

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

Priyanka Sharma, MD¹; William E. Barlow, PhD²; Andrew K. Godwin, PhD³; Eileen E. Parkes, PhD⁴; Laura A. Knight, PhD^{4,5}; Steven M. Walker, PhD^{4,5}; Richard D. Kennedy, MD, PhD^{4,5}; Denis P. Harkin, PhD^{4,5}; Gemma E. Logan, PhD⁵; Christopher J. Steele, PhD⁵; Shauna M. Lambe, MSc⁵; Sunil Badve, MD⁶; Yesim Gökmen-Polar, PhD⁶; Harsh B. Pathak, PhD³; Kamilla Isakova³; Hannah M. Linden, MD^{7,8}; Peggy Porter, MD⁸; Lajos Pusztai, MD, PhD⁹; Alastair M. Thompson, MD¹⁰; Debu Tripathy, MD¹¹; Gabriel N. Hortobagyi, MD¹¹; and Daniel F. Hayes, MD¹²

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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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

ASSOCIATED CONTENT

Appendix

Data Supplement

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

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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 $\geq 20\%$. 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 ($\geq 20\%$ v $< 20\%$), patients with sTILs density $\geq 20\%$ 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

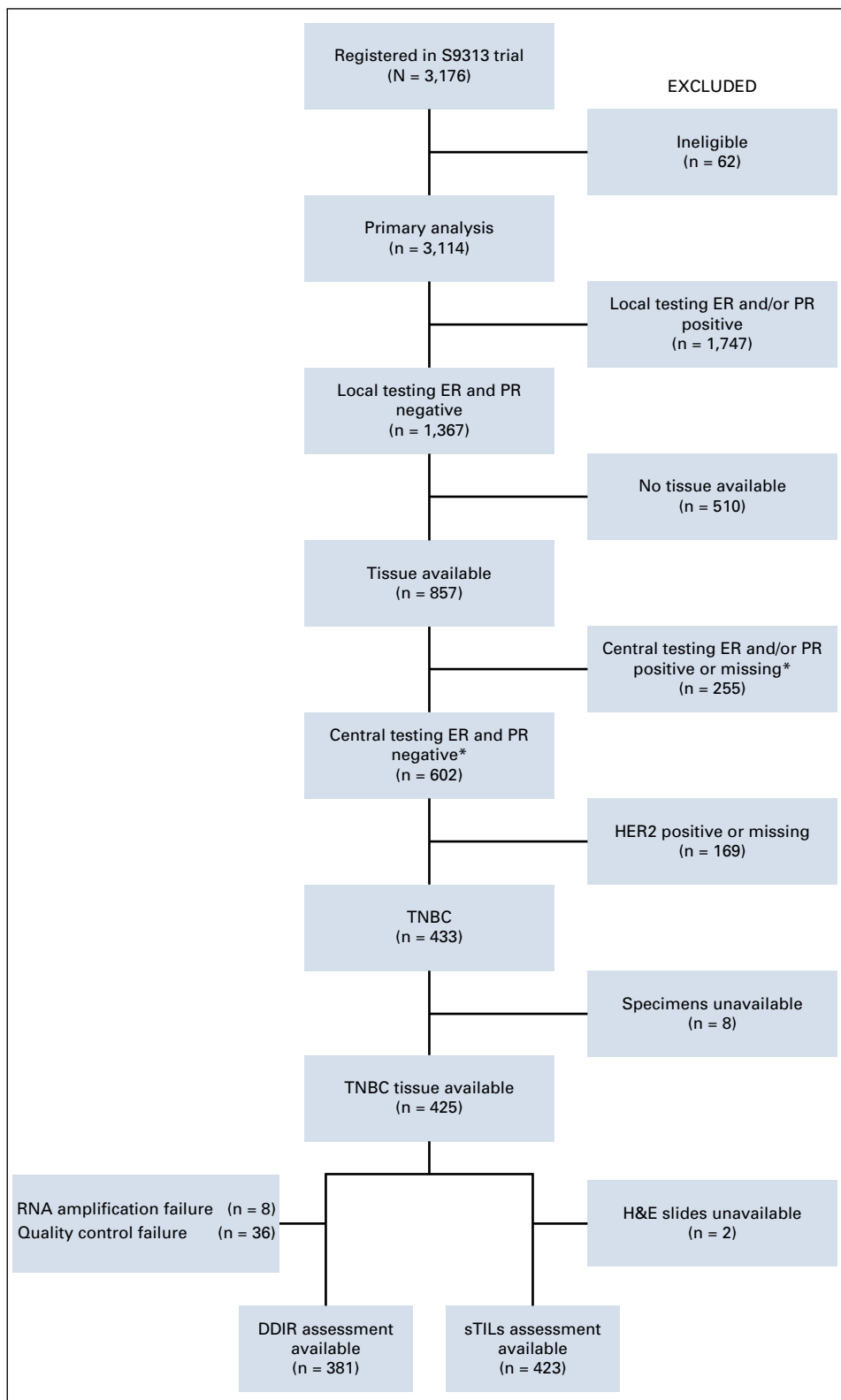


FIG 1. Reporting Recommendations for Tumor Marker Prognostic Studies (REMARK) diagram showing biomarker study subset of SWOG S9313 trial. (*) Central ER and PR testing were performed using the Allred scoring method. For the purpose of this biomarker study, ER and/or PR score > 0 was considered positive. 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

