSG00000196329 OTTHUMG00000157542	55340 100527949	*GIMAP1-GIMAP5* *GIMAP5*	GIMAP1-GIMAP5 readthrough GTPase, IMAP family member 5	2.53768	3.29336	−1.68842	1.64^{E-11}	2.19^{E-09}
ADXEC.6368.C1_s_at	ENSG00000124256 OTTHUMG00000032824	81030	*ZBP1*	Z-DNA–binding protein 1	3.12472	3.88008	−1.68804	2.30^{E-15}	5.60^{E-13}
ADXECADA.12783_at	—	—	—	—	4.05381	4.80889	−1.68773	2.29^{E-06}	0.000111145
ADXEC.12920.C1_at	ENSG00000110934	51411	*BIN2*	Bridging integrator 2	7.72358	8.47725	−1.68607	1.80^{E-15}	4.46^{E-13}
ADXEC.27278.C1_s_at	ENSG00000094755 OTTHUMG00000130443	2568	*GABRP*	GABA A receptor, pi	6.99519	7.7482	−1.68531	0.000336945	0.00751633
ADXEC.33505.C1_at	—	—	—	—	3.17411	3.92701	−1.68518	5.82^{E-11}	7.15^{E-09}
ADXEC.481.C4_s_at	ENSG00000204287 ENSG00000206308 ENSG00000226260 ENSG00000227993 ENSG00000228987 ENSG00000230726 ENSG00000234794 OTTHUMG00000012742 OTTHUMG00000031269 OTTHUMG00000031567 OTTHUMG00000138993 OTTHUMG00000149060 OTTHUMG00000149327 OTTHUMG00000149575	3122	*HLA-DRA*	Major histocompatibility complex, class II, DR alpha	10.6595	11.4108	−1.68333	2.67^{E-25}	3.42^{E-22}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXLCEC.116.C16_x_at	ENSG00000206505 ENSG00000223980 ENSG00000227715 ENSG00000231834 ENSG00000235657 OTTHUMG00000004793 OTTHUMG00000044844 OTTHUMG00000148897 OTTHUMG00000149177 OTTHUMG00000149428	3105	*HLA-A*	Major histocompatibility complex, class I, A	11.1624	11.9137	−1.68328	2.31^{E-14}	4.86^{E-12}
ADXECAD.24372_x_at	ENSG00000206450 ENSG00000223532 ENSG00000224608 ENSG00000228964 ENSG00000232126 ENSG00000234745 OTTHUMG00000031153 OTTHUMG00000031435 OTTHUMG00000036662 OTTHUMG00000149247 OTTHUMG00000149478 OTTHUMG00000149955	3106	*HLA-B*	Major histocompatibility complex, class I, B	5.91097	6.66222	−1.68325	3.98^{E-15}	9.33^{E-13}
ADXEC.119.C28_x_at	ENSG00000206505 ENSG00000223980 ENSG00000231834 OTTHUMG00000004793 OTTHUMG00000044844 OTTHUMG00000149177	3105	*HLA-A*	Major histocompatibility complex, class I, A	10.8214	11.5721	−1.68254	7.71^{E-16}	2.01^{E-13}
ADXEC.23683.C1_at	ENSG00000169508 OTTHUMG00000017263	1880	*GPR183*	G protein-coupled receptor 183	4.01164	4.76207	−1.6823	1.50^{E-10}	1.75^{E-08}
ADXECADA.20351_at	ENSG00000162676 OTTHUMG00000010897	2672	*GFI1*	Growth factor independent 1 transcription repressor	3.00246	3.75172	−1.68093	7.24^{E-11}	8.78^{E-09}
ADXEC.2026.C1_s_at	ENSG00000155629 OTTHUMG00000018838	118788	*PIK3AP1*	Phosphoinositide-3-kinase adaptor protein 1	3.00396	3.75218	−1.67973	2.18^{E-08}	1.74^{E-06}
ADXPCEC.11163.C1_at	—	—	—	—	3.9553	4.70171	−1.67761	3.18^{E-08}	2.44^{E-06}
ADXEC.7237.C1_s_at	ENSG00000005844 OTTHUMG00000176964	3683	*ITGAL*	Integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	6.01929	6.76555	−1.67743	4.84^{E-23}	4.33^{E-20}
ADXEC.16819.C1_at	ENSG00000126353 OTTHUMG00000133375	1236	*CCR7*	Chemokine (C-C motif) receptor 7	4.54962	5.29553	−1.67703	5.45^{E-13}	9.19^{E-11}
ADXEC.3276.C1_x_at	ENSG00000109861 OTTHUMG00000167290	1075	*CTSC*	Cathepsin C	5.75073	6.4956	−1.67583	3.96^{E-14}	7.94^{E-12}
ADXECADA.16167_at	—	—	—	—	2.78587	3.53074	−1.67582	1.73^{E-08}	1.42^{E-06}
ADXLCEC.128.C4_x_at	ENSG00000166710 OTTHUMG00000131247	567	*B2M*	Beta-2-microglobulin	5.59575	6.34013	−1.67525	7.36^{E-28}	1.33^{E-24}
ADXECRS.41932_x_at	ENSG00000172243 OTTHUMG00000133597	64581	*CLEC7A*	C-type lectin domain family 7, member A	4.03904	4.78328	−1.6751	3.92^{E-07}	2.34^{E-05}
ADXEC.21503.C1_x_at	—	643977	*FLJ32255*	Uncharacterized LOC643977	5.297	6.04118	−1.67502	1.40^{E-06}	7.30^{E-05}
ADXECAD.15721_at	ENSG00000197813 OTTHUMG00000184009	—	*CTC-30107.4* *OTTHUMG00000184009*	NULL NULL	7.43896	8.18136	−1.67296	1.49^{E-14}	3.19^{E-12}
ADXEC.22574.C1_at	ENSG00000163219 OTTHUMG00000152621	9938	*ARHGAP25*	Rho GTPase activating protein 25	5.26468	6.00707	−1.67294	1.75^{E-16}	5.28^{E-14}
ADXECAD.12444_s_at	ENSG00000107099 OTTHUMG00000078789	81704	*DOCK8*	Dedicator of cytokinesis 8	5.30217	6.04289	−1.671	1.19^{E-14}	2.58^{E-12}
ADXEC.10461.C2-a_s_at	ENSG00000093072 OTTHUMG00000030726	51816	*CECR1*	Cat eye syndrome chromosome region, candidate 1	3.81735	4.55693	−1.66969	3.26^{E-07}	1.99^{E-05}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.20728.C1_s_at	—	2634	*GBP2*	Guanylate binding protein 2, interferon-inducible	5.08911	5.82777	−1.66862	1.45^{E-08}	1.21^{E-06}
ADXECAD.2691_at	—	—	—	—	3.68679	4.42491	−1.66801	3.40^{E-10}	3.77^{E-08}
ADXECEMUTR.868_x_at	ENSG00000153283 OTTHUMG00000159275	10225	*CD96*	CD96 molecule	3.50414	4.24168	−1.66733	6.72^{E-11}	8.20^{E-09}
ADXLCEC.5698.C1_x_at	—	441108	*C5orf56*	Chromosome 5 open reading frame 56	3.85155	4.58885	−1.66706	2.25^{E-20}	1.31^{E-17}
ADXEC.119.C14_x_at	ENSG00000206450 ENSG00000223532 ENSG00000234745 OTTHUMG00000031153 OTTHUMG00000031435 OTTHUMG00000149955	3106	*HLA-B*	Major histocompatibility complex, class I, B	10.7923	11.529	−1.66639	1.81^{E-17}	6.62^{E-15}
ADXECADA.22573_s_at	ENSG00000117020 OTTHUMG00000039994	10000	*AKT3*	V-akt murine thymoma viral oncogene homolog 3 (protein kinase B, gamma)	4.41658	5.15234	−1.66527	3.69^{E-05}	0.00125105
ADXECAD.20735_at	ENSG00000048740 OTTHUMG00000017668	10659	*CELF2*	CUGBP, Elav-like family member 2	6.51308	7.24863	−1.66504	9.86^{E-12}	1.33^{E-09}
ADXEC.2989.C2_s_at	ENSG00000168384 ENSG00000206291 ENSG00000224103 ENSG00000228163 ENSG00000229685 ENSG00000231389 ENSG00000235844 ENSG00000236177 OTTHUMG00000012625 OTTHUMG00000031058 OTTHUMG00000031328 OTTHUMG00000140241 OTTHUMG00000148836 OTTHUMG00000149106 OTTHUMG00000149363 OTTHUMG00000149624	3113	*HLA-DPA1*	Major histocompatibility complex, class II, DP alpha 1	10.4259	11.1612	−1.66467	1.54^{E-09}	1.54^{E-07}
ADXPCEC.13546.C1_at	—	—	—	—	2.14138	2.87606	−1.66403	1.19^{E-12}	1.88^{E-10}
ADXEC.541.CB1_x_at	ENSG00000211896 ENSG00000253755 OTTHUMG00000152493 OTTHUMG00000152495	3500 3507 28396	*IGHG1* *IGHM* *IGHV4-31*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	11.3602	12.0949	−1.66403	1.89^{E-11}	2.49^{E-09}
ADXEC.17029.C1_s_at	ENSG00000088827 OTTHUMG00000031757	6614	*SIGLEC1*	Sialic acid binding Ig-like lectin 1, sialoadhesin	6.97946	7.71339	−1.66316	5.49^{E-17}	1.88^{E-14}
ADXEC.12685.C1_at	ENSG00000162511 OTTHUMG00000003707	7805	*LAPTM5*	Lysosomal protein transmembrane 5	5.59234	6.32373	−1.66024	8.57^{E-11}	1.03^{E-08}
ADXEC.22235.C1_at	ENSG00000066923 ENSG00000213413 OTTHUMG00000155183 OTTHUMG00000156798	10734 79037	*PVRIG* *STAG3*	Poliovirus receptor related immunoglobulin domain containing Stromal antigen 3	7.03191	7.76299	−1.65988	5.50^{E-07}	3.16^{E-05}
ADXECAD.19914_at	—	—	—	—	4.94455	5.67542	−1.65964	1.28^{E-19}	6.98^{E-17}
ADXEC.28931.C1_at	ENSG00000154642 OTTHUMG00000074509	54149	*C21orf91*	Chromosome 21 open reading frame 91	4.42579	5.15635	−1.65928	7.05^{E-05}	0.00215033
ADXECNTDJ.3401_x_at	—	10730	*YME1L1*	YME1-like 1 ATPase	3.83972	4.57019	−1.65918	4.10^{E-07}	2.43^{E-05}
ADXEC.541.C7_x_at	ENSG00000211897 ENSG00000253755 OTTHUMG00000152493 OTTHUMG00000152539	3502 3507 28396	*IGHG3* *IGHM* *IGHV4-31*	Immunoglobulin heavy constant gamma 3 (G3m marker) Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	6.04138	6.77086	−1.65803	9.96^{E-10}	1.03^{E-07}
ADXEC.9502.C1_at	ENSG00000101336 OTTHUMG00000032204	3055	*HCK*	Hemopoietic cell kinase	4.32305	5.05102	−1.6563	2.98^{E-08}	2.29^{E-06}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECRS.24793_x_at	ENSG00000146192 OTTHUMG00000014616	221472	*FGD2*	FYVE, RhoGEF and PH domain containing 2	5.56511	6.29239	−1.65552	4.07^{E-21}	2.69^{E-18}
ADXECAD.26949_s_at	ENSG00000179583 OTTHUMG00000129753	4261	*CIITA*	Class II, major histocompatibility complex, transactivator	6.0737	6.79841	−1.65257	2.09^{E-17}	7.61^{E-15}
ADXECAD.8106_s_at	—	—	—	—	5.37813	6.10276	−1.65248	5.10^{E-06}	0.000225069
ADXEC.20433.C1_at	ENSG00000197943 OTTHUMG00000176532	5336	*PLCG2*	Phospholipase C, gamma 2 (phosphatidylinositol-specific)	6.85967	7.58421	−1.65238	3.61^{E-09}	3.36^{E-07}
ADXECRS.44768_at	—	6672	*SP100*	SP100 nuclear antigen	4.66189	5.3862	−1.65211	1.37^{E-06}	7.16^{E-05}
ADXPCEC.4821.C5_x_at	ENSG00000211892 ENSG00000211893 ENSG00000211896 ENSG00000211897 ENSG00000253755 OTTHUMG00000152481 OTTHUMG00000152482 OTTHUMG00000152493 OTTHUMG00000152495 OTTHUMG00000152539	3500 3501 3502 3503 3507 28396	*IGHG1* *IGHG2* *IGHG3* *IGHG4* *IGHM* *IGHV4-31*	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant gamma 2 (G2m marker) Immunoglobulin heavy constant gamma 3 (G3m marker) Immunoglobulin heavy constant gamma 4 (G4m marker) Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	8.84974	9.57386	−1.65189	1.42^{E-12}	2.21^{E-10}
ADXEC.3942.C3_s_at	ENSG00000145287 OTTHUMG00000130294	51316	*PLAC8*	Placenta-specific 8	2.42296	3.14667	−1.65143	3.28^{E-07}	2.00^{E-05}
ADXECRS.408_x_at	ENSG00000243811 OTTHUMG00000151084	140564	*APOBEC3D*	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3D	7.71732	8.44046	−1.65077	1.14^{E-19}	6.26^{E-17}
ADXEC.21620.C1_at	ENSG00000113088 OTTHUMG00000097009	3003	*GZMK*	Granzyme K (granzyme 3; tryptase II)	3.7909	4.51378	−1.65047	1.28^{E-12}	2.02^{E-10}
ADXEC.23834.C1_x_at	ENSG00000187474 OTTHUMG00000183502	2359	*FPR3*	Formyl peptide receptor 3	5.22514	5.94792	−1.65036	4.95^{E-17}	1.71^{E-14}
ADXEC.18764.C1_at	ENSG00000171488 OTTHUMG00000010305	84230	*LRRC8C*	Leucine rich repeat containing 8 family, member C	3.51196	4.23407	−1.6496	3.21^{E-08}	2.46^{E-06}
ADXECAD.8513_at	—	—	—	—	4.67953	5.401	−1.64885	5.59^{E-09}	5.00^{E-07}
ADXEC.1477.C3_x_at	ENSG00000026950 OTTHUMG00000014449	11119	*BTN3A1*	Butyrophilin, subfamily 3, member A1	6.24846	6.96905	−1.64786	4.48^{E-17}	1.57^{E-14}
ADXEC.19534.C1_at	ENSG00000145088 OTTHUMG00000159424	55840	*EAF2*	ELL associated factor 2	3.72901	4.44912	−1.64731	2.68^{E-07}	1.66^{E-05}
ADXEC.8829.C1_at	ENSG00000094755 OTTHUMG00000130443	2568	*GABRP*	GABA A receptor, pi	8.83282	9.5523	−1.64659	0.00213074	0.0287375
ADXEC.1924.C10_s_at	ENSG00000165949 OTTHUMG00000171303	3429	*IFI27*	Interferon, alpha-inducible protein 27	5.31612	6.03363	−1.64434	8.65^{E-12}	1.18^{E-09}
ADXEC.32338.C1_at	ENSG00000135899 OTTHUMG00000133204	3431	*SP110*	SP110 nuclear body protein	4.50099	5.21798	−1.64375	1.78^{E-09}	1.77^{E-07}
ADXEC.12837.C1_at	ENSG00000069424 OTTHUMG00000000795	8514	*KCNAB2*	Potassium voltage-gated channel, shaker-related subfamily, beta member 2	7.88262	8.59892	−1.64296	1.03^{E-14}	2.27^{E-12}
ADXEC.4600.C1_s_at	ENSG00000160255 OTTHUMG00000090257	3689	*ITGB2*	Integrin, beta 2 (complement component 3 receptor 3 and 4 subunit)	6.40955	7.12513	−1.64214	2.24^{E-17}	8.07^{E-15}
ADXECNTDJ.1662_s_at	ENSG00000124103 ENSG00000213714 OTTHUMG00000032799 OTTHUMG00000032800	200232 388799	*FAM209A* *FAM209B*	Family with sequence similarity 209, member A Family with sequence similarity 209, member B	5.01834	5.73279	−1.64085	0.000191027	0.00482255
ADXECAD.16416_at	—	—	—	—	4.41088	5.12481	−1.64026	9.56^{E-17}	3.11^{E-14}
ADXECNTDJ.403_s_at	ENSG00000211866 OTTHUMG00000170944	—	*TRAJ23* *TRAJ23*	T-cell receptor alpha joining 23 NULL	3.68809	4.4018	−1.64002	9.88^{E-07}	5.30^{E-05}
ADXECADA.8117_at	—	—	—	—	5.2212	5.93466	−1.63974	1.37^{E-10}	1.61^{E-08}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.119.C1_x_at	ENSG00000206505 ENSG00000223980 ENSG00000227715 ENSG00000231834 ENSG00000235657 OTTHUMG00000004793 OTTHUMG00000044844 OTTHUMG00000148897 OTTHUMG00000149177 OTTHUMG00000149428	3105	*HLA-A*	Major histocompatibility complex, class I, A	10.77	11.4832	−1.63939	3.72^{E-16}	1.02^{E-13}
ADXECAD.28491_s_at	ENSG00000111537 OTTHUMG00000169113	3458	*IFNG*	Interferon, gamma	3.05809	3.77123	−1.63937	1.99^{E-08}	1.61^{E-06}
ADXECADA.15927_at	ENSG00000081189	4208	*MEF2C*	Myocyte enhancer factor 2C	4.78083	5.49317	−1.63845	9.49^{E-07}	5.11^{E-05}
ADXEC.7531.C1-a_s_at	ENSG00000041357 OTTHUMG00000143859	5685	*PSMA4*	Proteasome (prosome, macropain) subunit, alpha type, 4	4.17648	4.88849	−1.63808	7.11^{E-06}	0.000300514
ADXEC.13340.C1_at	ENSG00000187239 OTTHUMG00000020800	23048	*FNBP1*	Formin binding protein 1	5.8032	6.51513	−1.638	5.94^{E-14}	1.13^{E-11}
ADXEC.7250.C1_at	ENSG00000185862 OTTHUMG00000132869	2124	*EVI2B*	Ecotropic viral integration site 2B	4.48687	5.19875	−1.63793	6.12^{E-18}	2.38^{E-15}
ADXEC.6635.C2_s_at	ENSG00000138642 OTTHUMG00000160983	55008	*HERC6*	HECT and RLD domain containing E3 ubiquitin protein ligase family member 6	5.14391	5.85576	−1.63789	5.46^{E-11}	6.72^{E-09}
ADXECAD.14647_s_at	—	—	—	—	2.93491	3.6466	−1.63772	4.13^{E-07}	2.45^{E-05}
ADXEC.4208.C1_at	ENSG00000154124 OTTHUMG00000161762	90268	*FAM105B*	Family with sequence similarity 105, member B	5.82468	6.53511	−1.6363	0.000225727	0.00550193
ADXEC.25371.C1_at	ENSG00000166750 OTTHUMG00000179858	162394	*SLFN5*	Schlafen family member 5	5.51958	6.22996	−1.63623	1.41^{E-07}	9.45^{E-06}
ADXEC.8396.C1_at	ENSG00000026751 OTTHUMG00000024008	57823	*SLAMF7*	SLAM family member 7	3.4482	4.1577	−1.63523	5.37^{E-18}	2.15^{E-15}
ADXEC.11734.C1_at	ENSG00000184979 OTTHUMG00000150104	11274	*USP18*	Ubiquitin-specific peptidase 18	3.46738	4.17678	−1.63512	4.20^{E-11}	5.30^{E-09}
ADXEC.2739.C1_at	ENSG00000157873 OTTHUMG00000000792	8764	*TNFRSF14*	Tumor necrosis factor receptor superfamily, member 14	7.48352	8.19223	−1.63434	1.59^{E-13}	2.89^{E-11}
ADXECAD.15016_at	ENSG00000083799 OTTHUMG00000173404	1540	*CYLD*	Cylindromatosis (turban tumor syndrome)	4.32179	5.03021	−1.63401	0.000623068	0.0118496
ADXEC.26661.C1_at	—	—	—	—	4.6549	5.36179	−1.63228	3.62^{E-09}	3.36^{E-07}
ADXEC.18764.C1_x_at	ENSG00000171488 OTTHUMG00000010305	84230	*LRRC8C*	Leucine-rich repeat containing 8 family, member C	4.41917	5.12604	−1.63226	$6.84E^{-08}$	4.88^{E-06}
ADXEC.6664.C1_x_at	ENSG00000111335 OTTHUMG00000169802	4939	*OAS2*	2′-5′-Oligoadenylate synthetase 2, 69/71 kDa	6.08279	6.789	−1.63152	9.68^{E-13}	1.57^{E-10}
ADXEC.4004.C1_at	ENSG00000110042 OTTHUMG00000167336	23220	*DTX4*	Deltex homolog 4 (*Drosophila*)	3.6627	4.36837	−1.63089	3.12^{E-12}	4.53^{E-10}
ADXEC.3768.C2_x_at	ENSG00000140379 OTTHUMG00000144173	597	*BCL2A1*	BCL2-related protein A1	4.13156	4.83718	−1.63084	3.49^{E-08}	2.64^{E-06}
ADXEC.32000.C1_at	ENSG00000231578	—	—	—	2.31383	3.01942	−1.6308	3.53^{E-14}	7.12^{E-12}
ADXEC.1732.C2_s_at	ENSG00000113845 OTTHUMG00000159388	51300	*TIMMDC1*	Translocase of inner mitochondrial membrane domain containing 1	4.78788	5.49329	−1.63061	1.23^{E-07}	8.30^{E-06}
ADXEC.12372.C1_s_at	ENSG00000119922 OTTHUMG00000018707	3433	*IFIT2*	Interferon-induced protein with tetratricopeptide repeats 2	5.39497	6.10023	−1.63044	1.84^{E-12}	2.79^{E-10}
ADXECADA.10962_s_at	ENSG00000070190 OTTHUMG00000160974	27071	*DAPP1*	Dual adaptor of phosphotyrosine and 3-phosphoinositides	4.24276	4.94733	−1.62966	4.29^{E-10}	4.69^{E-08}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECAD.2593_at	ENSG00000171488 OTTHUMG00000010305	84230	*LRRC8C*	Leucine-rich repeat containing 8 family, member C	3.49226	4.19648	−1.62926	2.05^{E-08}	1.65^{E-06}
ADXEC.5286.C3_s_at	ENSG00000196954 OTTHUMG00000166078	837	*CASP4*	Caspase 4, apoptosis-related cysteine peptidase	6.66916	7.37203	−1.62773	1.58^{E-08}	1.31^{E-06}
ADXECEMUTR.6361_at	—	51561	*IL23A*	Interleukin 23, alpha subunit p19	4.97263	5.67548	−1.62772	2.43^{E-14}	5.08^{E-12}
ADXEC.6891.C1_at	ENSG00000117228 OTTHUMG00000010614	2633	*GBP1*	Guanylate-binding protein 1, interferon-inducible	3.87662	4.57937	−1.62761	9.72^{E-13}	1.57^{E-10}
ADXEC.7351.C1_s_at	ENSG00000165140 OTTHUMG00000020268	2203	*FBP1*	Fructose-1,6-bisphosphatase 1	4.5942	5.29571	−1.6262	6.91^{E-05}	0.00211391
ADXEC.19606.C1_s_at	ENSG00000105967 OTTHUMG00000023518	22797	*TFEC*	Transcription factor EC	2.63795	3.33881	−1.62548	3.49^{E-14}	7.05^{E-12}
ADXECAD.12222_at	ENSG00000240382	—	*IGKV1-17*	Immunoglobulin kappa variable 1-17	3.53499	4.23584	−1.62547	1.37^{E-10}	1.61^{E-08}
ADXEC.8312.C1_s_at	ENSG00000163565 OTTHUMG00000037108	3428	*IFI16*	Interferon, gamma-inducible protein 16	3.72553	4.42639	−1.62547	4.24^{E-09}	3.87^{E-07}
ADXEC.60.C3_x_at	ENSG00000116701 OTTHUMG00000035329	4688	*NCF2*	Neutrophil cytosolic factor 2	4.80998	5.51009	−1.62463	1.22^{E-08}	1.03^{E-06}
ADXEC.20554.C1_at	ENSG00000115935 OTTHUMG00000132334	7456	*WIPF1*	WAS/WASL interacting protein family, member 1	5.76995	6.46999	−1.62454	9.02^{E-13}	1.46^{E-10}
ADXEC.119.C16_at	—	—	—	—	7.47993	8.17945	−1.62396	2.95^{E-19}	1.47^{E-16}
ADXECAD.11127_s_at	ENSG00000131876 ENSG00000144158 OTTHUMG00000149871 OTTHUMG00000153382	6627	*SNRPA1*	Small nuclear ribonucleoprotein polypeptide A′	5.41283	6.11186	−1.62341	0.000534555	0.0105676
ADXEC.13347.C1_at	ENSG00000131018 OTTHUMG00000015841	23345	*SYNE1*	Spectrin repeat containing, nuclear envelope 1	3.95741	4.65643	−1.6234	1.73^{E-06}	8.75^{E-05}
ADXEC.27278.C2_at	ENSG00000094755 OTTHUMG00000130443	2568	*GABRP*	GABA A receptor, pi	6.10812	6.8071	−1.62336	0.00305297	0.0364148
ADXEC.22834.C1_x_at	ENSG00000135899 OTTHUMG00000133204	3431	*SP110*	SP110 nuclear body protein	4.27294	4.97079	−1.62209	1.15^{E-14}	2.50^{E-12}
ADXECAD.12181_s_at	ENSG00000137265 OTTHUMG00000016294	3662	*IRF4*	Interferon regulatory factor 4	4.51658	5.21336	−1.62087	1.30^{E-10}	1.53^{E-08}
ADXEC.4829.C1-a_s_at	ENSG00000134326 OTTHUMG00000151629	129607	*CMPK2*	Cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial	3.49544	4.19217	−1.62083	1.51^{E-15}	3.77^{E-13}
ADXECADA.20532_s_at	ENSG00000174946 OTTHUMG00000159861	29909	*GPR171*	G protein-coupled receptor 171	4.21846	4.915	−1.62062	1.14^{E-07}	7.75^{E-06}
ADXPCEC.12456.C1_at	—	—	—	—	4.12043	4.81675	−1.62037	2.85^{E-08}	2.21^{E-06}
ADXECNTDJ.4119_s_at	ENSG00000070190 OTTHUMG00000160974	27071	*DAPP1*	Dual adaptor of phosphotyrosine and 3-phosphoinositides	5.81361	6.50874	−1.61903	8.80^{E-11}	1.06^{E-08}
ADXEC.11929.C1_at	—	152926	*PPM1K*	Protein phosphatase, Mg2+/Mn2+ dependent, 1K	3.93553	4.63016	−1.61847	7.69^{E-09}	6.72^{E-07}
ADXEC.7199.C1_s_at	ENSG00000122862 OTTHUMG00000018369	5552	*SRGN*	Slycin	2.45511	3.14957	−1.61828	1.36^{E-08}	1.14^{E-06}
ADXEC.23398.C1_s_at	ENSG00000177272 OTTHUMG00000034493	3738	*KCNA3*	Potassium voltage-gated channel, shaker-related subfamily, member 3	2.34049	3.03453	−1.61781	5.82^{E-09}	5.20^{E-07}
ADXEC.3982.C1_s_at	ENSG00000137752 ENSG00000204397 OTTHUMG00000048072 OTTHUMG00000166157	834 114769	*CARD16* *CASP1*	Caspase recruitment domain family, member 16 Caspase 1, apoptosis-related cysteine peptidase	3.80538	4.49796	−1.61617	1.37^{E-08}	1.15^{E-06}
ADXEC.22709.C1_at	ENSG00000145779 OTTHUMG00000162949	25816	*TNFAIP8*	Tumor necrosis factor, alpha-induced protein 8	7.3595	8.05204	−1.61612	6.77^{E-17}	2.25^{E-14}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.17999.C1_at	ENSG00000154016 OTTHUMG00000059436	10750	*GRAP*	GRB2-related adaptor protein	4.63945	5.33188	−1.616	0.000988263	0.0166782
ADXECRS.41932_s_at	ENSG00000172243 OTTHUMG00000133597	64581	*CLEC7A*	C-type lectin domain family 7, member A	3.84526	4.5375	−1.6158	0.000269599	0.00629412
ADXECRS.41599_s_at	ENSG00000170085 OTTHUMG00000130663	202181 375484	*LOC202181* *SIMC1*	SUMO-interacting motifs containing 1 pseudogene SUMO-interacting motifs containing 1	4.23808	4.92973	−1.61513	0.00270521	0.0335997
ADXEC.18303.C1_at	—	55824	*PAG1*	Phosphoprotein associated with glycosphingolipid microdomains 1	3.20927	3.90075	−1.61493	6.17^{E-07}	3.49^{E-05}
ADXECRS.12890_s_at	ENSG00000089012 OTTHUMG00000031680	55423	*SIRPG*	Signal-regulatory protein gamma	5.03622	5.72749	−1.61471	1.45^{E-15}	3.66^{E-13}
ADXEC.10461.C2_x_at	ENSG00000093072	51816	*CECR1*	Cat eye syndrome chromosome region, candidate 1	6.97203	7.66112	−1.61226	2.35^{E-23}	2.24^{E-20}
ADXEC.9663.C1-a_s_at	ENSG00000162692 OTTHUMG00000010982	7412	*VCAM1*	Vascular cell adhesion molecule 1	2.70338	3.39233	−1.61212	6.10^{E-10}	6.53^{E-08}
ADXEC.19287.C1_s_at	ENSG00000164691 OTTHUMG00000015923	117289	*TAGAP*	T-cell activation RhoGTPase activating protein	2.77176	3.46069	−1.61209	8.39^{E-18}	3.14^{E-15}
ADXECAD.15016_x_at	ENSG00000083799 OTTHUMG00000173404	1540	*CYLD*	Cylindromatosis (turban tumor syndrome)	3.6816	4.37047	−1.61203	0.000151166	0.00399578
ADXECAD.4629_at	—	—	—	—	3.86072	4.54902	−1.61138	1.71^{E-10}	1.96^{E-08}
ADXEC.6180.C1_at	ENSG00000204673 OTTHUMG00000150246	84335	*AKT1S1*	AKT1 substrate 1 (proline-rich)	5.33689	6.02417	−1.61025	5.18^{E-06}	0.000227521
ADXECRS.29144_at	ENSG00000204267 ENSG00000206235 ENSG00000206299 ENSG00000223481 ENSG00000225967 ENSG00000228582 ENSG00000232326 ENSG00000237599 OTTHUMG00000012641 OTTHUMG00000031068 OTTHUMG00000031338 OTTHUMG00000041555 OTTHUMG00000148826 OTTHUMG00000149079 OTTHUMG00000149345 OTTHUMG00000149594	6891	*TAP2*	Transporter 2, ATP-binding cassette, subfamily B (MDR/TAP)	4.23028	4.91735	−1.61002	3.15^{E-09}	2.97^{E-07}
ADXEC.745.C1_s_at	ENSG00000010030 OTTHUMG00000014594	51513	*ETV7*	Ets variant 7	6.17561	6.86263	−1.60996	3.83^{E-25}	4.65^{E-22}
ADXEC.26927.C1_s_at	ENSG00000107742 OTTHUMG00000018430	9806	*SPOCK2*	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2	4.95745	5.64364	−1.60903	6.13^{E-08}	4.41^{E-06}
ADXECAD.23758_s_at	ENSG00000067066 OTTHUMG00000133203	6672	*SP100*	SP100 nuclear antigen	4.27392	4.95989	−1.60879	7.03^{E-07}	3.92^{E-05}
ADXECADA.22526_x_at	ENSG00000128335 OTTHUMG00000150634	23780	*APOL2*	Apolipoprotein L, 2	8.35313	9.03886	−1.60851	1.74^{E-23}	1.73^{E-20}
ADXECRS.38610_s_at	ENSG00000135838 OTTHUMG00000035321	80896	*NPL*	N-acetylneuraminate pyruvate lyase (dihydrodipicolinate synthase)	4.75083	5.43627	−1.60819	1.15^{E-07}	7.83^{E-06}
ADXECAD.18205_at	ENSG00000260655 OTTHUMG00000172730	—	*CTA-250D10.23* *OTTHUMG00000172730*	NULL NULL	3.09747	3.78225	−1.60745	1.56^{E-07}	1.0^{3E-05}
ADXEC.32510.C1_x_at	ENSG00000196684 OTTHUMG00000182256	84941	*HSH2D*	Hematopoietic SH2 domain containing	4.36801	5.0526	−1.60724	3.47^{E-15}	8.25^{E-13}
ADXEC.583.C2_s_at	ENSG00000173369 OTTHUMG00000002896	713	*C1QB*	Complement component 1, q subcomponent, B chain	6.54826	7.23195	−1.60624	1.85^{E-09}	1.82^{E-07}
ADXEC.3847.C3_s_at	ENSG00000100906 OTTHUMG00000140220	4792	*NFKBIA*	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	6.65423	7.33649	−1.60466	3.22^{E-08}	2.46^{E-06}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.5183.C1_s_at	ENSG00000173821 OTTHUMG00000161415	57674	*RNF213*	Ring finger protein 213	5.1164	5.79786	−1.60376	1.96^{E-13}	3.52^{E-11}
ADXEC.481.C13_x_at	ENSG00000204287 ENSG00000206308 ENSG00000226260 ENSG00000227993 ENSG00000228987 ENSG00000230726 ENSG00000234794 OTTHUMG00000012742 OTTHUMG00000031269 OTTHUMG00000031567 OTTHUMG00000138993 OTTHUMG00000149060 OTTHUMG00000149327 OTTHUMG00000149575	3122	*HLA-DRA*	Major histocompatibility complex, class II, DR alpha	4.4592	5.13627	−1.59888	6.55^{E-10}	6.97^{E-08}
ADXECEMUTR.1413_x_at	ENSG00000211666 ENSG00000211674 ENSG00000254709 OTTHUMG00000151225 OTTHUMG00000151235 OTTHUMG00000165670	100423062	*IGLL5*	Immunoglobulin lambda-like polypeptide 5	4.93804	5.61492	−1.59868	1.66^{E-12}	2.54^{E-10}
ADXEC.617.C1_s_at	ENSG00000111275 OTTHUMG00000169603	217	*ALDH2*	Aldehyde dehydrogenase 2 family (mitochondrial)	8.92411	9.60035	−1.59797	3.20^{E-11}	4.08^{E-09}
ADXEC.111.C193_s_at	ENSG00000211890 ENSG00000211895 OTTHUMG00000152472 OTTHUMG00000152494	3492 3493 3494	*IGH* *IGHA1* *IGHA2*	Immunoglobulin heavy locus Immunoglobulin heavy constant alpha 1 Immunoglobulin heavy constant alpha 2 (A2m marker)	8.39581	9.07205	−1.59797	0.000142684	0.00381645
ADXECADA.2949_at	—	55008	*HERC6*	HECT and RLD domain containing E3 ubiquitin protein ligase family member 6	2.73168	3.40775	−1.59778	4.33^{E-12}	6.22^{E-10}
ADXECAD.17927_at	ENSG00000173821 OTTHUMG00000161415	57674	*RNF213*	Ring finger protein 213	6.57402	7.24963	−1.59727	5.35^{E-17}	1.84^{E-14}
ADXECRS.22266_x_at	ENSG00000206505 OTTHUMG00000004793	3105	*HLA-A*	Major histocompatibility complex, class I, A	6.60567	7.27982	−1.59566	5.79^{E-12}	8.18^{E-10}
ADXEC.1056.C4_s_at	ENSG00000112096 OTTHUMG00000015940	6648 100129518	*LOC100129518* *SOD2*	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	7.67752	8.35143	−1.5954	1.12^{E-08}	9.59^{E-07}
ADXECADA.20312_x_at	ENSG00000105851 OTTHUMG00000157641	5294	*PIK3CG*	Phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit gamma	4.99884	5.67241	−1.59501	3.53^{E-07}	2.14^{E-05}
ADXECRS.17610_s_at	ENSG00000169554 OTTHUMG00000131834	9839	*ZEB2*	Zinc finger E-box binding homeobox 2	4.39199	5.0652	−1.59462	5.08^{E-08}	3.71^{E-06}
ADXECAD.7800_s_at	ENSG00000197872 OTTHUMG00000090615	81553	*FAM49A*	Family with sequence similarity 49, member A	5.0179	5.69003	−1.59343	0.000234641	0.0056689
ADXEC.7301.C1_at	ENSG00000116824 OTTHUMG00000022750	914	*CD2*	CD2 molecule	5.8015	6.47345	−1.59323	6.75^{E-18}	2.57^{E-15}
ADXECNTDJ.5601_at	ENSG00000188404 OTTHUMG00000034809	6402	*SELL*	Selectin L	4.6303	5.30188	−1.59282	1.87^{E-15}	4.61^{E-13}
ADXEC.23091.C1_at	ENSG00000135905 OTTHUMG00000153428	55619	*DOCK10*	Dedicator of cytokinesis 10	3.70869	4.37957	−1.59205	6.43^{E-15}	1.47^{E-12}
ADXECRS.6734_at	—	729230	*CCR2*	Chemokine (C-C motif) receptor 2	4.86222	5.53265	−1.59154	2.82^{E-14}	5.82^{E-12}
ADXEC.1428.C1_at	ENSG00000213809 ENSG00000255819 OTTHUMG00000168531 OTTHUMG00000168574	22914 100528032	*KLRC4-KLRK1* *KLRK1*	KLRC4-KLRK1 readthrough Killer cell lectin-like receptor subfamily K, member 1	3.64785	4.31821	−1.59147	2.73^{E-12}	3.99^{E-10}
ADXEC.15.C10_at	ENSG00000184371 OTTHUMG00000011646	1435	*CSF1*	Colony stimulating factor 1 (macrophage)	4.59879	5.26742	−1.58956	1.14^{E-08}	9.77^{E-07}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.8692.C1_s_at	ENSG00000125730 OTTHUMG00000150335	718	*C3*	Complement component 3	8.88893	9.55751	−1.58952	7.94^{E-08}	5.60^{E-06}
ADXEC.22991.C1_at	ENSG00000161921 OTTHUMG00000090761	58191	*CXCL16*	Chemokine (C-X-C motif) ligand 16	7.41762	8.08605	−1.58934	1.96^{E-05}	0.000727973
ADXEC.6719.C1_s_at	ENSG00000163131 OTTHUMG00000035010	1520	*CTSS*	Cathepsin S	3.26889	3.93622	−1.58812	1.25^{E-10}	1.48E-08
ADXEC.5662.C1_at	ENSG00000206337	10866	*HCP5*	HLA complex P5 (nonprotein coding)	2.45072	3.11636	−1.58627	4.55^{E-10}	4.93^{E-08}
ADXECADA.18168_at	ENSG00000163131	1520	*CTSS*	Cathepsin S	5.32749	5.99281	−1.58591	1.10^{E-15}	2.80^{E-13}
ADXEC.15.C10_x_at	ENSG00000184371 OTTHUMG00000011646	1435	*CSF1*	Colony stimulating factor 1 (macrophage)	5.15363	5.81883	−1.58579	1.53^{E-08}	1.27^{E-06}
ADXEC.11542.C2_s_at	ENSG00000073331 OTTHUMG00000132911	80216	*ALPK1*	Alpha-kinase 1	5.44374	6.10819	−1.58497	7.32^{E-12}	1.02^{E-09}
ADXEC.23396.C1_at	ENSG00000112096 OTTHUMG00000015940	6648 100129518	*LOC100129518* *SOD2*	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	3.43963	4.10135	−1.58197	2.81^{E-05}	0.000988428
ADXEC.12905.C1_x_at	ENSG00000101017 OTTHUMG00000033053	958	*CD40*	MD40 molecule, TNF receptor superfamily member 5	5.01986	5.68138	−1.58176	2.12^{E-16}	6.18^{E-14}
ADXEC.22939.C1-a_s_at	ENSG00000056558 OTTHUMG00000020578	7185	*TRAF1*	TNF receptor-associated factor 1	4.23635	4.89705	−1.58084	4.79^{E-07}	2.80^{E-05}
ADXEC.26430.C1_at	—	—	—	—	6.1926	6.85284	−1.58035	4.93^{E-14}	9.62^{E-12}
ADXEC.25169.C1_at	OTTHUMG00000184118	159013	*CXorf38*	Chromosome X open reading frame 38	4.6659	5.32544	−1.57958	9.48^{E-08}	6.55^{E-06}
3699890_at	ENSG00000065427	3735	*KARS*	Lysyl-tRNA synthetase	2.40414	3.06349	−1.57937	4.85^{E-06}	0.000215687
ADXEC.2863.C3_s_at	ENSG00000010610 ENSG00000268779 OTTHUMG00000168514	920	*CD4*	CD4 molecule	6.94849	7.60756	−1.57905	1.20^{E-09}	1.22^{E-07}
ADXEC.13057.C1_at	ENSG00000090339 OTTHUMG00000180403	3383	*ICAM1*	Intercellular adhesion molecule 1	7.14534	7.8043	−1.57894	1.58^{E-10}	1.83^{E-08}
ADXECAD.12819_s_at	—	—	—	—	5.52739	6.18588	−1.57843	1.27^{E-07}	8.60^{E-06}
ADXEC.22551.C1_at	—	—	—	—	5.01662	5.67447	−1.57773	2.35^{E-07}	1.48^{E-05}
ADXPCEC.5488.C1_s_at	ENSG00000111679 ENSG00000268954 OTTHUMG00000168518	5777	*PTPN6*	Protein tyrosine phosphatase, nonreceptor type 6	6.90145	7.55881	−1.5772	1.47^{E-06}	7.61^{E-05}
ADXEC.119.C12_x_at	ENSG00000204592 ENSG00000206493 ENSG00000225201 ENSG00000229252 ENSG00000230254 ENSG00000233904 ENSG00000236632 OTTHUMG00000004820 OTTHUMG00000031155 OTTHUMG00000031437 OTTHUMG00000132983 OTTHUMG00000148925 OTTHUMG00000149205 OTTHUMG00000149447	3133	*HLA-E*	Major histocompatibility complex, class I, E	5.76228	6.41883	−1.57631	2.17^{E-23}	2.09^{E-20}
ADXECAD.15087_s_at	ENSG00000166750 OTTHUMG00000179858	162394	*SLFN5*	Schlafen family member 5	4.79517	5.45147	−1.57604	3.66^{E-11}	4.63^{E-09}
ADXECADA.2898_at	—	—	—	—	2.70671	3.3625	−1.57548	1.93^{E-13}	3.49^{E-11}
ADXEC.2633.C2_x_at	ENSG00000115523 OTTHUMG00000130179	10578	*GNLY*	Granulysin	4.55366	5.20911	−1.5751	7.15^{E-11}	8.69^{E-09}
ADXEC.15758.C1_at	—	—	—	—	6.11037	6.76488	−1.57408	8.53^{E-09}	7.40^{E-07}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECADA.20383_s_at	ENSG00000134545 ENSG00000205809 OTTHUMG00000168532 OTTHUMG00000168584	3821 3822	*KLRC1* *KLRC2*	Killer cell lectin-like receptor subfamily C, member 1 Killer cell lectin-like receptor subfamily C, member 2	2.61451	3.26875	−1.57378	2.83^{E-07}	1.74^{E-05}
ADXEC.23287.C1_s_at	ENSG00000186407 OTTHUMG00000067605	342510	*CD300E*	CD300e molecule	3.55824	4.21165	−1.57289	0.000740565	0.0135284
ADXECADA.94_at	ENSG00000130487 OTTHUMG00000150250	113730	*KLHDC7B*	Kelch domain containing 7B	4.95823	5.61127	−1.57248	2.89^{E-11}	3.71^{E-09}
ADXEC.13225.C1_at	ENSG00000143390 OTTHUMG00000012495	5993	*RFX5*	Regulatory factor X, 5 (influences HLA class II expression)	4.19662	4.84931	−1.5721	3.79^{E-09}	3.50^{E-07}
ADXECAD.28806_s_at	ENSG00000107551 OTTHUMG00000018060	83937	*RASSF4*	Ras association (RalGDS/AF-6) domain family member 4	3.89503	4.5461	−1.57033	8.31^{E-10}	8.69^{E-08}
ADXEC.19598.C1_s_at	ENSG00000110077 OTTHUMG00000167241	64231	*MS4A6A*	Membrane-spanning 4-domains, subfamily A, member 6A	4.68995	5.34078	−1.57007	1.37^{E-08}	1.15^{E-06}
ADXEC.27278.C2_s_at	ENSG00000094755 OTTHUMG00000130443	2568	*GABRP*	GABA A receptor, pi	5.51708	6.16773	−1.56988	0.000167176	0.00432948
ADXEC.242.C9-a_s_at	ENSG00000240754	—	—	—	6.37127	7.02184	−1.56979	1.47^{E-07}	9.77^{E-06}
ADXEC.22822.C1_x_at	—	—	—	—	3.70863	4.35822	−1.56873	2.10^{E-08}	1.69^{E-06}
ADXECAD.23576_s_at	ENSG00000115165 OTTHUMG00000154551	9595	*CYTIP*	Cytohesin 1 interacting protein	2.32861	2.97814	−1.56867	3.15^{E-12}	4.55^{E-10}
ADXECADA.7015_at	ENSG00000158985	56990	*CDC42SE2*	CDC42 small effector 2	7.5615	8.21038	−1.56795	4.27^{E-14}	8.47^{E-12}
ADXECRS.6335_s_at	ENSG00000009790 OTTHUMG00000036480	80342	*TRAF3IP3*	TRAF3 interacting protein 3	4.25387	4.90128	−1.56635	1.73^{E-06}	8.73^{E-05}
ADXEC.5919.C2_s_at	ENSG00000008517 ENSG00000252561 OTTHUMG00000167498	9235	*IL32*	Interleukin 32	7.06257	7.70988	−1.56625	3.58^{E-08}	2.70^{E-06}
ADXLCEC.126.C9_x_at	ENSG00000215048 ENSG00000223865 ENSG00000226826 ENSG00000229295 ENSG00000230708 ENSG00000230763 ENSG00000236693 ENSG00000237710 OTTHUMG00000012659 OTTHUMG00000031076 OTTHUMG00000031346 OTTHUMG00000140240 OTTHUMG00000148842 OTTHUMG00000149113 OTTHUMG00000149370 OTTHUMG00000149629	3115	*HLA-DPB1*	Major histocompatibility complex, class II, DP beta 1	5.30857	5.95532	−1.56564	3.79^{E-08}	2.84^{E-06}
ADXECEMUTR.4384_at	ENSG00000244682 OTTHUMG00000074101	2212	*FCGR2A*	Fc fragment of IgG, low affinity IIa, receptor (CD32)	7.12069	7.76725	−1.56543	4.94^{E-07}	2.87^{E-05}
ADXECADA.20998_s_at	ENSG00000173391 OTTHUMG00000168527	4973	*OLR1*	Oxidized low density lipoprotein (lectin-like) receptor 1	5.45033	6.09655	−1.56506	3.76^{E-06}	0.000171701
ADXEC.7293.C1_at	ENSG00000134324 OTTHUMG00000119082	23175	*LPIN1*	Lipin 1	4.94776	5.59349	−1.56454	2.73^{E-07}	1.70^{E-05}
ADXECNTDJ.8757_at	ENSG00000134028 OTTHUMG00000097858	27299	*ADAMDEC1*	ADAM-like, decysin 1	2.83489	3.48009	−1.56395	1.24^{E-09}	1.26^{E-07}
ADXOCEC.3925.C1_at	—	—	—	—	4.04171	4.68658	−1.56359	9.88^{E-08}	6.77^{E-06}
ADXECNTDJ.4338_at	ENSG00000163564 OTTHUMG00000037109	149628	*PYHIN1*	Pyrin and HIN domain family, member 1	5.83906	6.48315	−1.56275	1.15^{E-14}	2.49^{E-12}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECEMUTR.2684_s_at	ENSG00000065413 OTTHUMG00000154411	91526	*ANKRD44*	Ankyrin repeat domain 44	2.38841	3.03249	−1.56273	6.29^{E-07}	3.56^{E-05}
ADXECAD.6399_at	ENSG00000166750 OTTHUMG00000179858	162394	*SLFN5*	Schlafen family member 5	5.44609	6.09006	−1.56262	2.31^{E-09}	2.24^{E-07}
ADXEC.21558.C1_at	—	—	—	—	4.89973	5.54326	−1.56215	3.62^{E-07}	2.19^{E-05}
ADXECNTDJ.2722_s_at	ENSG00000081237 ENSG00000262418 OTTHUMG00000035702 OTTHUMG00000175273	5788	*PTPRC*	Protein tyrosine phosphatase, receptor type, C	9.3271	9.96991	−1.56137	1.03^{E-12}	1.65^{E-10}
ADXECAD.16186_s_at	ENSG00000172349 OTTHUMG00000144186	3603	*IL16*	Interleukin 16	5.15747	5.79877	−1.55974	2.48^{E-11}	3.21^{E-09}
ADXEC.1477.C3_at	ENSG00000026950 OTTHUMG00000014449	11119	*BTN3A1*	Butyrophilin, subfamily 3, member A1	6.35856	6.99958	−1.55944	4.75^{E-17}	1.65^{E-14}
ADXECADA.980_s_at	—	—	—	—	4.02483	4.6643	−1.55775	5.94^{E-12}	8.36^{E-10}
ADXECRS.30490_s_at	ENSG00000267369 OTTHUMG00000179903	—	*OTTHUMG00000179903* *RP11-1094M14.8*	NULL NULL	2.28665	2.92592	−1.55754	2.59^{E-12}	3.81^{E-10}
ADXEC.16157.C1_s_at	ENSG00000012779 ENSG00000262552 OTTHUMG00000018081 OTTHUMG00000174846	240	*ALOX5*	Arachidonate 5-lipoxygenase	5.83744	6.47636	−1.55716	2.45^{E-09}	2.36^{E-07}
ADXEC.8964.C2_s_at	ENSG00000083799 OTTHUMG00000173404	1540	*CYLD*	Cylindromatosis (turban tumor syndrome)	4.87066	5.50943	−1.557	5.02^{E-12}	7.18^{E-10}
ADXECADA.10039_s_at	ENSG00000155962 ENSG00000268943 OTTHUMG00000022660	1193	*CLIC2*	Chloride intracellular channel 2	3.97167	4.61028	−1.55683	3.87^{E-06}	0.000176212
ADXECAD.11857_at	—	—	—	—	4.40157	5.04002	−1.55665	1.43^{E-10}	1.67^{E-08}
ADXECEMUTR.6354_at	—	—	—	—	4.37614	5.01444	−1.5565	6.94^{E-13}	1.15^{E-10}
ADXEC.11663.C1_s_at	ENSG00000185811 OTTHUMG00000155907	10320	*IKZF1*	IKAROS family zinc finger 1 (Ikaros)	4.86957	5.50763	−1.55623	2.24^{E-08}	1.78^{E-06}
ADXEC.23834.C1_at	ENSG00000187474 OTTHUMG00000183502	2359	*FPR3*	Formyl peptide receptor 3	4.55857	5.19648	−1.55608	6.52^{E-11}	7.98^{E-09}
ADXECAD.23981_s_at	ENSG00000114013 OTTHUMG00000159482	942	*CD86*	CD86 molecule	2.71726	3.35515	−1.55605	5.27^{E-14}	1.02^{E-11}
ADXEC.28199.C1_at	ENSG00000163545 OTTHUMG00000037196	81788	*NUAK2*	NUAK family, SNF1-like kinase, 2	5.02337	5.66054	−1.55528	4.84^{E-07}	2.82^{E-05}
ADXECAD.25110_s_at	ENSG00000254838	387751	*GVINP1*	GTPase, very large interferon inducible pseudogene 1	3.44813	4.08418	−1.55408	3.02^{E-12}	4.39^{E-10}
ADXEC.17921.C1_at	ENSG00000108798 OTTHUMG00000161306	51225	*ABI3*	ABI family, member 3	7.19284	7.82845	−1.55359	1.03^{E-16}	3.29^{E-14}
ADXEC.5919.C1_s_at	ENSG00000008517 OTTHUMG00000167498	9235	*IL32*	Interleukin 32	10.2236	10.8592	−1.55354	2.40^{E-14}	5.02^{E-12}
ADXEC.22774.C1_x_at	ENSG00000105639 OTTHUMG00000165648	3718	*JAK3*	Janus kinase 3	6.80387	7.439	−1.55308	2.06^{E-13}	3.70^{E-11}
ADXEC.22911.C1_at	ENSG00000171310 OTTHUMG00000169803	50515	*CHST11*	Carbohydrate (chondroitin 4) sulfotransferase 11	4.84233	5.47705	−1.55264	5.40^{E-07}	3.11^{E-05}
ADXEC.138.C3_x_at	ENSG00000166710 OTTHUMG00000131247	567	*B2M*	Beta-2-microglobulin	9.38774	10.0221	−1.55228	4.48^{E-29}	9.77^{E-26}
ADXEC.1136.C2_s_at	ENSG00000092010 OTTHUMG00000028795	5720	*PSME1*	Proteasome (prosome, macropain) activator subunit 1 (PA28 alpha)	5.62396	6.25664	−1.55044	1.39^{E-07}	9.31^{E-06}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECRS.27824_s_at	ENSG00000112493 ENSG00000206208 ENSG00000206281 ENSG00000231925 ENSG00000236490 OTTHUMG00000013076 OTTHUMG00000031090 OTTHUMG00000031360 OTTHUMG00000149094 OTTHUMG00000149610	6892	*TAPBP*	TAP binding protein (tapasin)	5.39007	6.02228	−1.54994	2.29^{E-08}	1.81^{E-06}
ADXECAD.5238_s_at	—	—	—	—	4.31148	4.94357	−1.54981	3.35^{E-09}	3.14^{E-07}
ADXECADA.13013_at	—	—	—	—	2.823	3.45378	−1.5484	1.02^{E-07}	6.95^{E-06}
ADXEC.19082.C1_x_at	—	—	—	—	4.46771	5.0982	−1.5481	1.64^{E-17}	6.03^{E-15}
ADXECAD.27653_at	ENSG00000254087 OTTHUMG00000044345	4067	*LYN*	V-yes-1 Yamaguchi sarcoma viral related oncogene homolog	4.85263	5.48307	−1.54803	2.72^{E-06}	0.000129988
ADXECNTDJ.9875_x_at	—	10730	*YME1L1*	YME1-like 1 ATPase	4.24633	4.87662	−1.54788	4.60^{E-13}	7.88^{E-11}
ADXEC.12647.C2_at	ENSG00000005810 OTTHUMG00000017105	23077	*MYCBP2*	MYC binding protein 2, E3 ubiquitin protein ligase	5.83426	6.46318	−1.5464	1.84^{E-06}	9.22^{E-05}
ADXECAD.1752_at	ENSG00000114127 OTTHUMG00000159251	54464	*XRN1*	5′-3′ Exoribonuclease 1	4.21768	4.84656	−1.54637	5.76^{E-07}	3.29^{E-05}
ADXEC.16953.C1_at	ENSG00000010810 OTTHUMG00000016305	2534	*FYN*	FYN oncogene related to SRC, FGR, YES	4.22615	4.85471	−1.54603	1.17^{E-06}	6.18^{E-05}
ADXEC.8622.C1_at	ENSG00000185811 OTTHUMG00000155907	10320	*IKZF1*	IKAROS family zinc finger 1 (Ikaros)	3.30977	3.93819	−1.54586	4.07^{E-09}	3.73^{E-07}
ADXECEMUTR.6379_at	—	203328	*SUSD3*	Sushi domain containing 3	4.93919	5.56738	−1.54563	2.93^{E-05}	0.00102496
ADXEC.14206.C1_at	ENSG00000130813 OTTHUMG00000180393	55337	*C19orf66*	Chromosome 19 open reading frame 66	6.43463	7.06272	−1.54553	3.43^{E-09}	3.21^{E-07}
ADXECNTDJ.8064_at	ENSG00000141682 OTTHUMG00000132765	5366	*PMAIP1*	Phorbol-12-myristate-13-acetate-induced protein 1	5.3069	5.93451	−1.54499	2.23^{E-05}	0.000813419
ADXECADA.19962_s_at	ENSG00000055332 OTTHUMG00000100962	5610	*EIF2AK2*	Eukaryotic translation initiation factor 2-alpha kinase 2	6.52976	7.15607	−1.54361	5.64^{E-11}	6.93^{E-09}
ADXEC.25236.C1_at	—	—	—	—	3.57675	4.20285	−1.54339	7.41^{E-13}	1.22^{E-10}
ADXEC.7155.C3-a_s_at	ENSG00000152926 ENSG00000213462 OTTHUMG00000156631 OTTHUMG00000165023	2086 51351	*ERV3-1* *ZNF117*	Endogenous retrovirus group 3, member 1 Zinc finger protein 117	4.36298	4.98858	−1.54286	2.09^{E-12}	3.13^{E-10}
ADXEC.2579.C1_s_at	ENSG00000185745 OTTHUMG00000018712	3434	*IFIT1*	Interferon-induced protein with tetratricopeptide repeats 1	4.27239	4.89764	−1.54248	2.43^{E-06}	0.000116874
ADXEC.21558.C1_x_at	—	—	—	—	5.02231	5.64751	−1.54243	1.46^{E-06}	7.58^{E-05}
ADXEC.20916.C1_at	ENSG00000174718 OTTHUMG00000128501	55196	*KIAA1551*	KIAA1551	6.06968	6.69461	−1.54213	4.34^{E-09}	3.96^{E-07}
ADXECAD.13559_at	—	—	—	—	5.33761	5.9624	−1.54199	1.85^{E-08}	1.51^{E-06}
ADXECRS.7275_x_at	ENSG00000263304 OTTHUMG00000179762	284021	*MILR1*	Mast cell immunoglobulin-like receptor 1	4.74695	5.37166	−1.54191	4.16^{E-06}	0.000188287
ADXEC.20716.C1_at	—	—	—	—	3.4593	4.08356	−1.54143	3.74^{E-09}	3.46^{E-07}
ADXECADA.15896_at	ENSG00000004468	952	*CD38*	CD38 molecule	2.21364	2.83788	−1.54139	2.30^{E-12}	3.41^{E-10}
ADXECAD.21664_s_at	ENSG00000137265 OTTHUMG00000016294	3662	*IRF4*	Interferon regulatory factor 4	4.38537	5.00915	−1.54091	5.06^{E-13}	8.59^{E-11}
ADXEC.4130.C1_s_at	ENSG00000172183 OTTHUMG00000148679	3669	*ISG20*	Interferon stimulated exonuclease gene 20 kDa	6.22322	6.84621	−1.54007	7.18^{E-16}	1.88^{E-13}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECNTDJ.4121_x_at	ENSG00000070190 OTTHUMG00000160974	27071	*DAPP1*	Dual adaptor of phosphotyrosine and 3-phosphoinositides	2.67844	3.30102	−1.53963	7.81^{E-08}	5.51^{E-06}
ADXEC.5570.C2_s_at	ENSG00000188313 OTTHUMG00000159427	5359	*PLSCR1*	Phospholipid scramblase 1	4.77119	5.39321	−1.53903	5.55^{E-07}	3.18^{E-05}
ADXECADA.7888_s_at	—	—	—	—	7.36678	7.98877	−1.53899	2.78^{E-16}	7.91^{E-14}
ADXEC.7382.C1_at	ENSG00000110777 OTTHUMG00000166659	5450	*POU2AF1*	POU class 2 associating factor 1	2.88859	3.51018	−1.53856	4.37^{E-08}	3.24^{E-06}
ADXEC.1056.C3_s_at	ENSG00000112096 OTTHUMG00000015940	6648 100129518	*LOC100129518* *SOD2*	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	6.78248	7.40386	−1.53835	1.41^{E-07}	9.43^{E-06}
ADXEC.17460.C1_s_at	ENSG00000167286 OTTHUMG00000166970	915	*CD3D*	CD3d molecule, delta (CD3-TCR complex)	5.74558	6.36491	−1.53617	8.88^{E-17}	2.90^{E-14}
ADXECAD.25972_s_at	ENSG00000185811 OTTHUMG00000155907	10320	*IKZF1*	IKAROS family zinc finger 1 (Ikaros)	5.7925	6.41146	−1.53577	2.73^{E-13}	4.81^{E-11}
ADXEC.15393.C1_at	ENSG00000198759 OTTHUMG00000021155	25975	*EGFL6*	EGF-like-domain, multiple 6	2.22312	2.84132	−1.53496	9.11^{E-07}	4.93^{E-05}
ADXECRS.30295_s_at	ENSG00000205045 OTTHUMG00000167707	100506736	*SLFN12L*	Schlafen family member 12-like	2.57006	3.18823	−1.53493	1.13^{E-08}	9.65^{E-07}
ADXECAD.27568_at	ENSG00000162747 ENSG00000203747 OTTHUMG00000034466 OTTHUMG00000074099	2215	*FCGR3B*	Fc fragment of IgG, low affinity IIIb, receptor (CD16b)	6.14472	6.76204	−1.53402	1.91^{E-08}	1.54^{E-06}
ADXEC.22774.C1_at	ENSG00000105639 OTTHUMG00000165648	3718	*JAK3*	Janus kinase 3	6.88633	7.50261	−1.53292	7.92^{E-13}	1.29^{E-10}
ADXECADA.4101_at	ENSG00000171488 OTTHUMG00000010305	84230	*LRRC8C*	Leucine rich repeat containing 8 family, member C	3.75074	4.36688	−1.53277	7.62^{E-06}	0.000320119
ADXEC.4424.C1_x_at	—	51014	*TMED7*	Transmembrane emp24 protein transport domain containing 7	4.00742	4.62355	−1.53276	1.68^{E-05}	0.000638555
ADXEC.6959.C2_at	ENSG00000179456 OTTHUMG00000040013	10472 57451	*TENM2* *ZBTB18*	Teneurin transmembrane protein 2 Zinc finger and BTB domain containing 18	9.10618	9.72214	−1.53257	1.38^{E-08}	1.16^{E-06}
ADXEC.1056.C2_s_at	ENSG00000112096 OTTHUMG00000015940	6648 100129518	*LOC100129518* *SOD2*	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	8.42621	9.04213	−1.53253	1.82^{E-09}	1.80^{E-07}
ADXEC.932.C3_at	ENSG00000101084 ENSG00000259399 OTTHUMG00000032382 OTTHUMG00000032384	55969 100527943	*C20orf24* *TGIF2-C20orf24*	Chromosome 20 open reading frame 24 TGIF2-C20orf24 readthrough	3.29697	3.91264	−1.53227	2.31^{E-07}	1.46^{E-05}
ADXPCEC.12496.C1_at	ENSG00000169085 OTTHUMG00000156998	254778	*C8orf46*	Chromosome 8 open reading frame 46	2.85924	3.4749	−1.53225	0.00055596	0.0108831
ADXECRS.15980_s_at	ENSG00000134255 OTTHUMG00000012357	10390	*CEPT1*	Choline/ethanolamine phosphotransferase 1	5.18895	5.80458	−1.53222	1.94^{E-10}	2.21^{E-08}
ADXEC.3796.C2_at	ENSG00000118503 OTTHUMG00000015664	7128	*TNFAIP3*	Tumor necrosis factor, alpha-induced protein 3	3.61964	4.23487	−1.53181	5.45^{E-14}	1.05^{E-11}
ADXEC.24229.C1_s_at	ENSG00000114127 OTTHUMG00000159251	54464	*XRN1*	5′-3′ Exoribonuclease 1	3.31757	3.93266	−1.53166	0.000272754	0.00634382
ADXEC.30934.C2_at	ENSG00000055332 OTTHUMG00000100962	5610	*EIF2AK2*	Eukaryotic translation initiation factor 2-alpha kinase 2	7.0837	7.69839	−1.53123	1.37^{E-12}	2.15^{E-10}
ADXECAD.17520_x_at	ENSG00000231486	—	—	—	4.0614	4.67577	−1.53089	6.00^{E-10}	6.43^{E-08}
ADXEC.23107.C1_at	ENSG00000188313 OTTHUMG00000159427	5359	*PLSCR1*	Phospholipid scramblase 1	4.25829	4.87237	−1.53058	7.75^{E-05}	0.00231628
ADXEC.21052.C1_at	ENSG00000168685 OTTHUMG00000090791	3575	*IL7R*	Interleukin 7 receptor	3.22746	3.84101	−1.53002	1.34^{E-09}	1.35^{E-07}
ADXECEMUTR.213_s_at	—	—	—	—	4.11874	4.73218	−1.5299	0.00352643	0.0401472