Model	Prognostic Factor	Disease-Free Survival				Overall Survival			
		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 $\geq 20\%$ 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 $\geq 30\%$). Five-year DFS for patients with DDIR positivity and sTILs $\geq 20\%$ 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

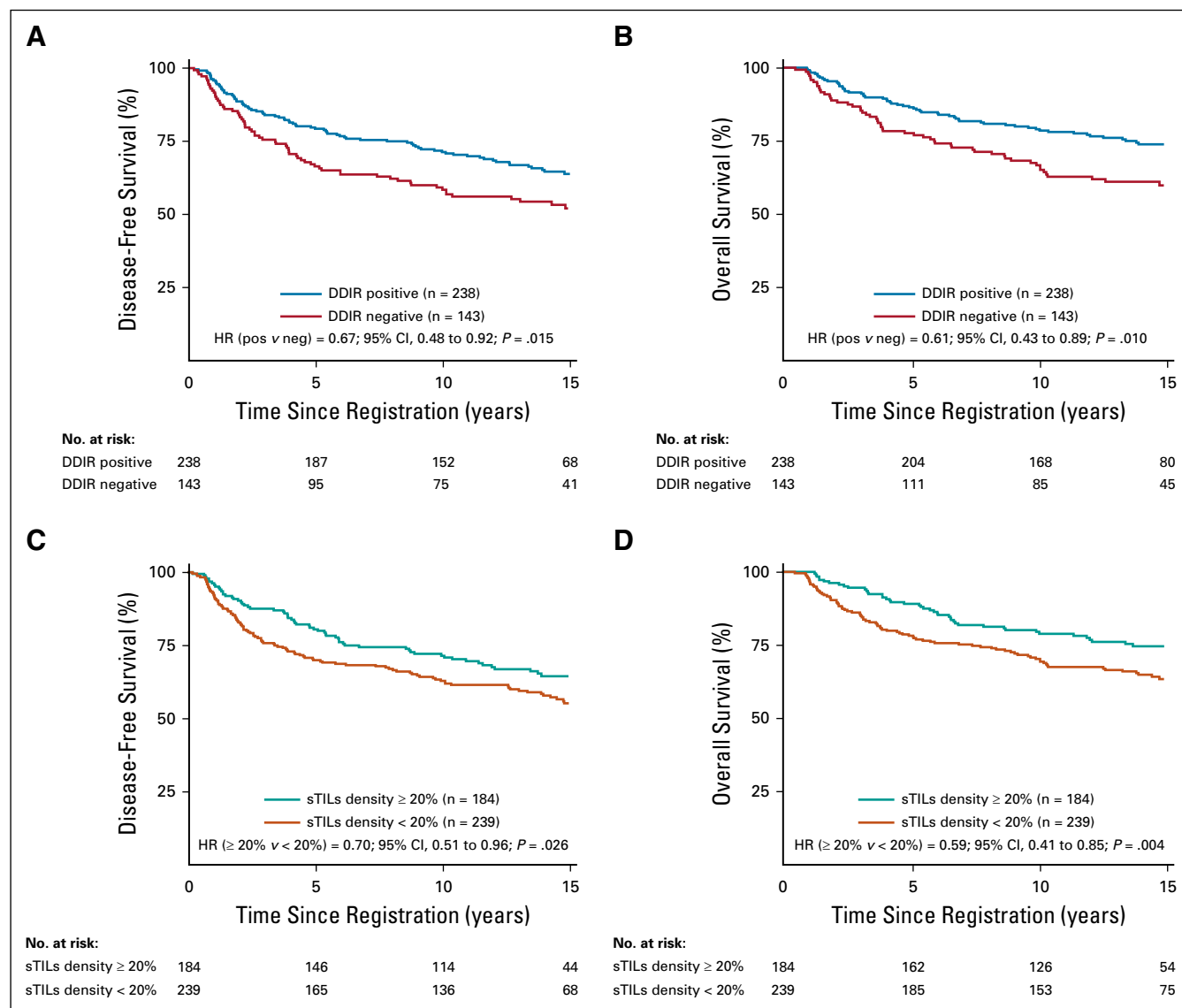


FIG 2. Kaplan-Meier survival analyses predicting (A) disease-free survival and (B) overall survival by DNA damage immune response (DDIR) signature status, and (C) disease-free survival and (D) overall survival by stromal tumor-infiltrating lymphocytes (sTILs) density. DDIR status is depicted as positive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