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.26133.C1_at	ENSG00000055332 OTTHUMG00000100962	5610	*EIF2AK2*	Eukaryotic translation initiation factor 2-alpha kinase 2	7.07571	7.68886	−1.52959	6.87^{E-07}	3.86^{E-05}
ADXEC.3377.C1_at	ENSG00000163131 OTTHUMG00000035010	1520	*CTSS*	Cathepsin S	3.51899	4.13211	−1.52956	4.17^{E-05}	0.0013912
ADXEC.31493.C3_s_at	ENSG00000143110 OTTHUMG00000011750	128346	*C1orf162*	Chromosome 1 open reading frame 162	5.68688	6.29915	−1.52866	3.27^{E-10}	3.65^{E-08}
ADXEC.30618.C1_s_at	ENSG00000173821 OTTHUMG00000161415	57674	*RNF213*	Ring finger protein 213	6.41799	7.02964	−1.52801	3.27^{E-10}	3.65^{E-08}
ADXEC.1131.CB4_s_at	ENSG00000236943 ENSG00000269501 OTTHUMG00000182426 OTTHUMG00000182668	727820 728855 728875	*LINC00623* *LOC727820* *LOC728875*	Long intergenic nonprotein coding RNA 623 Uncharacterized LOC727820 Uncharacterized LOC728875	6.92317	7.5347	−1.52788	3.64_{E-09}	3.38_{E-07}
ADXEC.6959.C2_x_at	ENSG00000179456 OTTHUMG00000040013	10472	*ZBTB18*	Zinc finger and BTB domain containing 18	7.49879	8.10919	−1.52668	1.90_{E-08}	1.54_{E-06}
ADXEC.648.C9-a_s_at	ENSG00000245105 OTTHUMG00000168289	144571	*A2M-AS1*	A2M antisense RNA 1	3.54624	4.15635	−1.52637	3.24_{E-06}	0.000151839
ADXECRS.42976_s_at	ENSG00000178104 ENSG00000264708 OTTHUMG00000013846	9659 728802 100996724 100996761 101060291 101060344 101060353 101060463 101060582	*LOC100996724* *LOC100996761* *LOC101060291* *LOC101060344* *LOC101060353* *LOC101060463* *LOC101060582* *LOC728802* *PDE4DIP*	Myomegalin-like Myomegalin-like Myomegalin-like Uncharacterized LOC101060344 Myomegalin-like Myomegalin-like Myomegalin-like Myomegalin-like Phosphodiesterase 4D interacting protein	4.51357	5.12366	−1.52635	1.32^{E-08}	1.12^{E-06}
ADXECRS.27706_x_at	ENSG00000188004 OTTHUMG00000035430	284677	*C1orf204*	Chromosome 1 open reading frame 204	5.39307	6.00292	−1.52611	2.68^{E-09}	2.57^{E-07}
ADXEC.19998.C1_s_at	ENSG00000171115 OTTHUMG00000158327	155038	*GIMAP8*	GTPase, IMAP family member 8	4.59579	5.2055	−1.52595	3.58^{E-05}	0.00121883
ADXEC.111.C86_s_at	ENSG00000130177 OTTHUMG00000017402	8881	*CDC16*	Cell division cycle 16	5.47636	6.08572	−1.52558	0.000254185	0.00602529
ADXECNTDJ.7388_at	—	—	—	—	4.51185	5.12111	−1.52548	1.70^{E-08}	1.39^{E-06}
ADXECAD.19112_at	ENSG00000135838 OTTHUMG00000035321	80896	*NPL*	N-acetylneuraminate pyruvate lyase (dihydrodipicolinate synthase)	3.60256	4.21174	−1.52539	8.41^{E-06}	0.000349319
ADXLCEC.126.C9_at	ENSG00000215048 ENSG00000223865 ENSG00000226826 ENSG00000229295 ENSG00000230708 ENSG00000230763 ENSG00000236693 ENSG00000237710 OTTHUMG00000012659 OTTHUMG00000031076 OTTHUMG00000031346 OTTHUMG00000140240 OTTHUMG00000148842 OTTHUMG00000149113 OTTHUMG00000149370 OTTHUMG00000149629	3115	*HLA-DPB1*	Major histocompatibility complex, class II, DP beta 1	3.11036	3.71847	−1.52426	4.36^{E-05}	0.00144296
ADXEC.548.C1_s_at	ENSG00000164430 OTTHUMG00000015034	115004	*MB21D1*	Mab-21 domain containing 1	2.93812	3.54558	−1.52357	2.91^{E-08}	2.25^{E-06}
ADXEC.3599.C1_s_at	ENSG00000025708 OTTHUMG00000150249	1890	*TYMP*	Thymidine phosphorylase	7.03706	7.64442	−1.52346	5.27^{E-21}	3.40^{E-18}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECRS.9321_s_at	ENSG00000171928 ENSG00000175106 OTTHUMG00000059052 OTTHUMG00000171461	51030 201158	*TVP23B* *TVP23C*	Transgolgi network vesicle protein 23 homolog B (*Saccharomyces cerevisiae*) *Trans*-golgi network vesicle protein 23 homolog C (*S cerevisiae*)	2.55371	3.15878	−1.52104	1.49^{E-05}	0.00057503
ADXEC.7877.C1_at	ENSG00000177409	219285	*SAMD9L*	Sterile alpha motif domain containing 9-like	4.83346	5.43828	−1.52078	2.13^{E-19}	1.09^{E-16}
ADXEC.23107.C1_x_at	ENSG00000188313 OTTHUMG00000159427	5359	*PLSCR1*	Phospholipid scramblase 1	3.96772	4.57074	−1.51889	7.63^{E-05}	0.00228802
ADXECRS.21321_s_at	ENSG00000101082 OTTHUMG00000032393	84174	*SLA2*	Src-like-adaptor 2	3.46651	4.06781	−1.51709	2.82^{E-12}	4.12^{E-10}
ADXEC.1119.C2_s_at	ENSG00000164104 OTTHUMG00000160799	3148	*HMGB2*	High mobility group box 2	4.00687	4.60817	−1.51708	0.00262967	0.0329469
ADXECRS.29962_s_at	ENSG00000165178 ENSG00000182487 ENSG00000261919 ENSG00000262960 ENSG00000262984 OTTHUMG00000149964 OTTHUMG00000156804	653361 654816 654817	*NCF1* *NCF1B* *NCF1C*	Neutrophil cytosolic factor 1 Neutrophil cytosolic factor 1B pseudogene Neutrophil cytosolic factor 1C pseudogene	6.27322	6.87315	−1.51564	1.93^{E-16}	5.68^{E-14}
ADXECEMUTR.4171_s_at	—	3537	*IGLC1*	Immunoglobulin lambda constant 1 (Mcg marker)	4.75746	5.35712	−1.51536	1.77E-06	8.91^{E-05}
ADXEC.1056.C2-a_s_at	ENSG00000112096 OTTHUMG00000015940	6648 100129518	*LOC100129518* *SOD2*	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	6.64396	7.24261	−1.5143	2.67^{E-07}	1.66^{E-05}
ADXEC.6447.C2_at	ENSG00000175309 OTTHUMG00000130892	85007	*PHYKPL*	5-Phosphohydroxy-L-lysine phospho-lyase	5.31662	5.91515	−1.51418	0.000180022	0.00459005
ADXEC.22601.C1_at	ENSG00000258588 ENSG00000258659 OTTHUMG00000066892 OTTHUMG00000066899	53840 445372	*TRIM34* *TRIM6-TRIM34*	Tripartite motif containing 34 TRIM6-TRIM34 readthrough	2.81314	3.41133	−1.51381	4.68^{E-08}	3.44^{E-06}
ADXEC.3438.C1_s_at	ENSG00000216490 ENSG00000268173 OTTHUMG00000150640 OTTHUMG00000183373	5296 10437	*IFI30* *PIK3R2*	Interferon, gamma-inducible protein 30 Phosphoinositide-3-kinase, regulatory subunit 2 (beta)	11.2518	11.8497	−1.51358	8.57^{E-21}	5.26^{E-18}
ADXEC.7753.C1_s_at	ENSG00000091490 OTTHUMG00000160331	23231	*SEL1L3*	Sel-1 suppressor of lin-12-like 3 (*C. elegans*)	4.38858	4.98653	−1.51357	2.18^{E-07}	1.39^{E-05}
ADXEC.13723.C1_s_at	ENSG00000187764 OTTHUMG00000020185	10507	*SEMA4D*	Sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4D	5.22214	5.82003	−1.5135	2.96^{E-14}	6.09^{E-12}
ADXEC.28662.C1_s_at	ENSG00000100219 OTTHUMG00000151094	7494	*XBP1*	X-box binding protein 1	4.17897	4.77664	−1.51327	3.13^{E-05}	0.00108381
ADXEC.25981.C1_s_at	ENSG00000227039 OTTHUMG00000090253	100505746	*ITGB2-AS1*	ITGB2 antisense RNA 1	5.55908	6.15666	−1.51318	1.68^{E-12}	2.56^{E-10}
ADXEC.17672.C1_at	ENSG00000083454 OTTHUMG00000090700	5026	*P2RX5*	Purinergic receptor P2X, ligand-gated ion channel, 5	3.43864	4.03608	−1.51303	3.50^{E-09}	3.26^{E-07}
ADXEC.32046.C1_at	ENSG00000132256 OTTHUMG00000066893	85363	*TRIM5*	Tripartite motif containing 5	3.99695	4.59392	−1.51253	3.67^{E-07}	2.21^{E-05}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.17390.C1_at	ENSG00000204252 ENSG00000206292 ENSG00000230141 ENSG00000231558 ENSG00000232957 ENSG00000232962 ENSG00000235744 OTTHUMG00000012644 OTTHUMG00000031211 OTTHUMG00000031511 OTTHUMG00000140242 OTTHUMG00000149105 OTTHUMG00000149362 OTTHUMG00000149623	3111	*HLA-DOA*	Major histocompatibility complex, class II, DO alpha	3.45379	4.05019	−1.51194	2.33^{E-07}	1.47^{E-05}
ADXEC.138.C20-a_s_at	ENSG00000166710 OTTHUMG00000131247	567	*B2M*	Beta-2-microglobulin	3.64376	4.24012	−1.5119	2.40^{E-16}	6.90^{E-14}
ADXEC.25371.C1-a_s_at	ENSG00000166750 OTTHUMG00000179858	162394	*SLFN5*	Schlafen family member 5	5.30949	5.90575	−1.5118	4.82^{E-08}	3.54^{E-06}
ADXEC.14637.C1-a_s_at	ENSG00000048740 OTTHUMG00000017668	10659	*CELF2*	CUGBP, Elav-like family member 2	4.38021	4.97646	−1.51179	1.78^{E-09}	1.77^{E-07}
ADXEC.409.C46_s_at	ENSG00000158417 OTTHUMG00000153242	9669	*EIF5B*	Eukaryotic translation initiation factor 5B	5.90573	6.50096	−1.51071	0.000519172	0.010375
ADXEC.10433.C2_s_at	ENSG00000050730 OTTHUMG00000132969	79931	*TNIP3*	TNFAIP3 interacting protein 3	7.1813	7.77623	−1.51039	2.87^{E-09}	2.72^{E-07}
ADXECAD.24936_s_at	ENSG00000103522 OTTHUMG00000131675	50615	*IL21R*	Interleukin 21 receptor	3.41336	4.0078	−1.50988	7.20^{E-13}	1.19^{E-10}
ADXEC.12444.C1_s_at	ENSG00000107551 OTTHUMG00000018060	83937	*RASSF4*	Ras association (RalGDS/AF-6) domain family member 4	5.58961	6.18346	−1.50926	1.19^{E-07}	8.04^{E-06}
ADXEC.7439.C1_at	ENSG00000116514 OTTHUMG00000004013	127544	*RNF19B*	Ring finger protein 19B	6.97816	7.57176	−1.50901	8.83^{E-07}	4.82^{E-05}
ADXEC.7875.C1_at	ENSG00000204487 ENSG00000206437 ENSG00000223448 ENSG00000227507 ENSG00000231314 ENSG00000236237 ENSG00000236925 ENSG00000238114 OTTHUMG00000031136 OTTHUMG00000031416 OTTHUMG00000040405 OTTHUMG00000148787 OTTHUMG00000149004 OTTHUMG00000149287 OTTHUMG00000149518 OTTHUMG00000149956	4050	*LTB*	Lymphotoxin beta (TNF superfamily, member 3)	5.83849	6.43183	−1.50874	9.10^{E-15}	2.02^{E-12}
ADXEC.4210.C1_at	ENSG00000110031 OTTHUMG00000167466	9404	*LPXN*	Leupaxin	4.48465	5.07777	−1.5085	6.55^{E-11}	8.00^{E-09}
ADXEC.22967.C1_at	ENSG00000139899 OTTHUMG00000171315	643866	*CBLN3*	Cerebellin 3 precursor	4.72925	5.32183	−1.50794	2.08^{E-09}	2.03^{E-07}
ADXOCEC.10150.C1_at	—	—	—	—	2.63251	3.2245	−1.50733	2.87^{E-06}	0.000136481
ADXEC.5919.C1_x_at	ENSG00000008517 OTTHUMG00000167498	9235	*IL32*	Interleukin 32	9.38765	9.97945	−1.50713	6.59^{E-15}	1.50^{E-12}
ADXLCEC.9139.C1_at	ENSG00000181631 OTTHUMG00000155745	53829	*P2RY13*	Purinergic receptor P2Y, G-protein coupled, 13	4.94806	5.53975	−1.507	1.95^{E-09}	1.92^{E-07}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.18512.C1_s_at	ENSG00000127951 OTTHUMG00000130681	10875	*FGL2*	Fibrinogen-like 2	5.26164	5.8531	−1.50677	1.40^{E-10}	1.63^{E-08}
ADXEC.7439.C1_x_at	ENSG00000116514 OTTHUMG00000004013	127544	*RNF19B*	Ring finger protein 19B	7.01813	7.60949	−1.50666	8.31^{E-07}	4.57^{E-05}
ADXEC.30545.C1_at	ENSG00000146094 OTTHUMG00000130850	79930	*DOK3*	Docking protein 3	5.78388	6.37515	−1.50657	2.09^{E-10}	2.38^{E-08}
ADXEC.5050.C1_at	ENSG00000164099 OTTHUMG00000161166	8492	*PRSS12*	Protease, serine, 12 (neurotrypsin, motopsin)	3.19981	3.79105	−1.50654	0.00113347	0.018384
ADXEC.7295.C1_at	ENSG00000254087 OTTHUMG00000044345	4067	*LYN*	V-yes-1 Yamaguchi sarcoma viral related oncogene homolog	2.75076	3.34196	−1.5065	1.69^{E-08}	1.39^{E-06}
ADXECADA.3464_at	—	—	—	—	2.86157	3.45234	−1.50604	1.16^{E-13}	2.15^{E-11}
ADXEC.14159.C1_s_at	ENSG00000106948	80709	*AKNA*	AT-hook transcription factor	4.17895	4.76946	−1.50578	0.00010569	0.00299432
ADXPCEC.161.C17_x_at	ENSG00000206435 ENSG00000206450 ENSG00000206452 ENSG00000223532 ENSG00000224608 ENSG00000228299 ENSG00000228964 ENSG00000232126 ENSG00000234745 ENSG00000237022 OTTHUMG00000031153 OTTHUMG00000031435 OTTHUMG00000036662 OTTHUMG00000037240 OTTHUMG00000148965 OTTHUMG00000149247 OTTHUMG00000149248 OTTHUMG00000149478 OTTHUMG00000149943 OTTHUMG00000149955	3106 3107	*HLA-B* *HLA-C*	Major histocompatibility complex, class I, B Major histocompatibility complex, class I, C	8.21596	8.80635	−1.50565	4.59^{E-16}	1.25^{E-13}
ADXEC.8403.C1_at	ENSG00000120899 OTTHUMG00000102082	2185	*PTK2B*	Protein tyrosine kinase 2 beta	5.25717	5.84684	−1.5049	1.12^{E-16}	3.56^{E-14}
ADXECRS.19227_s_at	ENSG00000181800 OTTHUMG00000017669	414196	*CELF2-AS1*	CELF2 antisense RNA 1	3.00391	3.593	−1.5043	6.86^{E-07}	3.85^{E-05}
ADXEC.7609.C6_s_at	ENSG00000128951 OTTHUMG00000172155	1854	*DUT*	Deoxyuridine triphosphatase	7.14391	7.73186	−1.50311	0.000178311	0.00455895
ADXEC.28196.C1_at	ENSG00000137403 ENSG00000204642 ENSG00000206509 ENSG00000229698 ENSG00000235220 ENSG00000237508 OTTHUMG00000004783 OTTHUMG00000031156 OTTHUMG00000031438 OTTHUMG00000041181 OTTHUMG00000148884 OTTHUMG00000149164	3134	*HLA-F*	Major histocompatibility complex, class I, F	3.95414	4.54204	−1.50305	2.37^{E-09}	2.30^{E-07}
ADXECAD.15610_s_at	ENSG00000157654 ENSG00000241978 OTTHUMG00000156811 OTTHUMG00000156812	11217 445815	*AKAP2* *PALM2-AKAP2*	A kinase (PRKA) anchor protein 2 PALM2-AKAP2 readthrough	5.54727	6.13424	−1.5021	0.00360816	0.0407665
ADXECAD.14381_at	ENSG00000170542 OTTHUMG00000014131	5272	*SERPINB9*	Serpin peptidase inhibitor, clade B (ovalbumin), member 9	6.06739	6.65417	−1.50189	7.28^{E-07}	4.05^{E-05}