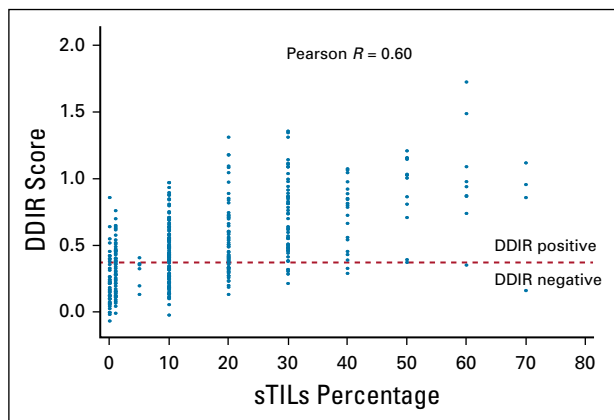


FIG 3. Scatterplot depicting the correlation of DNA damage immune response (DDIR) scores with stromal tumor-infiltrating lymphocytes (sTILs) density percentage in increments of 10 percentage points.

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.

AFFILIATIONS

¹University of Kansas Medical Center, Westwood, KS

²SWOG Statistical Center, Seattle, WA

³University of Kansas Medical Center, Kansas City, KS

⁴Queen's University Belfast, Belfast, UK

⁵Almac Group, Craigavon, UK

⁶Indiana University School of Medicine, Indianapolis, IN

⁷University of Washington, Seattle, WA

⁸Fred Hutchinson Cancer Research Center, Seattle, WA

⁹Yale Cancer Center, New Haven, CT

¹⁰Baylor College of Medicine, Houston, TX

¹¹The University of Texas MD Anderson Cancer Center, Houston, TX

¹²University of Michigan, Ann Arbor, MI

CORRESPONDING AUTHOR

Priyanka Sharma, MD, Department of Internal Medicine, Division of Medical Oncology, University of Kansas Medical Center, 2330 Shawnee Mission Parkway, Suite 210, MS 5003, Westwood, KS 66205; e-mail: psharma2@kumc.edu.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

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AUTHOR CONTRIBUTIONS

Conception and design: Priyanka Sharma, William E. Barlow, Steven M. Walker, Denis P. Harkin, Peggy Porter, Debu Tripathy, Gabriel N. Hortobagyi, Daniel F. Hayes

Financial support: Denis P. Harkin, Daniel F. Hayes

Administrative support: Denis P. Harkin, Gemma E. Logan, Lajos Pusztai, Gabriel N. Hortobagyi

Provision of study material or patients: Hannah M. Linden, Gabriel N. Hortobagyi

Collection and assembly of data: Priyanka Sharma, William E. Barlow, Andrew K. Godwin, Laura A. Knight, Steven M. Walker, Sunil Badve, Yesim Gökmen-Polar, Kamilla Isakova, Peggy Porter, Daniel F. Hayes

Data analysis and interpretation: Priyanka Sharma, William E. Barlow, Andrew K. Godwin, Eileen E. Parkes, Laura A. Knight, Steven M. Walker, Richard D. Kennedy, Denis P. Harkin, Gemma E. Logan, Christopher J. Steele, Shauna M. Lambe, Sunil Badve, Harsh B. Pathak, Hannah M. Linden, Lajos Pusztai, Alastair M. Thompson, Debu Tripathy, Gabriel N. Hortobagyi, Daniel F. Hayes

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT**Validation of the DNA Damage Immune Response Signature in Patients With Triple-Negative Breast Cancer From the SWOG 9313c Trial**

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Priyanka Sharma

Consulting or Advisory Role: TapImmune, Almac Diagnostics, AstraZeneca, Novartis, Pfizer, Myriad Genetics, Puma Biotechnology
Research Funding: Novartis (Inst), Celgene (Inst), Bristol-Myers Squibb (Inst), Cosmo Biosciences (Inst)
Travel, Accommodations, Expenses: AstraZeneca, Almac Diagnostics

William E. Barlow

Research Funding: AbbVie (Inst), Merck (Inst), AstraZeneca (Inst)

Andrew K. Godwin

Honoraria: Sinochips Kansas
Consulting or Advisory Role: NanoString Technologies, Personal Genome Diagnostics
Research Funding: BioFluidica (Inst)
Travel, Accommodations, Expenses: West China Cooperative Network of Pharmacy, Personal Genome Diagnostics

Eileen E. Parkes

Consulting or Advisory Role: Almac Diagnostics
Travel, Accommodations, Expenses: Almac Diagnostics

Laura A. Knight

Employment: Almac Diagnostics

Steven M. Walker

Employment: Almac Diagnostics
Patents, Royalties, Other Intellectual Property: Named inventor on Almac Diagnostics patents

Richard D. Kennedy

Employment: Almac Diagnostics
Honoraria: AstraZeneca, Tesaro

Denis P. Harkin

Employment: Almac Diagnostics
Patents, Royalties, Other Intellectual Property: Patents

Gemma E. Logan

Employment: Almac Diagnostic Services

Christopher J. Steele

Employment: Almac Diagnostics

Shauna M. Lambe

Employment: Almac Diagnostics

Sunil Badve

Leadership: YeSSGenomics
Stock and Other Ownership Interests: YeSSGenomics
Honoraria: Athenex
Consulting or Advisory Role: ClearLight
Speakers' Bureau: Genomic Health, Targos Molecular Pathology
Research Funding: Dako/Agilent Technologies
Patents, Royalties, Other Intellectual Property: EarlyR: signature for ER+ breast cancer (Inst), E-Score for predicting recurrence of DCIS (Inst)

Yesim Gökmen-Polar

Travel, Accommodations, Expenses: Thermo Fisher Scientific

Hannah M. Linden

Leadership: Evolent (I)
Stock and Other Ownership Interests: Evolent (I)
Consulting or Advisory Role: Genomic Health, Context Therapeutics, Syndax, AstraZeneca, Eisai
Research Funding: Eisai, Sanofi/Aventis (Inst), GTx (Inst)

Lajos Pusztai

Honoraria: Merck, AstraZeneca/MedImmune, Pfizer, Syndax, Almac Diagnostics, Pieris Pharmaceuticals, Genentech, Immunomedics, Eisai, Seattle Genetics/Astellas
Consulting or Advisory Role: H3 Biomedicine, Merck, Novartis, PierianDx, Seattle Genetics, Syndax, Athenex
Speakers' Bureau: bioTheranostics
Research Funding: Merck, Genentech, Seattle Genetics, AstraZeneca

Alastair M. Thompson

Honoraria: Novartis (I), Pfizer
Research Funding: Genentech/Roche
Travel, Accommodations, Expenses: Novartis (I), Pfizer

Debu Tripathy

Consulting or Advisory Role: Novartis, Nektar, Pfizer, Sellas Life Sciences, GlaxoSmithKline, Genomic Health, Polyphor
Research Funding: Novartis (Inst), Polyphor (Inst)
Travel, Accommodations, Expenses: Novartis

Gabriel N. Hortobagyi

Consulting or Advisory Role: Novartis, Peregrine Pharmaceuticals, Agendia
Research Funding: Novartis (Inst)
Travel, Accommodations, Expenses: Novartis

Daniel F. Hayes

Stock and Other Ownership Interests: OncImmune, InBiomotion, Cepheid, Freenome, Cellworks, CVS Caremark Breast Cancer Expert Panel, Agendia
Research Funding: AstraZeneca (Inst), Pfizer (Inst), Merrimack (Inst), Menarini Silicon Biosystems (Inst)
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Travel, Accommodations, Expenses: Menarini Silicon Biosystems
Other Relationship: Menarini