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXECNTDJ.8414_at	ENSG00000140968 OTTHUMG00000137648	3394	*IRF8*	Interferon regulatory factor 8	3.41792	4.00459	−1.50177	3.66^{E-13}	6.36^{E-11}
ADXEC.12846.C1_s_at	ENSG00000108691 OTTHUMG00000132887	6347	*CCL2*	Chemokine (C-C motif) ligand 2	4.63688	5.22338	−1.5016	4.37^{E-10}	4.76^{E-08}
ADXEC.1189.C30_x_at	ENSG00000211675 ENSG00000254709 OTTHUMG00000151218 OTTHUMG00000165670	3537 100423062	*IGLC1* *IGLL5*	Immunoglobulin lambda constant 1 (Mcg marker) Immunoglobulin lambda-like polypeptide 5	4.7742	5.35981	−1.50067	1.73^{E-09}	1.73^{E-07}
ADXEC.376.C1_s_at	ENSG00000091483 OTTHUMG00000039597	2271	*FH*	Fumarate hydratase	4.36579	4.95095	−1.50021	6.46^{E-05}	0.00199852
ADXEC.20273.C1_s_at	ENSG00000095585 ENSG00000262509 OTTHUMG00000018827 OTTHUMG00000182227	29760	*BLNK*	B-cell linker	3.28069	3.86583	−1.50019	2.76^{E-07}	1.71^{E-05}
ADXEC.6547.C1_at	ENSG00000198771 OTTHUMG00000035318	92241	*RCSD1*	RCSD domain containing 1	2.80294	3.38799	−1.5001	6.91^{E-08}	4.92^{E-06}
ADXEC.2639.C1_at	ENSG00000130635 OTTHUMG00000020891	1289	*COL5A1*	Collagen, type V, alpha 1	7.62186	7.0361	1.50083	2.92^{E-08}	2.25^{E-06}
ADXEC.1730.C1_at	ENSG00000130508 OTTHUMG00000059697	7837	*PXDN*	Peroxidasin homolog (*Drosophila*)	7.16843	6.58114	1.50242	2.76^{E-07}	1.71^{E-05}
ADXEC.2115.C1_at	ENSG00000162545 OTTHUMG00000002837	55450	*CAMK2N1*	Calcium/calmodulin-dependent protein kinase II inhibitor 1	4.95873	4.37039	1.50351	3.82^{E-06}	0.000174084
ADXEC.4587.C1_s_at	ENSG00000038427 OTTHUMG00000131321	1462	*VCAN*	Versican	8.20478	7.61468	1.50535	1.66^{E-07}	1.08^{E-05}
ADXPCEC.7986.C1_at	—	3164	*NR4A1*	Nuclear receptor subfamily 4, group A, member 1	7.8951	7.30449	1.50588	3.21^{E-06}	0.00015055
ADXEC.23162.C1_at	ENSG00000137801 OTTHUMG00000133665	7057	*THBS1*	Thrombospondin 1	8.50406	7.91329	1.50605	1.36^{E-05}	0.000532503
ADXEC.2011.C1-a_s_at	ENSG00000137801 OTTHUMG00000133665	7057	*THBS1*	Thrombospondin 1	7.04127	6.44987	1.50671	5.20^{E-06}	0.000228186
ADXEC.4452.C1_s_at	ENSG00000166033 OTTHUMG00000019186	5654	*HTRA1*	HtrA serine peptidase 1	7.45788	6.86483	1.50843	4.21^{E-08}	3.13^{E-06}
ADXECNTDJ.6318_at	ENSG00000165474 OTTHUMG00000016513	2706	*GJB2*	Gap junction protein, beta 2, 26 kDa	6.39062	5.79744	1.50857	0.00107151	0.0176431
ADXEC.26082.C1_s_at	ENSG00000099953 OTTHUMG00000150742	4320	*MMP11*	Matrix metallopeptidase 11 (stromelysin 3)	7.31721	6.72401	1.50859	0.000320306	0.00721671
ADXEC.823.C2_s_at	ENSG00000186847 ENSG00000226145 OTTHUMG00000059171 OTTHUMG00000133426	3861	*KRT14*	Keratin 14	6.44685	5.84772	1.5148	0.00134913	0.0208124
ADXEC.10326.C1_at	ENSG00000147257 OTTHUMG00000022448	2719	*GPC3*	Glypican 3	3.34438	2.745	1.51507	3.74^{E-05}	0.0012648
ADXEC.375.CB2_x_at	ENSG00000108821 OTTHUMG00000148674	1277	*COL1A1*	Collagen, type I, alpha 1	8.7259	8.12138	1.52048	6.88^{E-05}	0.00210701
ADXEC.10326.C1_x_at	ENSG00000147257 OTTHUMG00000022448	2719	*GPC3*	Glypican 3	3.32792	2.72295	1.52095	2.29^{E-05}	0.00083115
ADXECAD.6247_x_at	ENSG00000131711 OTTHUMG00000100952	4131	*MAP1B*	Microtubule-associated protein 1B	4.4032	3.79709	1.52215	9.00^{E-07}	4.88^{E-05}
ADXEC.18311.C1_s_at	ENSG00000187955 OTTHUMG00000149877	7373	*COL14A1*	Collagen, type XIV, alpha 1	4.00066	3.39386	1.52288	1.06^{E-06}	5.66^{E-05}
ADXEC.2446.C1_s_at	ENSG00000144063 OTTHUMG00000131196	7851 101060198	*LOC101060198* *MALL*	MARVEL domain-containing protein 1-like Mal, T-cell differentiation protein-like	6.00496	5.39762	1.52345	4.50^{E-06}	0.000201437