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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/m² and cyclophosphamide 1.2 g/m² intravenously [IV] every 3 weeks for six cycles) or (arm II) AC in sequence (A3C; doxorubicin 40.5 mg/m² IV days 1 and 2 of a 21-day cycle for four cycles, followed by cyclophosphamide 2.4 g/m² 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 (EnVision¹⁵; 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 ≥ 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 σ_{Bg} 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	Potential 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)
ADCEC.20415.C1_s_at	ENS00000131203 OTTHUMG00000164057	3620	IDO1	Indoleamine 2,3-dioxygenase 1	3.49155	6.43991	-7.71872	0	0
ADCEC.2464.C1_at	ENS00000138755 OTTHUMG00000160889	4283	CXCL9	Chemokine (C-X-C motif) ligand 9	5.33225	7.68033	-5.09146	9.99 ^{E-32}	3.53 ^{E-28}
ADCEC.6891.C2_at	ENS000002700154451 OTTHUMG0000010006	115362	GBP5	Guanylate-binding protein 5	2.20512	4.49763	-4.89908	2.61 ^{E-38}	4.85 ^{E-34}
ADCEC.17552_s_at	ENS000000211660	—	IGLV2-23	Immunoglobulin lambda variable 2-23	4.82631	6.86998	-4.12233	8.41 ^{E-14}	1.58 ^{E-11}
ADCEC.21261.C1_s_at	ENS000000204681 ENS000000206466 ENS000000206468 ENS000000206511 ENS000000206513 ENS000000213886 ENS000000224654 ENS000000226898 ENS000000228913 ENS000000231968 ENS000000232569 ENS000000232632 ENS000000237051 ENS000000237112 OTTHUMG00000004871 OTTHUMG000000004874 OTTHUMG000000031095 OTTHUMG000000031289 OTTHUMG000000031365 OTTHUMG000000031587 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}
ADCEC.6891.C2_s_at	ENS00000154451 OTTHUMG0000010006	3514 115362	IGKC GBP5	Immunoglobulin kappa constant Guanylate binding protein 5	5.60275 5.87049	7.59854 7.86447	-3.98836 -3.98335	3.58 ^{E-16} 3.36 ^{E-44}	9.91 ^{E-14} 8.31 ^{E-40}
ADCEC.1431_s_at	ENS000000211666 ENS000000211671 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}
ADCEC.10522_s_at	ENS000000211899 OTTHUMG00000152452	3507	IGHM	Immunoglobulin heavy constant mu	7.09846	8.98833	-3.6996	1.09 ^{E-19}	6.01 ^{E-17}
ADCEC.20299.C1_at	ENS00000156234 OTTHUMG00000130201	10563	CXCL13	Chemokine (C-X-C motif) ligand 13	3.44487	5.32918	-3.69177	7.85 ^{E-36}	1.12 ^{E-22}
ADCEC.11676.C1_at	ENS00000169245 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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.21261.C2_s_at	ENS00000204681	2550	<i>GABBR1</i>	GABA B receptor, 1	4.07237	5.89372	-3.53411	1.14 ^{E-33}	6.03 ^{E-30}
	ENS00000206466	10537	<i>UBD</i>	Ubiquitin D					
	ENS00000206468								
	ENS00000206511								
	ENS00000206513								
	ENS00000213886								
	ENS00000224654								
	ENS00000226898								
	ENS00000228913								
	ENS00000231968								
	ENS00000232569								
	ENS00000232632								
	ENS00000237051								
	ENS00000237112								
	OTTTHUMG0000004871								
	OTTTHUMG00000004874								
	OTTTHUMG00000031095								
	OTTTHUMG00000031289								
	OTTTHUMG00000031365								
	OTTTHUMG00000031587								
	OTTTHUMG00000148761								
	OTTTHUMG00000148765								
	OTTTHUMG00000148971								
	OTTTHUMG00000148975								
	OTTTHUMG00000149256								
	OTTTHUMG00000149260								
	OTTTHUMG00000149486								
	OTTTHUMG00000149490								
ADXC.11938.C5_at	—	—	—	—	3.98744	5.77275	-3.44693	5.24 ^{E-14}	1.01 ^{E-11}
ADXC.18512.C1_at	ENS00000127951	10875	<i>FGI2</i>	Fibrinogen-like 2	7.34208	8.9947	-3.14404	1.87 ^{E-27}	3.14 ^{E-24}
	OTTTHUMG00000130681								
ADXC.NTDJ.2312_s_at	ENS00000211892	3500	<i>IGHG1</i>	Immunoglobulin heavy constant gamma 1 (G1m marker)	8.06328	9.66083	-3.02629	1.94 ^{E-13}	3.51 ^{E-11}
	ENS00000211896	3502	<i>IGHG3</i>	Immunoglobulin heavy constant gamma 3 (G3m marker)					
	ENS00000211897	3503	<i>IGHG4</i>	Immunoglobulin heavy constant gamma 4 (G4m marker)					
	OTTTHUMG00000152481	3507	<i>IGHM</i>	Immunoglobulin heavy constant mu					
	OTTTHUMG00000152495	28396	<i>IGHV4-31</i>	Immunoglobulin heavy variable 4-31					
	OTTTHUMG00000152539								
ADXC.EMUTR.6415_at	—	3514	<i>IGKC</i>	Immunoglobulin kappa constant	3.22777	4.8108	-2.99598	1.62 ^{E-11}	2.16 ^{E-09}
ADXC.EDA.21030_at	—	6373	<i>CXCL11</i>	Chemokine (C-X-C motif) ligand 11	4.0256	5.60187	-2.98196	2.05 ^{E-31}	6.34 ^{E-28}
ADXC.EMUTR.1413_s_at	ENS00000211660	—	<i>IGLV2-23</i>	Immunoglobulin lambda variable 2-23	3.07738	4.62791	-2.92924	2.81 ^{E-11}	3.61 ^{E-09}
	OTTTHUMG00000151234		<i>IGLV2-23</i>	NULL					
ADXC.522.CB2_s_at	ENS00000230463	3125	<i>HLA-DRB3</i>	Major histocompatibility complex, class II, DR beta 3	6.58255	8.11696	-2.89669	3.00 ^{E-09}	2.83 ^{E-07}
	OTTTHUMG00000148818	3126	<i>HLA-DRB4</i>	Major histocompatibility complex, class II, DR beta 4					
ADXC.11938.C5_x_at	—	—	—	—	4.83419	6.36296	-2.88541	1.83 ^{E-14}	3.89 ^{E-12}
ADXC.17088.S_at	ENS00000239951	—	<i>IGKV3-20</i>	Immunoglobulin kappa variable 3-20	6.9432	8.47191	-2.88526	5.06 ^{E-14}	9.83 ^{E-12}
ADXC.52.at	ENS000000081237	5788	<i>PTPRC</i>	Protein tyrosine phosphatase, receptor type, C	4.25872	5.7863	-2.88302	2.61 ^{E-22}	1.98 ^{E-19}
	ENS00000262418								
	OTTTHUMG0000035702								
	OTTTHUMG00000175273								
ADXC.EMUTR.6415_s_at	—	3514	<i>IGKC</i>	Immunoglobulin kappa constant	4.02779	5.54022	-2.85289	6.74 ^{E-14}	1.28 ^{E-11}
ADXC.29879.C1_s_at	ENS00000004468	952	<i>CD38</i>	CD38 molecule	2.89588	4.3846	-2.80641	3.50 ^{E-30}	9.27 ^{E-27}
	OTTTHUMG00000048206								
ADXC.3225.C1-a_s_at	ENS00000125347	3659	<i>IRF1</i>	Interferon regulatory factor 1	4.44889	5.93458	-2.80051	1.18 ^{E-24}	1.39 ^{E-21}
	OTTTHUMG00000059497								

(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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.20355.C1_s_at	ENS00000211772 ENS00000260881 OTTTHUMG00000158912 OTTTHUMG00000174781	—	TRBC2 TRBC2	T-cell receptor beta constant 2 NULL	7.82604	9.26998	-2.72061	1.19 ^{E-22}	9.95 ^{E-20}
ADXC.6072.C2_a_s_at	ENS00000115415 OTTTHUMG00000132699	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}
ADXC.14394.C1_s_at	ENS00000239713 OTTTHUMG00000151081	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}
ADXC(NTDJ.4752)_at	ENS000000026751 OTTTHUMG00000124008	57823	SLAMF7	SLAM family member 7	3.16012	4.59049	-2.69515	4.78 ^{E-24}	5.21 ^{E-21}
ADXC.21236.C1_s_at	ENS00000181617 OTTTHUMG00000129393	260436	FDCSP	Follicular dendritic cell secreted protein	6.10901	7.53662	-2.69001	0.00344968	0.00768838
ADXC.14394.C2_x_at	ENS00000128383 OTTTHUMG00000151004	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}
ADXC.11453.C1_at	ENS00000188404 OTTTHUMG00000134809	6402	SELL	Selectin L	3.64657	5.06894	-2.68027	1.83 ^{E-25}	2.38 ^{E-22}
ADXC.9036.C1_s_at	ENS00000147168 OTTTHUMG00000121787	3561	IL2RG	Interleukin 2 receptor, gamma	7.14268	8.55525	-2.66212	1.42 ^{E-24}	1.65 ^{E-21}
ADXC.2957.C2_s_at	ENS00000168394 ENS00000206297 ENS00000224212 ENS00000224748 ENS00000226173 ENS00000227816 ENS00000230705 ENS00000232367 OTTTHUMG0000012640 OTTTHUMG00000131067 OTTTHUMG00000131337 OTTTHUMG00000140128 OTTTHUMG00000148832 OTTTHUMG00000149101 OTTTHUMG00000149358 OTTTHUMG00000149619	6890	TAP1	Transporter 1, ATP-binding cassette, subfamily B (MDR/TP)	6.47722	7.88574	-2.65465	2.07 ^{E-30}	5.91 ^{E-27}
ADXC.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}
ADXC.15996.C1_at	ENS00000108700 OTTTHUMG00000132883	6355	CCL8	Chemokine (C-C motif) ligand 8	4.18692	5.59299	-2.65014	2.57 ^{E-17}	9.11 ^{E-15}
ADXC.1903.C1_s_at	ENS00000132465 OTTTHUMG00000129909	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}
ADXC.830.C8_s_at	ENS00000115917 OTTTHUMG00000118708	3437	IFI73	Interferon-induced protein with tetratricopeptide repeats 3	3.67353	5.07483	-2.64139	8.59E-22	6.07 ^{E-19}
ADXC.119.C3_s_at	ENS00000137403 ENS00000202462 ENS00000206509 ENS00000229698 ENS00000235220 ENS00000237508 OTTTHUMG00000004783 OTTTHUMG00000111556 OTTTHUMG00000131438 OTTTHUMG00000141181 OTTTHUMG00000148884 OTTTHUMG00000149164	3134	HLA-F	Major histocompatibility complex, class I, F	9.10266	10.5026	-2.63897	4.15 ^{E-32}	1.62 ^{E-28}
ADXC.6681.C1_at	ENS00000115267 OTTTHUMG00000132055	64135	IFIH1	Interferon induced with helicase C domain 1	3.74073	5.1233	-2.60731	3.30 ^{E-15}	7.89 ^{E-13}