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TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.5310.C1-a_s_at	ENSG00000163359 OTTHUMG00000150020	1293	*COL6A3*	Collagen, type VI, alpha 3	6.60048	5.9926	1.52401	5.08^{E-05}	0.00164365
ADXEC.679.C1_s_at	ENSG00000081853 ENSG00000204956 ENSG00000240184 ENSG00000240764 ENSG00000242419 ENSG00000253159 ENSG00000253305 ENSG00000253485 ENSG00000253537 ENSG00000253731 ENSG00000253767 ENSG00000253846 ENSG00000253910 ENSG00000253953 ENSG00000254122 ENSG00000254221 ENSG00000254245 ENSG00000261934 ENSG00000262209 ENSG00000262576 OTTHUMG00000129611 OTTHUMG00000129613 OTTHUMG00000129624 OTTHUMG00000129625 OTTHUMG00000163678 OTTHUMG00000163679 OTTHUMG00000163680 OTTHUMG00000163681 OTTHUMG00000163682 OTTHUMG00000163683 OTTHUMG00000163684 OTTHUMG00000163685 OTTHUMG00000163686 OTTHUMG00000163687 OTTHUMG00000163688 OTTHUMG00000164053 OTTHUMG00000164054 OTTHUMG00000177471 OTTHUMG00000177473 OTTHUMG00000177593	5098 8641 9708 26025 56097 56098 56099 56100 56101 56102 56103 56104 56105 56106 56107 56108 56109 56110 56111 56112 56113 56114	*PCDHGA1* *PCDHGA10* *PCDHGA11* *PCDHGA12* *PCDHGA2* *PCDHGA3* *PCDHGA4* *PCDHGA5* *PCDHGA6* *PCDHGA7* *PCDHGA8* *PCDHGA9* *PCDHGB1* *PCDHGB2* *PCDHGB3* *PCDHGB4* *PCDHGB5* *PCDHGB6* *PCDHGB7* *PCDHGC3* *PCDHGC4* *PCDHGC5*	Protocadherin gamma subfamily A, 1 Protocadherin gamma subfamily A, 10 Protocadherin gamma subfamily A, 11 Protocadherin gamma subfamily A, 12 Protocadherin gamma subfamily A, 2 Protocadherin gamma subfamily A, 3 Protocadherin gamma subfamily A, 4 Protocadherin gamma subfamily A, 5 Protocadherin gamma subfamily A, 6 Protocadherin gamma subfamily A, 7 Protocadherin gamma subfamily A, 8 Protocadherin gamma subfamily A, 9 Protocadherin gamma subfamily B, 1 Protocadherin gamma subfamily B, 2 Protocadherin gamma subfamily B, 3 Protocadherin gamma subfamily B, 4 Protocadherin gamma subfamily B, 5 Protocadherin gamma subfamily B, 6 Protocadherin gamma subfamily B, 7 Protocadherin gamma subfamily C, 3 Protocadherin gamma subfamily C, 4 Protocadherin gamma subfamily C, 5	6.75854	6.15018	1.52452	1.97^{E-08}	1.59^{E-06}
ADXEC.5091.C2_s_at	ENSG00000118523 OTTHUMG00000015573	1490	*CTGF*	Connective tissue growth factor	9.30794	8.69914	1.52498	1.88^{E-05}	0.000702362
ADXEC.8706.C1-a_s_at	ENSG00000152268 ENSG00000262655 OTTHUMG00000165751 OTTHUMG00000181576	10418	*SPON1*	Spondin 1, extracellular matrix protein	5.19453	4.58418	1.52662	1.11^{E-07}	7.56^{E-06}
ADXEC.12292.C1_at	ENSG00000156535 OTTHUMG00000015040	135228	*CD109*	CD109 molecule	4.52579	3.91504	1.52705	8.91^{E-07}	4.85^{E-05}
ADXECAD.21682_s_at	ENSG00000038427 OTTHUMG00000131321	1462	*VCAN*	Versican	6.97476	6.36109	1.53014	1.70^{E-05}	0.000644035
ADXEC.2446.C2_at	ENSG00000144063 OTTHUMG00000131196	7851 101060198	*LOC101060198* *MALL*	MARVEL domain-containing protein 1-like Mal, T-cell differentiation protein-like	6.80165	6.18694	1.53125	1.88^{E-05}	0.000704211
ADXEC.10090.C1_at	ENSG00000134909 OTTHUMG00000165774	9743	*ARHGAP32*	Rho GTPase activating protein 32	5.4699	4.85497	1.53148	1.46^{E-07}	9.74^{E-06}
ADXEC.8092.C1_s_at	—	—	—	—	5.86387	5.2482	1.53227	2.19^{E-07}	1.40^{E-05}
ADXEC.5091.C1_s_at	ENSG00000118523 OTTHUMG00000015573	1490	*CTGF*	Connective tissue growth factor	6.90153	6.28471	1.53349	2.64^{E-05}	0.000939203