(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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXCERS.21496_s_at	ENS00000111335 OTTTHUMG00000169802	4939	OAS2	2'-5'-Oligoadenylate synthetase 2, 6971 kDa	5.76494	7.1395	-2.59289	4.88 ^{E-16}	1.32 ^{E-13}
ADXCACD.25710_s_at	ENS00000121858 OTTTHUMG00000156917	8743	TNFSF10	Tumor necrosis factor (ligand) superfamily, member 10	6.29476	7.66481	-2.5848	3.45 ^{E-14}	6.99 ^{E-12}
ADXCACD.9742_at	ENS00000117409 OTTTHUMG00000155807	219285	SAMD9L	Sterile alpha motif domain containing 9-like	5.5574	6.91652	-2.56529	3.32 ^{E-31}	9.84 ^{E-28}
ADXC.23233.C1_at	ENS00000162654 OTTTHUMG00000106663	115361	GBP4	Guanylate binding protein 4	7.22905	8.58763	-2.56433	1.42 ^{E-26}	2.20 ^{E-23}
ADXC.30159.C1_at	—	10964	IFI44L	Interferon-induced protein 44-like	5.39292	6.7467	-2.55403	2.19 ^{E-18}	9.86 ^{E-16}
ADXC.8915.C1_at	ENS000001081237	5788	PTPRC	Protein tyrosine phosphatase, receptor type, C	6.02686	7.37536	-2.54647	9.18 ^{E-42}	3.41 ^{E-28}
ADXCOC.12110.C2_s_at	ENS00000137959 OTTTHUMG00000009724	10964	IFI44L	Interferon-induced protein 44-like	6.21706	7.56043	-2.53743	6.76 ^{E-21}	4.25 ^{E-18}
ADXC.6079.C1_x_at	ENS00000137959 OTTTHUMG00000009724	10964	IFI44L	Interferon-induced protein 44-like	3.23779	4.5572	-2.49564	1.57 ^{E-25}	2.12 ^{E-22}
ADXC.25108.C1_at	—	—	—	—	2.43289	3.74809	-2.48837	1.39 ^{E-14}	2.99 ^{E-12}
ADXC.6681.C1_x_at	ENS00000115267 OTTTHUMG00000132055	64135	IFIH1	Interferon induced with helicase C domain 1	3.18326	4.49549	-2.48325	5.61 ^{E-18}	2.21 ^{E-15}
ADXCADA.11564_at	—	64135	IFIH1	Interferon induced with helicase C domain 1	3.81146	5.11924	-2.47561	3.16 ^{E-23}	2.96 ^{E-20}
ADXC.20258.C1_s_at	ENS00000117409 OTTTHUMG00000155807	219285	SAMD9L	Sterile alpha motif domain containing 9-like	5.78852	7.09197	-2.46819	1.89 ^{E-31}	6.10 ^{E-28}
ADXC.14394.C2_at	ENS00000128383 OTTTHUMG00000151004	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}
ADXC.31983.C1_at	—	—	—	—	7.13675	8.42223	-2.43764	9.38 ^{E-30}	2.32 ^{E-26}
ADXCCEMUTR.3815_at	ENS00000173193 OTTTHUMG00000159552	54625	PARP14	Poly (ADP-ribose) polymerase family, member 14	4.76144	6.04678	-2.4374	6.13 ^{E-34}	6.59 ^{E-21}
ADXC.6996.C1_s_at	ENS00000115415 OTTTHUMG00000132699	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}
ADXC.15369.C1_s_at	ENS00000126340 ENS00000025594 OTTTHUMG00000165670	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}
ADXC.1189.C27_x_at	ENS00000111675 ENS000000254709 OTTTHUMG00000151218 OTTTHUMG00000165670	100423062	IGLL5	Immunoglobulin lambda-like polypeptide 5	9.82726	11.0963	-2.40998	2.96 ^{E-13}	5.18 ^{E-11}
ADXC.6079.C1_at	ENS00000137959 OTTTHUMG00000009724	10964	IFI44L	Interferon-induced protein 44-like	2.20162	3.46871	-2.40676	1.08 ^{E-30}	6.48 ^{E-18}
ADXC.6683.C1_s_at	ENS00000157601 OTTTHUMG00000086755	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}
ADXC.3561.C1_s_at	ENS00000111331 OTTTHUMG00000169795	4940	OAS3	2'-5'-Oligoadenylate synthetase 3, 100 kDa	7.04131	8.29673	-2.38737	2.20 ^{E-22}	1.70 ^{E-19}
ADXC.541.C2_x_at	ENS00000121896 OTTTHUMG00000152495	3500 3507	IGHG1 IGHM	Immunoglobulin heavy constant gamma 1 (G1m marker) Immunoglobulin heavy constant mu	7.8503	9.10497	-2.38613	2.53 ^{E-09}	2.43 ^{E-07}
ADXC.22975.C1_s_at	ENS00000115956 OTTTHUMG00000129562	5341	PLEK	Immunoglobulin heavy variable 4-31 Pleckstrin	4.87621	6.1304	-2.38534	1.33 ^{E-35}	8.97 ^{E-32}
ADXCCEMUTR.3438_at	ENS00000173193 OTTTHUMG00000159552	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)
ADXC.23233.C1_x_at	ENS00000162654 OTTTHUMG0000010663	115361	GBP4	Guanylate binding protein 4	6.23062	7.42447	-2.28764	2.66 ^{E-26}	4.02 ^{E-23}