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.4995.C1_s_at	—	—	—	—	9.25918	8.63663	1.53959	4.63^{E-07}	2.71^{E-05}
ADXEC.1186.C3_at	—	—	—	—	9.0131	8.38755	1.5428	0.00386913	0.0428133
ADXEC.31194.C1_s_at	ENSG00000144810 OTTHUMG00000148669	1295	*COL8A1*	Collagen, type VIII, alpha 1	6.84868	6.22181	1.54421	0.000411994	0.00872587
ADXEC.2177.C5-a_s_at	ENSG00000134775 OTTHUMG00000182381	80206	*FHOD3*	Formin homology 2 domain containing 3	4.57732	3.94789	1.54696	0.00018306	0.00465789
ADXEC.4573.C1-a_s_at	ENSG00000050165 OTTHUMG00000165709	27122	*DKK3*	Dickkopf WNT signaling pathway inhibitor 3	5.68713	5.05659	1.54814	4.98^{E-06}	0.000220209
ADXEC.20484.C1_at	ENSG00000140937	1009	*CDH11*	Cadherin 11, type 2, OB-cadherin (osteoblast)	6.26948	5.63778	1.54939	3.73^{E-08}	2.81^{E-06}
ADXEC.716.C1_s_at	ENSG00000115461 OTTHUMG00000133058	3488	*IGFBP5*	Insulin-like growth factor binding protein 5	8.83455	8.20176	1.55055	1.76^{E-05}	0.000664677
ADXECAD.1745_s_at	ENSG00000133110 OTTHUMG00000016751	10631	*POSTN*	Periostin, osteoblast specific factor	7.68107	7.04816	1.55069	3.97^{E-06}	0.000180044
ADXEC.4684.C1_at	ENSG00000213190 OTTHUMG00000035160	10962	*MLLT11*	Myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, *Drosophila*); translocated to, 11	6.60293	5.97001	1.5507	0.000166659	0.00432061
ADXEC.14670.C3_at	ENSG00000138162 OTTHUMG00000019181	10579	*TACC2*	Transforming, acidic coiled-coil containing protein 2	8.77267	8.1328	1.55818	3.52^{E-08}	2.65^{E-06}
ADXEC.14012.C1_s_at	ENSG00000152377 OTTHUMG00000129157	6695	*SPOCK1*	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 1	4.6098	3.96766	1.56065	8.52^{E-07}	4.68^{E-05}
ADXOCEC.9628.C1_at	—	—	—	—	7.96442	7.32116	1.56186	0.000205971	0.00512294
ADXECAD.17188_s_at	ENSG00000038427 OTTHUMG00000131321	1462	*VCAN*	Versican	7.49486	6.85147	1.562	5.26^{E-05}	0.00169081
ADXEC.8730.C1_at	ENSG00000113140 OTTHUMG00000130122	6678	*SPARC*	Secreted protein, acidic, cysteine-rich (osteonectin)	5.33696	4.69116	1.5646	1.55^{E-05}	0.000594706
ADXEC.5783.C3_at	ENSG00000145423 OTTHUMG00000161559	6423	*SFRP2*	Secreted frizzled-related protein 2	6.66635	6.01753	1.56789	1.42^{E-05}	0.000549962
ADXEC.8089.C1_at	ENSG00000154553	27295	*PDLIM3*	PDZ and LIM domain 3	3.75771	3.09976	1.57783	3.89^{E-08}	2.91^{E-06}
ADXEC.2007.CB1_x_at	—	1278	*COL1A2*	Collagen, type I, alpha 2	10.5618	9.90281	1.57893	2.08^{E-08}	1.67^{E-06}
ADXECRS.2356_x_at	ENSG00000188219 ENSG00000196604 ENSG00000250852 OTTHUMG00000153536 OTTHUMG00000153628	445582 728378	*POTEE* *POTEF*	POTE ankyrin domain family, member E POTE ankyrin domain family, member F	5.40113	4.73913	1.58228	0.00178296	0.0253904
ADXEC.11777.C1_at	ENSG00000156535 OTTHUMG00000015040	135228	*CD109*	CD109 molecule	3.92596	3.26214	1.58428	3.83^{E-06}	0.000174204
ADXEC.9153.C1_at	ENSG00000106819 OTTHUMG00000020227	54829	*ASPN*	Asporin	6.20075	5.53179	1.58993	8.94^{E-07}	4.86^{E-05}
ADXEC.3805.C1_x_at	ENSG00000013588 OTTHUMG00000168710	9052	*GPRC5A*	G protein-coupled receptor, family C, group 5, member A	6.21978	5.54974	1.59111	6.01^{E-06}	0.000258989
ADXEC.6819.C2_at	ENSG00000185479 OTTHUMG00000169593	3854	*KRT6B*	Keratin 6B	5.07303	4.4027	1.59144	0.000691341	0.0128258
ADXEC.18997.C1_s_at	ENSG00000176641 OTTHUMG00000132774	220441	*RNF152*	Ring finger protein 152	5.1647	4.49194	1.59413	1.35^{E-06}	7.07^{E-05}
ADXEC.34426.C1_x_at	ENSG00000104490 OTTHUMG00000164876	83988	*NCALD*	Neurocalcin delta	6.02504	5.3516	1.59487	0.00130069	0.0202718
ADXEC.2007.CB1_at	—	1278	*COL1A2*	Collagen, type I, alpha 2	10.0905	9.41681	1.59517	7.06^{E-07}	3.93^{E-05}
ADXEC.2011.C1_s_at	ENSG00000137801 OTTHUMG00000133665	7057	*THBS1*	Thrombospondin 1	7.80905	7.11766	1.61484	1.55^{E-06}	7.94^{E-05}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.3805.C1_at	ENSG00000013588 OTTHUMG00000168710	9052	*GPRC5A*	G protein-coupled receptor, family C, group 5, member A	7.0137	6.31732	1.62043	9.21^{E-05}	0.0026655
ADXEC.8917.C1_s_at	ENSG00000060718 OTTHUMG00000010872	1301	*COL11A1*	Collagen, type XI, alpha 1	5.51833	4.82141	1.62104	1.26^{E-05}	0.000497687
ADXEC.159.CB2_s_at	ENSG00000163017 OTTHUMG00000129813	72	*ACTG2*	Actin, gamma 2, smooth muscle, enteric	8.25579	7.55284	1.62783	0.00336674	0.0389206
ADXEC.34426.C1_at	ENSG00000104490 OTTHUMG00000164876	83988	*NCALD*	Neurocalcin delta	6.52002	5.81381	1.63151	0.00215697	0.028946
ADXECADA.15978_at	ENSG00000133110 OTTHUMG00000016751	10631	*POSTN*	Periostin, osteoblast specific factor	4.175	3.46534	1.63542	2.05^{E-09}	2.01^{E-07}
ADXECAD.22446_s_at	ENSG00000170577 OTTHUMG00000152421	10736	*SIX2*	SIX homeobox 2	7.12574	6.41207	1.63996	0.00203424	0.0278754
ADXEC.3415.C1_s_at	ENSG00000133110 OTTHUMG00000016751	10631	*POSTN*	Periostin, osteoblast specific factor	6.81472	6.09846	1.64292	1.12^{E-06}	5.93^{E-05}
ADXEC.13772.C1_at	ENSG00000184828 OTTHUMG00000180322	201501	*ZBTB7C*	Zinc finger and BTB domain containing 7C	5.52516	4.80225	1.6505	0.000335408	0.00750228
ADXECAD.17850_at	—	—	—	—	4.34139	3.61843	1.65056	0.000900326	0.0156206
ADXEC.21625.C1_s_at	ENSG00000164692 OTTHUMG00000148675	1278	*COL1A2*	Collagen, type I, alpha 2	5.68997	4.95734	1.66167	1.66^{E-07}	1.08^{E-05}
ADXEC.298.C2_s_at	ENSG00000167244 ENSG00000240801 OTTHUMG00000009394 OTTHUMG00000009395	3481 723961	*IGF2* *INS-IGF2*	Insulin-like growth factor 2 (somatomedin A) INS-IGF2 readthrough	7.56643	6.82653	1.67006	4.38^{E-09}	3.99^{E-07}
ADXECAD.6887_at	—	—	—	—	6.89192	6.14456	1.67872	2.32^{E-08}	1.83^{E-06}
ADXEC.5080.C2_at	ENSG00000144810 OTTHUMG00000148669	1295	*COL8A1*	Collagen, type VIII, alpha 1	5.59182	4.84394	1.67932	8.72^{E-08}	6.08^{E-06}
ADXEC.15995.C1_at	ENSG00000152377 OTTHUMG00000129157	6695	*SPOCK1*	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 1	4.50347	3.75469	1.68037	3.75^{E-08}	2.82^{E-06}
ADXECEMUTR.4185_s_at	ENSG00000038427 OTTHUMG00000131321	1462	*VCAN*	Versican	7.74793	6.99775	1.68199	5.95^{E-05}	0.00186183
ADXEC.8917.C1_at	ENSG00000060718 OTTHUMG00000010872	1301	*COL11A1*	Collagen, type XI, alpha 1	5.39171	4.64064	1.68304	0.000278483	0.00644271
ADXEC.9217.C1-a_s_at	—	—	—	—	7.37404	6.61365	1.69394	3.58^{E-06}	0.000164778
ADXEC.25223.C1_at	ENSG00000137745 ENSG00000262325 OTTHUMG00000165850	4322	*MMP13*	Matrix metallopeptidase 13 (collagenase 3)	5.5192	4.75493	1.69851	3.14^{E-05}	0.00108627
ADXEC.298.C3_s_at	ENSG00000167244 ENSG00000240801 OTTHUMG00000009394 OTTHUMG00000009395	3481 723961	*IGF2* *INS-IGF2*	Insulin-like growth factor 2 (somatomedin A) INS-IGF2 readthrough	7.62159	6.85105	1.7059	2.63^{E-09}	2.52^{E-07}
ADXEC.8579.C2_s_at	ENSG00000197614 OTTHUMG00000168703	8076	*MFAP5*	Microfibrillar associated protein 5	7.31694	6.5356	1.71873	4.81^{E-05}	0.00157199
ADXEC.18200.C1_at	ENSG00000197614 OTTHUMG00000168703	8076	*MFAP5*	Microfibrillar associated protein 5	7.63057	6.83318	1.73795	8.59^{E-06}	0.0003556
ADXEC.823.C1_s_at	ENSG00000128422 ENSG00000173801 OTTHUMG00000133505	3728 3872	*JUP* *KRT17*	Junction plakoglobin Keratin 17	9.83313	9.03249	1.74187	3.29^{E-05}	0.00113386
ADXEC.3014.C5_s_at	ENSG00000149591 OTTHUMG00000167067	6876	*TAGLN*	Transgelin	8.43101	7.62493	1.74846	0.000167142	0.00432948
ADXECEMUTR.5466_s_at	ENSG00000176641 OTTHUMG00000132774	220441	*RNF152*	Ring finger protein 152	3.82722	3.01331	1.75797	1.71^{E-07}	1.11^{E-05}

(continued on following page)

TABLE A4. Differentially Expressed Genes Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Probe Set ID	Ensembl	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	*P*	*P* (FDR)
ADXEC.21861.C1_s_at	ENSG00000167244 OTTHUMG00000009395	3481 723961	*IGF2* *INS-IGF2*	Insulin-like growth factor 2 (somatomedin A) INS-IGF2 readthrough	10.148	9.32616	1.76769	1.86^{E-08}	1.51^{E-06}
ADXECAD.20866_at	ENSG00000129965 ENSG00000167244 OTTHUMG00000009395 OTTHUMG00000166213	3481 723961	*IGF2* *INS-IGF2*	Insulin-like growth factor 2 (somatomedin A) INS-IGF2 readthrough	7.78117	6.9562	1.7715	3.48^{E-08}	2.63^{E-06}
ADXECAD.20866_x_at	ENSG00000129965 ENSG00000167244 OTTHUMG00000009395 OTTHUMG00000166213	3481 723961	*IGF2* *INS-IGF2*	Insulin-like growth factor 2 (somatomedin A) INS-IGF2 readthrough	7.84451	7.00865	1.78492	2.32^{E-08}	1.83^{E-06}
ADXEC.15009.C1_at	ENSG00000164176 OTTHUMG00000119047	10085	*EDIL3*	EGF-like repeats and discoidin I-like domains 3	3.66375	2.82545	1.78794	3.43^{E-08}	2.60^{E-06}
ADXEC.6924.C1_at	ENSG00000169604 OTTHUMG00000129575	84168	*ANTXR1*	Anthrax toxin receptor 1	7.13904	6.29525	1.79476	1.80^{E-07}	1.17^{E-05}
ADXECNTDJ.3932_s_at	ENSG00000152377 OTTHUMG00000129157	6695	*SPOCK1*	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 1	5.80313	4.92105	1.84304	1.56^{E-07}	1.03^{E-05}

Abbreviations: DDIR, DNA damage immune response; DDRD, DNA damage repair deficient; FDR, false discovery rate; GABA, gamma-aminobutyric acid; MAD, median absolute deviation.

TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0006955	Immune response	206	1,424	.0000	.0000	LILRB4, IL7R, LST1, MILR1, HCK, IRF4, ZC3HAV1, POU2AF1, NFKBIA, TNIP3, IFI16, PSMA4, BTN3A1, CLEC7A, ZAP70, IFNG, CXCL10, IFIT1, LAMP3, IL16, CSF1, IL12RB1, CCL8, SLA2, TNFSF13B, C1QA, TNFSF10, BLNK, LCP2, HERC5, NCF4, HLA-F, GBP1, KLHL6, IGLC2, CD96, EIF2AK2, VCAM1, IDO1, CCL5, HLA-C, IL24, HLA-DPB1, PTAFR, OAS3, GBP5, IGHM, PXDN, APOBEC3D, ITGB2, OAS2, CTSS, LILRB2, RSAD2, NCF2, OAS1, IFI30, FCGR2C, CD3D, C1QC, CD74, ERAP2, MX1, PLSCR1, HLA-DRA, PAG1, APOL1, C19orf66, KLRK1, MS4A1, CD300E, CASP4, IFITM1, HLA-DPA1, TRAF3, HLA-DRB1, FYB, CCR2, CD4, SEMA4D, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, THBS1, RBCK1, SPN, IL32, CD40, LGALS9, CLEC2D, PIK3AP1, APBB1IP, HLA-B, CXCL16, IGHA1, GZMB, CXCL13, PLCG2, FCGR3B, RNF19B, JAK3, TRIM22, LTB, TAP1, CCR1, HLA-DOA, LAX1, HLA-DMB, HAVCR2, ZBP1, IRF7, LTF, CYBB, LYN, HLA-A, THEMIS2, MB21D1, ISG20, CD86, LCP1, IGHG4, DDX58, CFB, PRKCB, CD3E, SP100, JAK2, COL1A2, IGHG1, GPR183, TNFAIP3, NR1H3, CD8A, CIITA, APOBEC3G, IGF2, LILRB1, XAF1, CCL2, BTN3A3, TRIM34, RAC2, COL1A1, LPXN, CXCL11, C1QB, STAT1, IFIH1, TRIM5, SECTM1, ADAMDEC1, TRIM21, TAPBP, SAMHD1, TRAC, NLRC5, TNFRSF14, ITGAL, APOBEC3B, B2M, HMGB2, APOBEC3A, IGKC, SELL, PIK3CG, PTPN6, TAP2, CCL19, PSME1, AIM2, IRF8, CCR7, CYLD, GBP2, FCGR3A, CD38, IGLL5, GFI1, XBP1, SERPINB9, KLRC2, LAIR1, SLAMF7, IL18, CD79A, FCRL5, IGSF6, HLA-DOB, PSMB9, WIPF1, IFIT3, MEF2C, IFIT2, BIRC3, STAP1, USP18, HLA-E, FCER1G, PTPRC, IL2RG, C3, IFI27, CTSC
GO:0002376	Immune system process	237	2,307	.0000	.0000	LILRB4, IFI44L, IL7R, LST1, MILR1, HCK, IRF4, ZC3HAV1, POU2AF1, TNIP3, PSMA4, NFKBIA, IFI16, BTN3A1, ZAP70, CLEC7A, IFNG, CXCL10, SFRP2, IFIT1, LAMP3, IL16, IL12RB1, CSF1, SLA2, CCL8, TNFSF13B, TNFSF10, C1QA, BLNK, LCP2, HERC5, NCF4, HLA-F, GBP1, KLHL6, IGLC2, CD96, EIF2AK2, VCAM1, IDO1, CCL5, HLA-C, HLA-DPB1, IL24, PTAFR, OAS3, GBP5, IGHM, PXDN, APOBEC3D, ITGB2, CTSS, OAS2, LILRB2, NCF2, RSAD2, OAS1, IFI30, FCGR2C, CD3D, C1QC, ERAP2, MX1, CD74, PLSCR1, HLA-DRA, PAG1, APOL1, C19orf66, KLRK1, MS4A1, CD300E, CASP4, IFITM1, HLA-DPA1, TRAF3, HLA-DRB1, FYB, CCR2, CD4, SEMA4D, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, BANK1, RHOH, THBS1, RBCK1, SPN, IL32, CD40, BCL11B, LGALS9, CLEC2D, PIK3AP1, APBB1IP, HLA-B, CXCL16, IGHA1, CXCL13, GZMB, PLCG2, FCGR3B, RNF19B, JAK3, PLEK, TRIM22, TAP1, LTB, ALPK1, CCR1, HLA-DOA, LAX1, IKZF3, HLA-DMB, HAVCR2, ZBP1, IRF7, CYBB, LTF, LYN, HLA-A, PMAIP1, THEMIS2, MB21D1, ISG20, CD86, IGHG4, LCP1, DDX58, CFB, MFAP5, PRKCB, SP100, GPR171, CD3E, JAK2, GPC3, SIRPG, IGHG1, COL1A2, TNFAIP3, HERC6, GPR183, NR1H3, CD8A, CIITA, APOBEC3G, IGF2, LILRB1, XAF1, CCL2, BTN3A3, TRIM34, COL1A1, RAC2, LPXN, CXCL11, STAT1, C1QB, HTRA1, LRMP, IFIH1, TRIM5, SECTM1, TRIM21, ORM2, ADAMDEC1, TAPBP, SAMHD1, TRAC, NLRC5, TNFRSF14, APOBEC3B, ITGAL, B2M, HMGB2, APOBEC3A, OLR1, SNX10, IGKC, SELL, PIK3CG, RASAL3, CD2, PTPN6, TAP2, CCL19, PSME1, IRF8, AIM2, CD48, CCR7, IL21R, CYLD, CD109, GBP2, FCGR3A, IGLL5, CD38, GFI1, SERPINB9, XBP1, IKZF1, KCNAB2, KLRC2, LAIR1, SLAMF7, IL18, NLRC3, FCRL5, CD79A, IGSF6, HLA-DOB, PSMB9, WIPF1, IFIT3, HCLS1, MEF2C, IFIT2, DOCK8, STAP1, BIRC3, USP18, HLA-E, PLA2G2D, FCER1G, PTPRC, IL2RG, ATM, C3, IFI27, CTSC
GO:0006952	Defense response	167	1,444	.0000	.0000	IFI44L, HCK, IRF4, ZC3HAV1, NFKBIA, TNIP3, IFI16, PSMA4, CLEC7A, ZAP70, IFNG, CXCL10, IFIT1, PLAC8, CSF1, APOL2, IL12RB1, CCL8, C1QA, BLNK, HERC5, HLA-F, GBP1, IGLC2, EIF2AK2, VCAM1, IDO1, CCL5, HLA-C, IL24, HLA-DPB1, PTAFR, OAS3, GBP5, IGHM, APOBEC3D, ITGB2, OAS2, CTSS, RSAD2, OAS1, NCF2, IFI30, C1QC, CD74, MX1, PLSCR1, HLA-DRA, APOL1, C19orf66, KLRK1, CD300E, CASP4, HCP5, IFITM1, HLA-DPA1, TRAF3, HLA-DRB1, CCR2, CD4, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, THBS1, SPN, IL32, CD40, LGALS9, PIK3AP1, HLA-B, CXCL16, IGHA1, GZMB, CXCL13, PLCG2, FCGR3B, AOAH, ALOX5, JAK3, TRIM22, TAP1, CCR1, ALPK1, LYZ, HAVCR2, ZBP1, IRF7, LTF, CYBB, LYN, HLA-A, PMAIP1, THEMIS2, MB21D1, ISG20, CD86, IGHG4, DDX58, APOL3, CFB, SP100, JAK2, IGHG1, TNFAIP3, CASP1, CD8A, NR1H3, CIITA, APOBEC3G, IGF2, LILRB1, XAF1, CCL2, TRIM34, CXCL11, SERPINA1, C1QB, STAT1, HTRA1, IFIH1, TRIM5, TRIM21, ORM2, SAMHD1, NLRC5, TNFRSF14, ITGAL, APOBEC3B, B2M, APOBEC3A, HMGB2, OLR1, IGKC, PIK3CG, PTPN6, P2RX1, CCL19, PSME1, IRF8, AIM2, CD48, CCR7, CYLD, GBP2, IGLL5, GFI1, SERPINB9, KLRC2, SLAMF7, IL18, PSMB9, IFIT3, SIGLEC1, MEF2C, IFIT2, BIRC3, USP18, HLA-E, PLA2G2D, FCER1G, GNLY, PTPRC, C3, IFI27

(continued on following page)

TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0002682	Regulation of immune system process	159	1,306	.0000	.0000	LILRB4, IL7R, LST1, HCK, IRF4, ZC3HAV1, NFKBIA, TNIP3, IFI16, PSMA4, BTN3A1, CLEC7A, ZAP70, IFNG, CXCL10, IFIT1, CSF1, IL12RB1, CCL8, SLA2, TNFSF13B, C1QA, LCP2, HERC5, HLA-F, KLHL6, IGLC2, CD96, EIF2AK2, VCAM1, IDO1, CCL5, HLA-C, HLA-DPB1, PTAFR, GBP5, IGHM, ITGB2, CTSS, LILRB2, RSAD2, CD3D, C1QC, CD74, PLSCR1, HLA-DRA, PAG1, KLRK1, CD300E, IFITM1, HLA-DPA1, TRAF3, HLA-DRB1, FYB, CCR2, CD4, FYN, ICAM1, IRF1, CXCL9, PTK2B, BANK1, THBS1, RBCK1, SPN, CD40, LGALS9, CLEC2D, PIK3AP1, HLA-B, IGHA1, CXCL13, PLCG2, FCGR3B, JAK3, TAP1, CCR1, ALPK1, HLA-DOA, LAX1, HLA-DMB, IKZF3, HAVCR2, IRF7, LTF, LYN, HLA-A, THEMIS2, MB21D1, CD86, IGHG4, CFB, DDX58, PRKCB, GPR171, CD3E, JAK2, COL1A2, IGHG1, SIRPG, GPR183, TNFAIP3, CD8A, NR1H3, APOBEC3G, IGF2, LILRB1, CCL2, RAC2, COL1A1, LPXN, CXCL11, C1QB, STAT1, HTRA1, IFIH1, TRIM5, ORM2, SAMHD1, TRAC, NLRC5, TNFRSF14, ITGAL, B2M, HMGB2, IGKC, SELL, RASAL3, PTPN6, CD2, CCL19, PSME1, AIM2, CCR7, CYLD, FCGR3A, CD38, IGLL5, GFI1, SERPINB9, XBP1, LAIR1, SLAMF7, IL18, CD79A, FCRL5, PSMB9, WIPF1, HCLS1, MEF2C, STAP1, BIRC3, USP18, PLA2G2D, HLA-E, FCER1G, PTPRC, ATM, C3
GO:0050776	Regulation of immune response	127	795	.0000	.0000	LTF, IL7R, LYN, HLA-A, HCK, IRF4, ZC3HAV1, NFKBIA, IFI16, PSMA4, TNIP3, THEMIS2, MB21D1, BTN3A1, CLEC7A, CD86, ZAP70, IFNG, IGHG4, DDX58, CFB, PRKCB, CD3E, JAK2, IL12RB1, SLA2, C1QA, IGHG1, COL1A2, LCP2, TNFAIP3, CD8A, NR1H3, IGF2, HLA-F, LILRB1, KLHL6, IGLC2, CD96, VCAM1, IDO1, COL1A1, RAC2, LPXN, CCL5, HLA-C, PTAFR, HLA-DPB1, C1QB, STAT1, GBP5, IFIH1, IGHM, TRIM5, ITGB2, SAMHD1, CTSS, TRAC, NLRC5, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, C1QC, CD74, HMGB2, PLSCR1, IGKC, HLA-DRA, PAG1, SELL, PTPN6, KLRK1, CCL19, PSME1, CD300E, AIM2, IFITM1, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, CCR2, IGLL5, CD38, CD4, SERPINB9, GFI1, FYN, XBP1, ICAM1, IRF1, LAIR1, SPN, RBCK1, SLAMF7, CD40, CD79A, FCRL5, PSMB9, LGALS9, CLEC2D, WIPF1, PIK3AP1, HLA-B, IGHA1, MEF2C, CXCL13, PLCG2, STAP1, BIRC3, JAK3, USP18, HLA-E, FCER1G, TAP1, PTPRC, C3, LAX1, HLA-DMB, HAVCR2, IRF7
GO:0045087	Innate immune response	121	754	.0000	.0000	LTF, CYBB, LYN, HLA-A, HCK, IRF4, ZC3HAV1, NFKBIA, IFI16, PSMA4, TNIP3, MB21D1, ISG20, CLEC7A, CD86, ZAP70, IFNG, IGHG4, DDX58, IFIT1, SP100, JAK2, CSF1, IL12RB1, CCL8, C1QA, IGHG1, TNFAIP3, NR1H3, HERC5, CIITA, APOBEC3G, IGF2, HLA-F, LILRB1, GBP1, XAF1, CCL2, TRIM34, IGLC2, EIF2AK2, VCAM1, CCL5, HLA-C, PTAFR, OAS3, HLA-DPB1, C1QB, STAT1, GBP5, IFIH1, IGHM, APOBEC3D, TRIM5, ITGB2, TRIM21, SAMHD1, OAS2, CTSS, NLRC5, RSAD2, NCF2, OAS1, IFI30, APOBEC3B, B2M, C1QC, APOBEC3A, MX1, HMGB2, PLSCR1, IGKC, HLA-DRA, PIK3CG, APOL1, PTPN6, C19orf66, KLRK1, CCL19, CASP4, PSME1, CD300E, IRF8, AIM2, IFITM1, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, GBP2, IGLL5, SERPINB9, GFI1, FYN, ICAM1, IRF1, PTK2B, CCL18, KLRC2, SLAMF7, PSMB9, LGALS9, PIK3AP1, HLA-B, CXCL16, IFIT3, IGHA1, IFIT2, GZMB, PLCG2, BIRC3, JAK3, USP18, HLA-E, TRIM22, FCER1G, TAP1, IFI27, HAVCR2, ZBP1, IRF7
GO:0002684	Positive regulation of immune system process	123	831	.0000	.0000	LTF, IL7R, LYN, HLA-A, HCK, IRF4, ZC3HAV1, NFKBIA, IFI16, TNIP3, PSMA4, THEMIS2, MB21D1, BTN3A1, CLEC7A, CD86, ZAP70, IFNG, CXCL10, IGHG4, DDX58, CFB, PRKCB, CD3E, CSF1, IL12RB1, CCL8, SLA2, TNFSF13B, C1QA, SIRPG, IGHG1, LCP2, GPR183, TNFAIP3, NR1H3, IGF2, LILRB1, KLHL6, CCL2, IGLC2, VCAM1, IDO1, RAC2, LPXN, CCL5, CXCL11, PTAFR, HLA-DPB1, C1QB, GBP5, IFIH1, IGHM, TRIM5, ITGB2, CTSS, TRAC, NLRC5, LILRB2, RSAD2, TNFRSF14, B2M, CD3D, C1QC, CD74, HMGB2, PLSCR1, IGKC, HLA-DRA, PAG1, RASAL3, PTPN6, CD2, KLRK1, CCL19, PSME1, AIM2, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, CCR2, IGLL5, CD38, CD4, GFI1, FYN, XBP1, ICAM1, CXCL9, PTK2B, THBS1, SPN, RBCK1, IL18, CD40, CD79A, FCRL5, PSMB9, LGALS9, WIPF1, PIK3AP1, HLA-B, HCLS1, IGHA1, MEF2C, CXCL13, PLCG2, STAP1, BIRC3, JAK3, HLA-E, FCER1G, CCR1, PTPRC, C3, LAX1, HLA-DMB, HAVCR2, IRF7
GO:0050778	Positive regulation of immune response	99	578	.0000	.0000	LTF, LYN, HLA-A, HCK, IRF4, ZC3HAV1, NFKBIA, IFI16, PSMA4, TNIP3, THEMIS2, MB21D1, BTN3A1, CLEC7A, CD86, ZAP70, IFNG, IGHG4, DDX58, CFB, PRKCB, CD3E, IL12RB1, SLA2, C1QA, IGHG1, LCP2, TNFAIP3, NR1H3, LILRB1, KLHL6, IGLC2, IDO1, LPXN, CCL5, PTAFR, HLA-DPB1, C1QB, GBP5, IFIH1, TRIM5, IGHM, ITGB2, CTSS, TRAC, NLRC5, RSAD2, TNFRSF14, B2M, CD3D, C1QC, CD74, HMGB2, PLSCR1, IGKC, HLA-DRA, PAG1, PTPN6, KLRK1, CCL19, PSME1, AIM2, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, CCR2, IGLL5, CD38, CD4, GFI1, FYN, XBP1, RBCK1, CD40, CD79A, FCRL5, PSMB9, LGALS9, WIPF1, PIK3AP1, HLA-B, IGHA1, MEF2C, PLCG2, BIRC3, STAP1, JAK3, HLA-E, FCER1G, PTPRC, C3, LAX1, HLA-DMB, HAVCR2, IRF7

(continued on following page)

TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0002252	Immune effector process	108	712	.0000	.0000	IFI44L, IL7R, LYN, MILR1, HLA-A, HCK, IRF4, ZC3HAV1, PMAIP1, IFI16, MB21D1, ISG20, CLEC7A, CD86, ZAP70, IFNG, CXCL10, IGHG4, LCP1, DDX58, CFB, IFIT1, IL12RB1, SLA2, C1QA, IGHG1, GPR183, TNFAIP3, CD8A, HERC5, APOBEC3G, IGF2, LILRB1, GBP1, CCL2, BTN3A3, TRIM34, IGLC2, EIF2AK2, RAC2, PTAFR, OAS3, C1QB, STAT1, HTRA1, IFIH1, APOBEC3D, TRIM5, SAMHD1, OAS2, NLRC5, RSAD2, OAS1, TNFRSF14, APOBEC3B, ITGAL, B2M, C1QC, CD74, APOBEC3A, MX1, PLSCR1, IGKC, PIK3CG, PTPN6, C19orf66, KLRK1, CCL19, AIM2, IFITM1, TRAF3, HLA-DRB1, FCGR3A, CCR2, SERPINB9, FYN, XBP1, ICAM1, CXCL9, IRF1, PTK2B, KLRC2, SPN, SLAMF7, CD40, LGALS9, WIPF1, APBB1IP, HLA-B, IFIT3, IFIT2, GZMB, PLCG2, FCGR3B, STAP1, BIRC3, JAK3, TRIM22, HLA-E, FCER1G, TAP1, PTPRC, ALPK1, C3, HLA-DMB, HAVCR2, CTSC, IRF7
GO:0051707	Response to other organism	111	844	.0000	.0000	LTF, IFI44L, LYN, CMPK2, HLA-A, HCK, ZC3HAV1, PMAIP1, NFKBIA, IFI16, SPARC, TNIP3, MB21D1, ISG20, CLEC7A, CD86, IFNG, CXCL10, IGHG4, DDX58, IFIT1, PLAC8, JAK2, IL12RB1, CCL8, IGHG1, IL10RA, TNFAIP3, CASP1, CD8A, NR1H3, HERC5, APOBEC3G, LILRB1, GBP1, CCL2, TRIM34, IGLC2, EIF2AK2, VCAM1, IDO1, CCL5, CXCL11, PTAFR, IL24, OAS3, STAT1, HTRA1, IFIH1, IGHM, APOBEC3D, TRIM5, SAMHD1, OAS2, NLRC5, LILRB2, RSAD2, TNFRSF14, OAS1, APOBEC3B, B2M, APOBEC3A, MX1, HMGB2, PLSCR1, IGKC, C19orf66, KLRK1, IFI44, CCL19, IRF8, AIM2, IFITM1, CCR7, TRAF3, HLA-DRB1, CCR2, IGLL5, CD4, SERPINB9, GFI1, XBP1, ICAM1, CXCL9, IRF1, SPN, IL18, CD40, PSMB9, LGALS9, WIPF1, HLA-B, CXCL16, IFIT3, IGHA1, MEF2C, IFIT2, CXCL13, PLCG2, FCGR3B, STAP1, BIRC3, TRIM22, HLA-E, FCER1G, PTPRC, ALPK1, GNLY, LYZ, HAVCR2, IRF7
GO:0043207	Response to external biotic stimulus	111	844	.0000	.0000	LTF, IFI44L, LYN, CMPK2, HLA-A, HCK, ZC3HAV1, PMAIP1, NFKBIA, IFI16, SPARC, TNIP3, MB21D1, ISG20, CLEC7A, CD86, IFNG, CXCL10, IGHG4, DDX58, IFIT1, PLAC8, JAK2, IL12RB1, CCL8, IGHG1, IL10RA, TNFAIP3, CASP1, CD8A, NR1H3, HERC5, APOBEC3G, LILRB1, GBP1, CCL2, TRIM34, IGLC2, EIF2AK2, VCAM1, IDO1, CCL5, CXCL11, PTAFR, IL24, OAS3, STAT1, HTRA1, IFIH1, IGHM, APOBEC3D, TRIM5, SAMHD1, OAS2, NLRC5, LILRB2, RSAD2, TNFRSF14, OAS1, APOBEC3B, B2M, APOBEC3A, MX1, HMGB2, PLSCR1, IGKC, C19orf66, KLRK1, IFI44, CCL19, IRF8, AIM2, IFITM1, CCR7, TRAF3, HLA-DRB1, CCR2, IGLL5, CD4, SERPINB9, GFI1, XBP1, ICAM1, CXCL9, IRF1, SPN, IL18, CD40, PSMB9, LGALS9, WIPF1, HLA-B, CXCL16, IFIT3, IGHA1, MEF2C, IFIT2, CXCL13, PLCG2, FCGR3B, STAP1, BIRC3, TRIM22, HLA-E, FCER1G, PTPRC, ALPK1, GNLY, LYZ, HAVCR2, IRF7
GO:0001775	Cell activation	102	700	.0000	.0000	IL7R, LST1, LYN, MILR1, HLA-A, IRF4, BTN3A1, CLEC7A, CD86, ZAP70, IFNG, CXCL10, IGHG4, LCP1, PRKCB, CD3E, JAK2, IL12RB1, SLA2, TNFSF13B, SIRPG, IGHG1, BLNK, LCP2, GPR183, TNFAIP3, CD8A, IGF2, LILRB1, CCL2, IGLC2, VCAM1, IDO1, RAC2, CCL5, PTAFR, HLA-DPB1, IGHM, ITGB2, TRAC, LILRB2, RSAD2, TNFRSF14, CTGF, ITGAL, B2M, CD3D, CD74, PLSCR1, IGKC, HLA-DRA, PIK3CG, PAG1, RASAL3, PTPN6, CD2, KLRK1, CCL19, MS4A1, CCR7, HLA-DPA1, IL21R, CYLD, HLA-DRB1, CCR2, IGLL5, CD38, CD4, XBP1, FYN, IKZF1, ICAM1, IRF1, PTK2B, RHOH, BANK1, THBS1, SPN, SLAMF7, NLRC3, IL18, CD40, CD79A, BCL11B, LGALS9, APBB1IP, IGHA1, MEF2C, DOCK8, PLCG2, STAP1, JAK3, PLA2G2D, HLA-E, FCER1G, PTPRC, ATM, HLA-DOA, LAX1, IKZF3, HLA-DMB, HAVCR2
GO:0009607	Response to biotic stimulus	112	877	.0000	.0000	LTF, IFI44L, LYN, CMPK2, HLA-A, HCK, ZC3HAV1, PMAIP1, NFKBIA, IFI16, SPARC, TNIP3, MB21D1, ISG20, CLEC7A, CD86, IFNG, CXCL10, IGHG4, DDX58, IFIT1, PLAC8, JAK2, IL12RB1, CCL8, IGHG1, IL10RA, TNFAIP3, CASP1, CD8A, NR1H3, HERC5, APOBEC3G, LILRB1, GBP1, CCL2, TRIM34, IGLC2, EIF2AK2, VCAM1, IDO1, CCL5, CXCL11, PTAFR, IL24, OAS3, STAT1, HTRA1, IFIH1, IGHM, APOBEC3D, TRIM5, SAMHD1, OAS2, NLRC5, LILRB2, RSAD2, OAS1, TNFRSF14, APOBEC3B, B2M, APOBEC3A, MX1, HMGB2, PLSCR1, IGKC, C19orf66, KLRK1, IFI44, CCL19, IRF8, AIM2, IFITM1, CCR7, TRAF3, HLA-DRB1, CCR2, IGLL5, CD4, SERPINB9, GFI1, XBP1, ICAM1, CXCL9, IRF1, CCL18, SPN, IL18, CD40, PSMB9, LGALS9, WIPF1, HLA-B, CXCL16, IFIT3, IGHA1, MEF2C, IFIT2, CXCL13, PLCG2, FCGR3B, STAP1, BIRC3, TRIM22, HLA-E, FCER1G, PTPRC, ALPK1, GNLY, LYZ, HAVCR2, IRF7

(continued on following page)

TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0045321	Leukocyte activation	99	668	.0000	.0000	IL7R, LST1, LYN, MILR1, HLA-A, IRF4, BTN3A1, CLEC7A, CD86, ZAP70, IFNG, IGHG4, LCP1, PRKCB, CD3E, IL12RB1, SLA2, TNFSF13B, SIRPG, IGHG1, BLNK, LCP2, GPR183, TNFAIP3, CD8A, IGF2, LILRB1, CCL2, IGLC2, VCAM1, IDO1, RAC2, CCL5, PTAFR, HLA-DPB1, IGHM, ITGB2, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, PLSCR1, IGKC, HLA-DRA, PIK3CG, PAG1, RASAL3, PTPN6, CD2, KLRK1, CCL19, MS4A1, CCR7, HLA-DPA1, IL21R, CYLD, HLA-DRB1, CCR2, IGLL5, CD38, CD4, XBP1, FYN, IKZF1, ICAM1, IRF1, PTK2B, RHOH, BANK1, THBS1, SPN, SLAMF7, NLRC3, IL18, CD40, CD79A, BCL11B, LGALS9, APBB1IP, IGHA1, MEF2C, DOCK8, PLCG2, STAP1, JAK3, PLA2G2D, HLA-E, FCER1G, PTPRC, ATM, HLA-DOA, LAX1, HLA-DMB, IKZF3, HAVCR2
GO:0019221	Cytokine-mediated signaling pathway	88	518	.0000	.0000	IL7R, HLA-A, HCK, IRF4, PSMA4, ISG20, IFNG, CXCL10, IFIT1, SP100, JAK2, CSF1, IL12RB1, CCL8, TNFSF13B, IL10RA, TNFAIP3, NR1H3, CIITA, HLA-F, GBP1, XAF1, CCL2, TRIM34, VCAM1, TRAF1, CCL5, HLA-C, CXCL11, PTAFR, OAS3, HLA-DPB1, STAT1, TRIM5, PXDN, TRIM21, SAMHD1, OAS2, NLRC5, RSAD2, TNFRSF14, OAS1, IFI30, B2M, CD74, MX1, HLA-DRA, PTPN6, CSF2RB, CCL19, PSME1, AIM2, IFITM1, IRF8, CCR7, HLA-DPA1, IL21R, TRAF3, CYLD, HLA-DRB1, GBP2, CCR2, GFI1, ICAM1, CXCL9, IRF1, PTK2B, CCL18, RBCK1, CD40, PSMB9, HLA-B, IFIT3, IFIT2, CXCL13, BIRC3, STAP1, JAK3, USP18, TRIM22, HLA-E, LTB, CCR1, ASPN, PTPRC, IL2RG, IFI27, IRF7
GO:0046649	Lymphocyte activation	93	592	.0000	.0000	IL7R, LST1, LYN, HLA-A, IRF4, BTN3A1, CLEC7A, CD86, ZAP70, IFNG, IGHG4, LCP1, PRKCB, CD3E, IL12RB1, SLA2, TNFSF13B, SIRPG, IGHG1, BLNK, GPR183, TNFAIP3, CD8A, IGF2, LILRB1, CCL2, IGLC2, VCAM1, IDO1, RAC2, CCL5, HLA-DPB1, IGHM, ITGB2, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, IGKC, HLA-DRA, PIK3CG, PAG1, RASAL3, PTPN6, CD2, KLRK1, CCL19, MS4A1, CCR7, HLA-DPA1, IL21R, CYLD, HLA-DRB1, CCR2, IGLL5, CD38, CD4, XBP1, FYN, IKZF1, ICAM1, IRF1, PTK2B, RHOH, BANK1, SPN, SLAMF7, NLRC3, IL18, CD40, CD79A, BCL11B, LGALS9, APBB1IP, IGHA1, MEF2C, DOCK8, PLCG2, JAK3, PLA2G2D, HLA-E, FCER1G, PTPRC, ATM, HLA-DOA, LAX1, HLA-DMB, IKZF3, HAVCR2
GO:0034097	Response to cytokine	104	765	.0000	.0000	IL7R, HLA-A, HCK, IRF4, NFKBIA, SPARC, PSMA4, ISG20, CD86, IFNG, CXCL10, IFIT1, LAMP3, SP100, JAK2, CSF1, IL12RB1, CCL8, TNFSF13B, IL10RA, TNFAIP3, NR1H3, CIITA, HLA-F, GBP1, XAF1, CCL2, TRIM34, EIF2AK2, VCAM1, TRAF1, COL1A1, CCL5, HLA-C, CXCL11, POSTN, PTAFR, IL24, OAS3, HLA-DPB1, STAT1, GBP5, TRIM5, PXDN, TRIM21, SAMHD1, OAS2, NLRC5, RSAD2, OAS1, TNFRSF14, IFI30, B2M, CD74, MX1, PLSCR1, HLA-DRA, PTPN6, C19orf66, CSF2RB, CCL19, PSME1, IRF8, AIM2, IFITM1, CCR7, HLA-DPA1, TRAF3, IL21R, CYLD, HLA-DRB1, GBP2, CCR2, CD38, GFI1, XBP1, ICAM1, CXCL9, IRF1, PTK2B, CCL18, RBCK1, CD40, LGALS9, PSMB9, HLA-B, HCLS1, CXCL16, IFIT3, IFIT2, CXCL13, BIRC3, STAP1, JAK3, USP18, TRIM22, HLA-E, LTB, CCR1, PTPRC, ASPN, IL2RG, IFI27, IRF7
GO:0071345	Cellular response to cytokine stimulus	97	659	.0000	.0000	IL7R, HLA-A, HCK, IRF4, NFKBIA, PSMA4, ISG20, CD86, IFNG, CXCL10, IFIT1, SP100, JAK2, CSF1, IL12RB1, CCL8, TNFSF13B, IL10RA, TNFAIP3, NR1H3, CIITA, HLA-F, GBP1, XAF1, CCL2, TRIM34, VCAM1, TRAF1, COL1A1, CCL5, HLA-C, CXCL11, POSTN, PTAFR, IL24, OAS3, HLA-DPB1, STAT1, GBP5, TRIM5, PXDN, TRIM21, SAMHD1, OAS2, NLRC5, RSAD2, TNFRSF14, OAS1, IFI30, B2M, CD74, MX1, HLA-DRA, PTPN6, CSF2RB, CCL19, PSME1, IRF8, AIM2, IFITM1, CCR7, HLA-DPA1, IL21R, TRAF3, CYLD, HLA-DRB1, GBP2, CCR2, XBP1, GFI1, ICAM1, CXCL9, IRF1, PTK2B, CCL18, RBCK1, CD40, LGALS9, PSMB9, HLA-B, HCLS1, IFIT3, IFIT2, CXCL13, BIRC3, STAP1, JAK3, USP18, TRIM22, HLA-E, LTB, CCR1, ASPN, PTPRC, IL2RG, IFI27, IRF7
GO:0002253	Activation of immune response	79	455	.0000	.0000	LTF, LYN, IRF4, HCK, ZC3HAV1, IFI16, NFKBIA, TNIP3, PSMA4, THEMIS2, MB21D1, BTN3A1, ZAP70, CLEC7A, IFNG, CD86, IGHG4, CFB, DDX58, PRKCB, CD3E, SLA2, C1QA, IGHG1, LCP2, TNFAIP3, NR1H3, KLHL6, IGLC2, LPXN, HLA-DPB1, C1QB, IFIH1, IGHM, TRIM5, ITGB2, CTSS, TRAC, RSAD2, CD3D, C1QC, IGKC, PLSCR1, HLA-DRA, PAG1, PTPN6, KLRK1, PSME1, AIM2, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, IGLL5, CD38, CD4, FYN, GFI1, RBCK1, FCRL5, CD79A, LGALS9, PSMB9, WIPF1, PIK3AP1, IGHA1, MEF2C, PLCG2, BIRC3, STAP1, FCER1G, PTPRC, C3, LAX1, HAVCR2, IRF7

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TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0050865	Regulation of cell activation	75	420	.0000	.0000	IL7R, LST1, LYN, IRF4, HLA-A, ZAP70, IFNG, CD86, IGHG4, CD3E, JAK2, IL12RB1, SLA2, TNFSF13B, SIRPG, IGHG1, GPR183, TNFAIP3, IGF2, LILRB1, CCL2, IGLC2, VCAM1, IDO1, CCL5, RAC2, PTAFR, HLA-DPB1, IGHM, TRAC, LILRB2, TNFRSF14, CTGF, CD3D, CD74, IGKC, PLSCR1, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, IGLL5, CD38, CD4, FYN, XBP1, IRF1, BANK1, THBS1, SPN, IL18, CD40, LGALS9, IGHA1, MEF2C, STAP1, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, ATM, HLA-DOA, LAX1, IKZF3, HLA-DMB, HAVCR2
GO:0002694	Regulation of leukocyte activation	73	415	.0000	.0000	IL7R, LST1, LYN, IRF4, HLA-A, ZAP70, IFNG, CD86, IGHG4, CD3E, IL12RB1, SLA2, TNFSF13B, SIRPG, IGHG1, GPR183, TNFAIP3, IGF2, LILRB1, CCL2, IGLC2, VCAM1, IDO1, CCL5, RAC2, PTAFR, HLA-DPB1, IGHM, TRAC, LILRB2, TNFRSF14, CD3D, CD74, IGKC, PLSCR1, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, IGLL5, CD38, CD4, FYN, XBP1, IRF1, BANK1, THBS1, SPN, IL18, CD40, LGALS9, IGHA1, MEF2C, STAP1, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, ATM, HLA-DOA, LAX1, HLA-DMB, IKZF3, HAVCR2
GO:0002764	Immune response–regulating signaling pathway	74	432	.0000	.0000	LTF, LYN, IRF4, HCK, ZC3HAV1, NFKBIA, TNIP3, PSMA4, THEMIS2, BTN3A1, ZAP70, CLEC7A, IFNG, CD86, IGHG4, DDX58, PRKCB, CD3E, SLA2, IGHG1, LCP2, TNFAIP3, NR1H3, LILRB1, KLHL6, IGLC2, LPXN, HLA-DPB1, IFIH1, IGHM, TRIM5, ITGB2, CTSS, TRAC, LILRB2, RSAD2, CD3D, IGKC, PLSCR1, HLA-DRA, PAG1, PTPN6, KLRK1, PSME1, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, IGLL5, CD38, CD4, FYN, GFI1, RBCK1, CD40, FCRL5, CD79A, LGALS9, PSMB9, PIK3AP1, WIPF1, IGHA1, MEF2C, PLCG2, STAP1, BIRC3, FCER1G, PTPRC, LAX1, HAVCR2, IRF7
GO:0002757	Immune response–activating signal transduction	71	399	.0000	.0000	LTF, LYN, IRF4, HCK, ZC3HAV1, NFKBIA, TNIP3, PSMA4, THEMIS2, BTN3A1, ZAP70, CLEC7A, IFNG, CD86, IGHG4, DDX58, PRKCB, CD3E, SLA2, IGHG1, LCP2, TNFAIP3, NR1H3, KLHL6, IGLC2, LPXN, HLA-DPB1, IFIH1, IGHM, TRIM5, ITGB2, CTSS, TRAC, RSAD2, CD3D, IGKC, PLSCR1, HLA-DRA, PAG1, PTPN6, KLRK1, PSME1, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, IGLL5, CD38, CD4, FYN, GFI1, RBCK1, FCRL5, CD79A, LGALS9, PSMB9, PIK3AP1, WIPF1, IGHA1, MEF2C, PLCG2, STAP1, BIRC3, FCER1G, PTPRC, LAX1, HAVCR2, IRF7
GO:0051249	Regulation of lymphocyte activation	68	372	.0000	.0000	IL7R, LST1, LYN, IRF4, HLA-A, ZAP70, IFNG, CD86, IGHG4, CD3E, IL12RB1, SLA2, TNFSF13B, SIRPG, IGHG1, GPR183, TNFAIP3, IGF2, LILRB1, CCL2, IGLC2, VCAM1, IDO1, CCL5, RAC2, HLA-DPB1, IGHM, TRAC, LILRB2, TNFRSF14, CD3D, CD74, IGKC, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, CD38, CD4, IGLL5, FYN, XBP1, IRF1, BANK1, SPN, IL18, CD40, LGALS9, IGHA1, MEF2C, JAK3, HLA-E, PLA2G2D, PTPRC, ATM, HLA-DOA, LAX1, HLA-DMB, IKZF3, HAVCR2
GO:0007166	Cell surface receptor signaling pathway	170	2,460	.0000	.0000	IL7R, HCK, IRF4, PSMA4, NFKBIA, BTN3A1, ZAP70, CLEC7A, IFNG, CXCL10, SFRP2, IFIT1, IL12RB1, CSF1, SLA2, CCL8, TNFSF13B, TNFSF10, BLNK, LCP2, IL10RA, P2RY13, NCF4, HLA-F, GBP1, KLHL6, IGLC2, VCAM1, CCL5, HLA-C, HLA-DPB1, OAS3, PTAFR, IGHM, PXDN, ITGB2, OAS2, LILRB2, NCF2, MLLT11, RSAD2, OAS1, IFI30, CD3D, MX1, CD74, PLSCR1, HLA-DRA, PAG1, CHST11, KLRK1, P2RX5, IFITM1, HLA-DPA1, TRAF3, HLA-DRB1, FYB, CCR2, CD4, SEMA4D, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, THBS1, RBCK1, SPN, CD40, CLEC2D, HLA-B, IGHA1, CXCL13, PLCG2, JAK3, PLEK, TRIM22, LTB, CCR1, LAX1, IRF7, CYBB, LTF, LYN, HLA-A, PMAIP1, THEMIS2, ISG20, IGHG4, PRKCB, SP100, CD3E, GPR171, JAK2, GPC3, IGHG1, COL1A2, CD53, TNFAIP3, NR1H3, CD8A, CIITA, IGF2, LILRB1, XAF1, CCL2, TRIM34, TRAF1, DKK3, LPXN, COL1A1, CXCL11, POSTN, STAT1, HTRA1, TRIM5, TRIM21, IGFBP5, SAMHD1, TRAC, NLRC5, TNFRSF14, ITGAL, CTGF, B2M, HMGB2, IGKC, CD2, PTPN6, CSF2RB, P2RX1, CCL19, PSME1, AIM2, IRF8, GPRC5A, CCR7, IL21R, CYLD, ZEB2, GBP2, CD109, BCL2A1, FCGR3A, IGLL5, CD38, GFI1, XBP1, AKT1S1, IL18, CD79A, FCRL5, IGSF6, PSMB9, DTX4, WIPF1, IFIT3, MEF2C, IFIT2, BIRC3, STAP1, RNF213, USP18, HLA-E, FCER1G, PTPRC, ASPN, IL2RG, IFI27
GO:0034341	Response to interferon-gamma	47	155	.0000	.0000	HLA-DRA, IRF4, HLA-A, HCK, C19orf66, CCL19, IFNG, CD86, IRF8, IFITM1, SP100, JAK2, HLA-DPA1, IL12RB1, CCL8, HLA-DRB1, GBP2, ICAM1, IRF1, NR1H3, CCL18, CIITA, HLA-F, GBP1, CCL2, TRIM34, LGALS9, VCAM1, HLA-B, CXCL16, CCL5, HLA-C, HLA-DPB1, PTAFR, OAS3, GBP5, STAT1, TRIM22, HLA-E, TRIM5, TRIM21, OAS2, NLRC5, OAS1, IFI30, B2M, IRF7

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TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0048584	Positive regulation of response to stimulus	145	1,875	.0000	.0000	HCK, IRF4, ZC3HAV1, NFKBIA, TNIP3, IFI16, PSMA4, BTN3A1, CLEC7A, ZAP70, IFNG, CXCL10, SFRP2, IL16, CSF1, IL12RB1, CCL8, SLA2, C1QA, TNFSF10, BLNK, LCP2, KLHL6, IGLC2, EIF2AK2, IDO1, CCL5, IL24, HLA-DPB1, PTAFR, GBP5, IGHM, ITGB2, CTSS, MLLT11, RSAD2, CD3D, C1QC, CD74, PLSCR1, HLA-DRA, PAG1, KLRK1, P2RX5, HLA-DPA1, TRAF3, HLA-DRB1, FYB, CCR2, CD4, SEMA4D, FYN, ICAM1, CXCL9, CCL18, PTK2B, BANK1, THBS1, RBCK1, CD40, LGALS9, PIK3AP1, HLA-B, IGHA1, GZMB, CXCL13, PLCG2, JAK3, TRIM22, CCR1, LAX1, HLA-DMB, HAVCR2, IRF7, LTF, LYN, HLA-A, PMAIP1, THEMIS2, MB21D1, CD86, IGHG4, APOL3, CFB, DDX58, PRKCB, CD3E, JAK2, GPC3, IGHG1, GPR183, TNFAIP3, CASP1, CD8A, NR1H3, IGF2, LILRB1, CCL2, RAC2, COL1A1, LPXN, PDCD5, CXCL11, GRAP, C1QB, IFIH1, TRIM5, SECTM1, IGFBP5, TRAC, NLRC5, TNFRSF14, CTGF, B2M, HMGB2, IGKC, PIK3CG, PTPN6, CCL19, PSME1, AIM2, CCR7, CYLD, ZEB2, FCGR3A, CD38, IGLL5, GFI1, XBP1, FGD2, IL18, CD79A, FCRL5, PSMB9, WIPF1, HCLS1, MEF2C, STAP1, BIRC3, HLA-E, FCER1G, PTPRC, ATM, C3, CTSC
GO:0050867	Positive regulation of cell activation	59	287	.0000	.0000	IGKC, IL7R, HLA-DRA, LYN, HLA-A, RASAL3, PTPN6, CD2, KLRK1, CCL19, ZAP70, IFNG, CD86, IGHG4, CCR7, CD3E, JAK2, IL12RB1, HLA-DPA1, TNFSF13B, HLA-DRB1, SIRPG, IGHG1, CCR2, IGLL5, CD4, CD38, XBP1, FYN, GPR183, THBS1, IGF2, SPN, LILRB1, IL18, CCL2, CD40, IGLC2, LGALS9, VCAM1, CCL5, IGHA1, MEF2C, HLA-DPB1, PTAFR, STAP1, JAK3, HLA-E, FCER1G, IGHM, PTPRC, TRAC, LILRB2, TNFRSF14, CTGF, HLA-DMB, HAVCR2, CD3D, CD74
GO:0071346	Cellular response to interferon-gamma	43	133	.0000	.0000	HLA-DRA, IRF4, HLA-A, HCK, CCL19, IFNG, IRF8, SP100, JAK2, HLA-DPA1, IL12RB1, CCL8, HLA-DRB1, GBP2, ICAM1, IRF1, NR1H3, CCL18, CIITA, HLA-F, GBP1, CCL2, TRIM34, LGALS9, VCAM1, HLA-B, CCL5, HLA-C, PTAFR, OAS3, HLA-DPB1, GBP5, STAT1, HLA-E, TRIM22, TRIM5, TRIM21, OAS2, NLRC5, OAS1, IFI30, B2M, IRF7
GO:0098542	Defense response to other organism	74	500	.0000	.0000	LTF, IFI44L, HLA-A, ZC3HAV1, PMAIP1, IFI16, MB21D1, ISG20, IFNG, CD86, CXCL10, IGHG4, DDX58, IFIT1, PLAC8, IL12RB1, IGHG1, TNFAIP3, CD8A, HERC5, APOBEC3G, LILRB1, GBP1, TRIM34, IGLC2, EIF2AK2, OAS3, STAT1, HTRA1, IFIH1, IGHM, TRIM5, APOBEC3D, SAMHD1, OAS2, NLRC5, RSAD2, OAS1, TNFRSF14, APOBEC3B, B2M, APOBEC3A, HMGB2, MX1, IGKC, PLSCR1, C19orf66, KLRK1, AIM2, IRF8, IFITM1, TRAF3, CCR2, IGLL5, CD4, CXCL9, IRF1, SPN, CD40, IFIT3, IGHA1, CXCL13, IFIT2, FCGR3B, BIRC3, TRIM22, HLA-E, FCER1G, ALPK1, PTPRC, GNLY, LYZ, HAVCR2, IRF7
GO:0007159	Leukocyte cell-cell adhesion	70	452	.0000	.0000	IL7R, LYN, IRF4, HLA-A, BTN3A1, ZAP70, CLEC7A, IFNG, CD86, LCP1, CD3E, IL12RB1, SLA2, SIRPG, CD8A, IGF2, LILRB1, CCL2, VCAM1, IDO1, CCL5, RAC2, PTAFR, HLA-DPB1, ITGB2, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, OLR1, PIK3CG, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, SEMA4D, CD4, FYN, XBP1, ICAM1, IRF1, RHOH, SPN, NLRC3, IL18, BCL11B, LGALS9, APBB1IP, DOCK8, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, HLA-DOA, LAX1, HLA-DMB, HAVCR2
GO:0002696	Positive regulation of leukocyte activation	57	284	.0000	.0000	IGKC, IL7R, HLA-DRA, LYN, HLA-A, RASAL3, PTPN6, CD2, KLRK1, CCL19, ZAP70, IFNG, CD86, IGHG4, CCR7, CD3E, IL12RB1, HLA-DPA1, TNFSF13B, HLA-DRB1, SIRPG, IGHG1, CCR2, IGLL5, CD4, CD38, XBP1, FYN, GPR183, THBS1, IGF2, SPN, LILRB1, IL18, CCL2, CD40, IGLC2, LGALS9, VCAM1, CCL5, IGHA1, MEF2C, HLA-DPB1, PTAFR, STAP1, JAK3, HLA-E, FCER1G, IGHM, PTPRC, TRAC, LILRB2, TNFRSF14, HLA-DMB, HAVCR2, CD3D, CD74
GO:0002250	Adaptive immune response	58	299	.0000	.0000	LILRB4, IL7R, PAG1, PIK3CG, LYN, IRF4, HLA-A, TAP2, KLRK1, CCL19, BTN3A1, ZAP70, IFNG, CD86, LAMP3, PRKCB, JAK2, IL12RB1, SLA2, HLA-DRB1, CCR2, CD4, FYN, GPR183, TNFAIP3, ICAM1, CD8A, IRF1, PTK2B, LAIR1, SPN, LILRB1, SLAMF7, IL18, KLHL6, CD40, BTN3A3, CD79A, HLA-B, MEF2C, CXCL13, RNF19B, JAK3, HLA-E, FCER1G, IGHM, TAP1, PTPRC, CTSS, LILRB2, RSAD2, LAX1, B2M, CTSC, HAVCR2, IRF7, CD74, ERAP2
GO:0070486	Leukocyte aggregation	67	419	.0000	.0000	IL7R, LYN, IRF4, HLA-A, BTN3A1, ZAP70, CLEC7A, IFNG, CD86, LCP1, CD3E, IL12RB1, SLA2, SIRPG, CD8A, IGF2, LILRB1, CCL2, VCAM1, IDO1, CCL5, RAC2, HLA-DPB1, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, PIK3CG, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, SEMA4D, CD4, FYN, XBP1, ICAM1, IRF1, RHOH, SPN, NLRC3, IL18, BCL11B, LGALS9, APBB1IP, DOCK8, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, HLA-DOA, LAX1, HLA-DMB, HAVCR2

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TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0060333	Interferon-gamma–mediated signaling pathway	35	83	.0000	.0000	HLA-DRA, IRF4, HLA-A, HCK, IFNG, IRF8, SP100, JAK2, HLA-DPA1, HLA-DRB1, GBP2, ICAM1, IRF1, NR1H3, CIITA, HLA-F, GBP1, TRIM34, VCAM1, HLA-B, HLA-C, OAS3, PTAFR, HLA-DPB1, STAT1, HLA-E, TRIM22, TRIM5, TRIM21, OAS2, NLRC5, OAS1, IFI30, B2M, IRF7
GO:0042110	T-cell activation	66	413	.0000	.0000	IL7R, LYN, IRF4, HLA-A, BTN3A1, ZAP70, CLEC7A, IFNG, CD86, LCP1, CD3E, IL12RB1, SLA2, SIRPG, CD8A, IGF2, LILRB1, CCL2, VCAM1, IDO1, CCL5, RAC2, HLA-DPB1, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, PIK3CG, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, CD4, FYN, XBP1, ICAM1, IRF1, RHOH, SPN, NLRC3, IL18, BCL11B, LGALS9, APBB1IP, DOCK8, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, HLA-DOA, LAX1, HLA-DMB, HAVCR2
GO:0070489	T-cell aggregation	66	413	.0000	.0000	IL7R, LYN, IRF4, HLA-A, BTN3A1, ZAP70, CLEC7A, IFNG, CD86, LCP1, CD3E, IL12RB1, SLA2, SIRPG, CD8A, IGF2, LILRB1, CCL2, VCAM1, IDO1, CCL5, RAC2, HLA-DPB1, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, PIK3CG, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, CD4, FYN, XBP1, ICAM1, IRF1, RHOH, SPN, NLRC3, IL18, BCL11B, LGALS9, APBB1IP, DOCK8, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, HLA-DOA, LAX1, HLA-DMB, HAVCR2
GO:0071593	Lymphocyte aggregation	66	414	.0000	.0000	IL7R, LYN, IRF4, HLA-A, BTN3A1, ZAP70, CLEC7A, IFNG, CD86, LCP1, CD3E, IL12RB1, SLA2, SIRPG, CD8A, IGF2, LILRB1, CCL2, VCAM1, IDO1, CCL5, RAC2, HLA-DPB1, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, PIK3CG, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, CD4, FYN, XBP1, ICAM1, IRF1, RHOH, SPN, NLRC3, IL18, BCL11B, LGALS9, APBB1IP, DOCK8, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, HLA-DOA, LAX1, HLA-DMB, HAVCR2
GO:0006950	Response to stress	195	3,379	.0000	.0000	IFI44L, UBA7, HCK, IRF4, ZC3HAV1, TNIP3, SPARC, PSMA4, NFKBIA, IFI16, ZAP70, TFEC, CLEC7A, IFNG, CXCL10, SFRP2, COL5A1, IFIT1, PLAC8, APOL2, IL12RB1, CSF1, CCL8, C1QA, BLNK, DTX3L, RNF152, HERC5, HLA-F, GBP1, IGLC2, EIF2AK2, VCAM1, IDO1, CCL5, HLA-C, HLA-DPB1, IL24, PTAFR, OAS3, GBP5, IGHM, PXDN, APOBEC3D, ITGB2, CTSS, OAS2, NCF2, RSAD2, OAS1, IFI30, C1QC, MX1, CD74, MMP13, PLSCR1, HLA-DRA, APOL1, C19orf66, KLRK1, SOD2, CD300E, HCP5, CASP4, P2RX5, IFITM1, HLA-DPA1, TRAF3, GJB2, HLA-DRB1, CCR2, CD4, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, THBS1, SPN, IL32, CD40, LGALS9, PIK3AP1, HLA-B, CXCL16, IGHA1, CXCL13, GZMB, PLCG2, FCGR3B, AOAH, ALOX5, JAK3, TRIM22, TAP1, ALPK1, CCR1, LYZ, HAVCR2, ZBP1, IRF7, CYBB, LTF, LYN, HLA-A, PMAIP1, THEMIS2, MB21D1, ISG20, CD86, IGHG4, LCP1, DDX58, CFB, APOL3, PRKCB, SP100, JAK2, IGHG1, COL1A2, TNFAIP3, CASP1, NR1H3, CD8A, CIITA, APOBEC3G, IGF2, LILRB1, XAF1, CCL2, TRIM34, COL1A1, CXCL11, POSTN, SERPINA1, STAT1, C1QB, UBE2L6, HTRA1, IFIH1, TRIM5, ORM2, TRIM21, SAMHD1, NLRC5, TNFRSF14, ITGAL, CTGF, APOBEC3B, B2M, HMGB2, APOBEC3A, OLR1, IGKC, PIK3CG, PTPN6, P2RX1, CCL19, PSME1, AIM2, IRF8, CD48, CCR7, CYLD, ZEB2, GBP2, CD109, BCL2A1, IGLL5, CD38, GFI1, SERPINB9, XBP1, KLRC2, SLAMF7, AKT1S1, IL18, FGD2, PSMB9, IFIT3, SIGLEC1, MEF2C, IFIT2, DOCK8, BIRC3, USP18, HLA-E, PLA2G2D, FCER1G, PTPRC, GNLY, ATM, C3, IFI27
GO:0048583	Regulation of response to stimulus	199	3,556	.0000	.0000	TAGAP, IL7R, HCK, IRF4, ZC3HAV1, TNIP3, PSMA4, NFKBIA, IFI16, BTN3A1, ZAP70, CLEC7A, GABBR1, IFNG, CXCL10, SFRP2, IFIT1, IL16, IL12RB1, CSF1, SLA2, CCL8, TNFSF10, C1QA, BLNK, LCP2, RNF152, HERC5, HLA-F, GBP1, KLHL6, IGLC2, CD96, EIF2AK2, VCAM1, IDO1, CCL5, HLA-C, CLIC2, HLA-DPB1, IL24, PTAFR, GBP5, ARHGAP32, IGHM, PXDN, ITGB2, CTSS, LILRB2, MLLT11, RSAD2, CD3D, C1QC, CD74, PLSCR1, HLA-DRA, PAG1, CHST11, KLRK1, SOD2, CD300E, CASP4, P2RX5, IFITM1, HLA-DPA1, TRAF3, HLA-DRB1, FYB, CCR2, CD4, SEMA4D, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, BANK1, THBS1, RHOH, RBCK1, SPN, CD40, LGALS9, CLEC2D, PIK3AP1, HLA-B, IGHA1, CXCL13, GZMB, PLCG2, FCGR3B, JAK3, PLEK, TRIM22, TAP1, ARHGAP9, ALPK1, CCR1, LAX1, HLA-DMB, HAVCR2, IRF7, LTF, LYN, HLA-A, PMAIP1, THEMIS2, MB21D1, CD86, IGHG4, DDX58, CFB, APOL3, PRKCB, SP100, CD3E, JAK2, GPC3, IGHG1, COL1A2, TNFAIP3, GPR183, CASP1, NR1H3, CD8A, APOBEC3G, FBP1, IGF2, LILRB1, CCL2, TRAF1, DKK3, RAC2, LPXN, ARHGAP25, COL1A1, PDCD5, CXCL11, POSTN, GRAP, STAT1, C1QB, HTRA1, IFIH1, TRIM5, SECTM1, IGFBP5, SAMHD1, TRAC, NLRC5, ARHGAP15, TNFRSF14, ITGAL, CTGF, B2M, HMGB2, IGKC, SELL, PIK3CG, RASAL3, PTPN6, CCL19, PSME1, AIM2, GPRC5A, CCR7, CYLD, ZEB2, CD109, FCGR3A, IGLL5, CD38, GFI1, SERPINB9, XBP1, LAIR1, SLAMF7, AKT1S1, IL18, NLRC3, FGD2, FCRL5, CD79A, PSMB9, WIPF1, HCLS1, MEF2C, BIRC3, STAP1, RNF213, USP18, HLA-E, FCER1G, PTPRC, ASPN, ATM, C3, CTSC

(continued on following page)

TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0070661	Leukocyte proliferation	52	261	.0000	.0000	IL7R, LST1, PIK3CG, LYN, HLA-A, RASAL3, PTPN6, CCL19, BTN3A1, ZAP70, IFNG, CD86, MS4A1, CD3E, CSF1, IL12RB1, HLA-DPA1, CCL8, TNFSF13B, HLA-DRB1, CCR2, CD4, CD38, FYN, GPR183, TNFAIP3, IRF1, IGF2, SPN, LILRB1, IL18, CD40, CD79A, LGALS9, VCAM1, IDO1, RAC2, CCL5, MEF2C, DOCK8, HLA-DPB1, JAK3, PLA2G2D, HLA-E, PTPRC, ATM, LILRB2, TNFRSF14, IKZF3, HLA-DMB, HAVCR2, CD74
GO:0051251	Positive regulation of lymphocyte activation	52	262	.0000	.0000	IGKC, IL7R, HLA-DRA, LYN, HLA-A, RASAL3, PTPN6, KLRK1, CCL19, ZAP70, IFNG, CD86, IGHG4, CCR7, CD3E, IL12RB1, HLA-DPA1, TNFSF13B, HLA-DRB1, SIRPG, IGHG1, CCR2, IGLL5, CD4, CD38, XBP1, FYN, GPR183, IGF2, SPN, LILRB1, IL18, CCL2, CD40, IGLC2, LGALS9, VCAM1, CCL5, IGHA1, MEF2C, HLA-DPB1, JAK3, HLA-E, IGHM, PTPRC, TRAC, LILRB2, TNFRSF14, HLA-DMB, HAVCR2, CD3D, CD74
GO:0009605	Response to external stimulus	143	2,040	.0000	.0000	IFI44L, HCK, ZC3HAV1, NFKBIA, TNIP3, IFI16, SPARC, CLEC7A, IFNG, CXCL10, SFRP2, IFIT1, PLAC8, IL16, CSF1, IL12RB1, CCL8, IL10RA, RNF152, HERC5, COL11A1, GBP1, IGLC2, EIF2AK2, VCAM1, IDO1, CCL5, IL24, PTAFR, OAS3, GBP5, IGHM, APOBEC3D, ITGB2, OAS2, LILRB2, RSAD2, OAS1, BIN2, CD74, MX1, MMP13, PLSCR1, C19orf66, KLRK1, CASP4, IFITM1, TRAF3, HLA-DRB1, CCR2, CD4, SEMA4D, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, THBS1, SPN, FPR3, CD40, BCL11B, LGALS9, PIK3AP1, HLA-B, CXCL16, IGHA1, CXCL13, PLCG2, FCGR3B, ALOX5, TRIM22, CCR1, ALPK1, LYZ, HAVCR2, IRF7, LTF, CMPK2, LYN, HLA-A, PMAIP1, MB21D1, ISG20, CD86, IGHG4, CFB, DDX58, CD3E, JAK2, IGHG1, TNFAIP3, CASP1, CD8A, NR1H3, APOBEC3G, IGF2, LILRB1, CCL2, TRIM34, RAC2, COL1A1, CXCL11, POSTN, TYMP, STAT1, HTRA1, IFIH1, TRIM5, SAMHD1, NLRC5, TNFRSF14, APOBEC3B, B2M, APOBEC3A, HMGB2, IGKC, PIK3CG, IFI44, CCL19, IRF8, AIM2, CCR7, CD109, IGLL5, SERPINB9, XBP1, GFI1, IL18, PSMB9, WIPF1, IFIT3, MEF2C, IFIT2, STAP1, BIRC3, NR4A1, HLA-E, FCER1G, GNLY, PTPRC, C3
GO:0032943	Mononuclear cell proliferation	50	247	.0000	.0000	IL7R, LST1, PIK3CG, LYN, HLA-A, RASAL3, PTPN6, BTN3A1, CCL19, ZAP70, IFNG, CD86, MS4A1, CD3E, CSF1, HLA-DPA1, IL12RB1, TNFSF13B, HLA-DRB1, CCR2, CD4, CD38, FYN, GPR183, IRF1, SPN, IGF2, LILRB1, IL18, CD79A, CD40, LGALS9, VCAM1, IDO1, CCL5, RAC2, MEF2C, HLA-DPB1, DOCK8, JAK3, HLA-E, PLA2G2D, PTPRC, ATM, TNFRSF14, LILRB2, IKZF3, HLA-DMB, HAVCR2, CD74
GO:0001817	Regulation of cytokine production	70	532	.0000	.0000	LTF, LYN, UBA7, HLA-A, IRF4, ZC3HAV1, IFI16, MB21D1, CD86, IFNG, DDX58, CD3E, JAK2, IL12RB1, TNFAIP3, CASP1, HERC5, LILRB1, GBP1, CCL2, SRGN, EIF2AK2, IDO1, POSTN, PTAFR, HLA-DPB1, GBP5, UBE2L6, IFIH1, TRIM21, NLRC5, LILRB2, RSAD2, TNFRSF14, B2M, CD74, HMGB2, CD2, KLRK1, CCL19, AIM2, IRF8, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, CCR2, CD4, XBP1, IRF1, BANK1, THBS1, SPN, IL18, NLRC3, CD40, LGALS9, DTX4, HLA-B, PLCG2, BIRC3, JAK3, HLA-E, LTB, FCER1G, C3, HAVCR2, IRF7, ZBP1
GO:0001816	Cytokine production	73	586	.0000	.0000	LTF, LYN, UBA7, HLA-A, IRF4, ZC3HAV1, IFI16, MB21D1, BTN3A1, CD86, IFNG, DDX58, CD3E, JAK2, IL12RB1, LCP2, TNFAIP3, CASP1, HERC5, LILRB1, GBP1, CCL2, SRGN, EIF2AK2, IDO1, POSTN, PTAFR, HLA-DPB1, GBP5, UBE2L6, IFIH1, TRIM21, NLRC5, LILRB2, RSAD2, TNFRSF14, B2M, CD74, HMGB2, PIK3CG, CD2, KLRK1, CCL19, AIM2, IRF8, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, CCR2, CD4, XBP1, IRF1, BANK1, THBS1, SPN, IL18, NLRC3, CD40, LGALS9, DTX4, HLA-B, PLCG2, BIRC3, JAK3, HLA-E, LTB, FCER1G, C3, HAVCR2, IRF7, ZBP1
GO:0070663	Regulation of leukocyte proliferation	45	197	.0000	.0000	LST1, LYN, HLA-A, RASAL3, PTPN6, CCL19, ZAP70, IFNG, CD86, CD3E, CSF1, HLA-DPA1, IL12RB1, CCL8, TNFSF13B, HLA-DRB1, CCR2, CD4, CD38, TNFAIP3, GPR183, IRF1, SPN, IGF2, LILRB1, IL18, CD40, LGALS9, VCAM1, IDO1, CCL5, RAC2, MEF2C, HLA-DPB1, JAK3, HLA-E, PLA2G2D, PTPRC, ATM, TNFRSF14, LILRB2, HLA-DMB, IKZF3, HAVCR2, CD74
GO:0046651	Lymphocyte proliferation	49	244	.0000	.0000	IL7R, LST1, PIK3CG, LYN, HLA-A, RASAL3, PTPN6, BTN3A1, CCL19, ZAP70, IFNG, CD86, MS4A1, CD3E, HLA-DPA1, IL12RB1, TNFSF13B, HLA-DRB1, CCR2, CD4, CD38, FYN, GPR183, IRF1, SPN, IGF2, LILRB1, IL18, CD79A, CD40, LGALS9, VCAM1, IDO1, CCL5, RAC2, MEF2C, HLA-DPB1, DOCK8, JAK3, HLA-E, PLA2G2D, PTPRC, ATM, TNFRSF14, LILRB2, HLA-DMB, IKZF3, HAVCR2, CD74

(continued on following page)

TABLE A5. Functional Analysis for Biologic Process of the DEGs Between DDIR Signature-Positive and DDIR Signature-Negative Patient Subgroups (continued)

Group	Description	Query	Total	*P*	*P* (FDR)	Genes
GO:0050896	Response to stimulus	310	7,722	.0000	.0000	TAGAP, IL7R, MILR1, HCK, IRF4, ZC3HAV1, PSMA4, TNIP3, IFI16, GABBR1, ZAP70, TFEC, CXCL10, SFRP2, IL16, APOL2, IL12RB1, SLA2, BLNK, LCP2, IL10RA, P2RY13, CDC42EP4, HERC5, NCF4, HLA-F, RASSF4, KLHL6, CD96, IGLC2, EIF2AK2, VCAM1, IDO1, CCL5, KRT14, OAS3, PTAFR, TEAD2, ARHGAP32, IGHM, APOBEC3D, CTSS, LILRB2, OAS1, RSAD2, C1QC, MX1, ERAP2, MMP13, C19orf66, KLRK1, NCALD, SOD2, MS4A1, HCP5, P2RX5, HLA-DPA1, HLA-DRB1, CCR2, CD4, SEMA4D, FYN, IRF1, CCL18, PTK2B, BANK1, RBCK1, SPN, FPR3, IL32, CLEC2D, HLA-B, CXCL13, PLCG2, ALOX5, RNF19B, JAK3, PLEK, TRIM22, LTB, ARHGAP9, CCR1, LGALS3BP, HLA-DOA, LYZ, LAX1, HLA-DMB, IRF7, CMPK2, LYN, HLA-A, LCP1, IGHG4, DDX58, CFB, PRKCB, SP100, JAK2, GPC3, SP110, ANTXR1, SIRPG, GPR183, CASP1, CD8A, NR1H3, APOBEC3G, IGF2, LILRB1, XAF1, TRIM34, DKK3, COL1A1, RAC2, ARHGAP25, PDCD5, POSTN, GRAP, IFIH1, SECTM1, ADAMDEC1, ORM2, TRIM21, SAMHD1, NUAK2, NLRC5, B2M, APOBEC3A, OLR1, IGKC, SELL, PIK3CG, RASAL3, CD2, TAP2, CCL19, AIM2, IRF8, GPRC5A, IL21R, GBP2, FCGR3A, IGLL5, CD38, SERPINB9, LAIR1, IL18, CD79A, IGSF6, HLA-DOB, WIPF1, SIGLEC1, DOCK8, NR4A1, USP18, HLA-E, PLA2G2D, FCER1G, ATM, C3, LILRB4, IFI44L, LST1, UBA7, POU2AF1, SPARC, NFKBIA, DOK3, BTN3A1, IFNG, CLEC7A, COL5A1, IFIT1, PLAC8, LAMP3, CSF1, CCL8, TNFSF10, TNFSF13B, C1QA, DTX3L, RNF152, COL11A1, GBP1, DOCK10, SRGN, SPOCK2, HLA-C, CLIC2, HLA-DPB1, IL24, LPIN1, GBP5, PXDN, ITGB2, OAS2, MLLT11, NCF2, IFI30, FCGR2C, CD3D, BIN2, CD74, PLSCR1, HLA-DRA, PAG1, CHST11, APOL1, GABRP, CASP4, CD300E, IFITM1, TRAF3, GJB2, FYB, ICAM1, CXCL9, THBS1, RHOH, CD40, BCL11B, LGALS9, PIK3AP1, APBB1IP, CXCL16, IGHA1, GZMB, FCGR3B, AOAH, TAP1, ALPK1, HAVCR2, ZBP1, CYBB, LTF, PMAIP1, THEMIS2, DAPP1, MB21D1, ISG20, CD86, APOL3, GPR171, CD3E, IGHG1, COL1A2, CD53, TNFAIP3, AKT3, CIITA, FBP1, CCL2, BTN3A3, TRAF1, LPXN, CXCL11, SERPINA1, UBE2L6, TYMP, STAT1, C1QB, HTRA1, TRIM5, TAPBP, IGFBP5, TRAC, TNFRSF14, ARHGAP15, CTGF, ITGAL, APOBEC3B, HMGB2, SLC24A1, PTPN6, RTP4, CSF2RB, IFI44, P2RX1, PSME1, CD48, CCR7, CYLD, ZEB2, CD109, BCL2A1, XBP1, GFI1, KLRC2, KRT17, SLAMF7, AKT1S1, NLRC3, FGD2, FCRL5, PSMB9, DTX4, IFIT3, HCLS1, MEF2C, IFIT2, STAP1, BIRC3, RNF213, PTPRC, GNLY, ASPN, IL2RG, SPOCK1, IFI27, CTSC
GO:0032944	Regulation of mononuclear cell proliferation	43	188	.0000	.0000	LST1, LYN, HLA-A, RASAL3, PTPN6, CCL19, ZAP70, IFNG, CD86, CD3E, CSF1, HLA-DPA1, IL12RB1, TNFSF13B, HLA-DRB1, CCR2, CD4, CD38, GPR183, IRF1, SPN, IGF2, LILRB1, IL18, CD40, LGALS9, VCAM1, IDO1, CCL5, RAC2, MEF2C, HLA-DPB1, JAK3, HLA-E, PLA2G2D, PTPRC, ATM, TNFRSF14, LILRB2, HLA-DMB, IKZF3, HAVCR2, CD74

Abbreviations: DDIR, DNA damage immune response; DEGS, differentially expressed genes; FDR, false discovery rate.