ADXCADA.13828_at	—	—	—	—	2.90485	4.09801	-2.28653	3.99 ^{E-16}	1.10 ^{E-13}
ADXC.20343.C1_at	ENS00000239457 ENS00000241106 ENS00000241386 ENS00000241910 ENS00000243496 ENS00000243612 OTTTHUMG0000031213 OTTTHUMG0000031513 OTTTHUMG0000040121 OTTTHUMG0000048824 OTTTHUMG0000049075 OTTTHUMG0000049590	3112	HLA-DQB	Major histocompatibility complex, class II, DQ beta	4.47646	5.66962	-2.28653	6.87 ^{E-16}	1.80 ^{E-13}
ADXC.6902.C1_s_at	ENS000000026751 OTTTHUMG0000024008	57823	SLAMF7	SLAM family member 7	5.26608	6.45804	-2.28463	2.39 ^{E-18}	1.07 ^{E-15}
ADXC.RS.21496_at	ENS00000111335 OTTTHUMG00000169802	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/M97936_s_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}
ADXCAD.12596_at	ENS00000156738 OTTTHUMG00000167614	931	MSH41	Membrane-spanning 4-domains, subfamily A, member 1	2.64181	3.83088	-2.28006	1.28 ^{E-12}	2.02 ^{E-10}
ADXCCEMUTR.669_at	ENS00000143297 OTTTHUMG0000017481	83416	FCRL5	Fc receptor-like 5	2.79311	3.98051	-2.27742	5.75 ^{E-15}	1.32 ^{E-12}
ADXC.8308.C1-a_s_at	ENS00000134321 OTTTHUMG00000090352	91543	RSAD2	Radical S-adenosyl methionine domain containing 2	3.64213	4.82885	-2.27319	8.80 ^{E-16}	2.27 ^{E-13}
ADXC.NTID1.1088_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-s_s_at	ENS00000115415 OTTTHUMG00000132699	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}
ADXC.224.C4_s_at	ENS00000206305 ENS00000257473 OTTTHUMG0000012723	3117 28823 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
ADXC.6072.C2_at	ENS00000115415 OTTTHUMG00000132699	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}
ADXC.1022.CB2_s_at	ENS00000211592 ENS00000231486 OTTTHUMG00000151684 OTTTHUMG00000151686	3514 50802	IGK IGKC	Immunoglobulin kappa locus Immunoglobulin kappa constant	10.4595	11.6305	-2.25172	9.85 ^{E-11}	1.18 ^{E-08}
ADXC.224.C28-a_s_at	ENS00000206305 ENS00000257473 OTTTHUMG0000012723	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
ADXC.1189.CB1_x_at	ENS00000211677 ENS00000211679 OTTTHUMG00000151214 OTTTHUMG00000151217	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}
ADXC.1189.CB4_x_at	ENS00000211677 ENS00000211679 OTTTHUMG00000151214 OTTTHUMG00000151217	—	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}
ADXCADA.9938_at	ENS00000103351 OTTTHUMG00000177581	23059	CLUAP1	Clusterin associated protein 1	3.3281	4.49558	-2.23887	6.48 ^{E-16}	1.72 ^{E-13}
ADXC.23345.C1_at	ENS00000132274 OTTTHUMG00000166904	10346	TRIM22	Tripartite motif containing 22	6.29911	7.46145	-2.2382	4.36 ^{E-21}	2.86 ^{E-18}
ADXC.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)
ADXCAD.1735_x_at	ENS00000161570 OTTHUMG00000132949	6352	CCL5	Chemokine (C-C motif) ligand 5	5.84976	7.00732	-2.23079	4.54 ^{E-18}	1.86 ^{E-15}
ADXC.7218.C1_s_at	ENS00000012223 OTTHUMG00000156325	4057	LTF	Lactotransferrin	7.88753	9.04341	-2.22821	4.74 ^{E-06}	0.000211081
ADXC.5349.C4-a_s_at	ENS0000017193 OTTHUMG00000159552	54625	PARP14	Poly (ADP-ribose) polymerase family, member 14	7.39454	8.54074	-2.22807	2.43 ^{E-04}	2.69 ^{E-21}
ADXC.72569.C1_s_at	ENS00000132274 OTTHUMG00000066904	10346	TRIM22	Tripartite motif containing 22	4.25785	5.41293	-2.22697	2.79 ^{E-25}	3.51 ^{E-22}
ADXC.31505.C1_at	—	4261	CMTA	Class II, major histocompatibility complex, transactivator	5.44674	6.59947	-2.22333	3.90 ^{E-19}	1.92 ^{E-16}
ADXC.1477.C1_s_at	ENS00000111801 ENS00000186470 OTTHUMG00000144450 OTTHUMG00000144451	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}
ADXC.3496.C1_s_at	ENS00000006074 OTTHUMG00000133001	6362 101060271	CCL18 LOC101060271	Chemokine (C-C motif) ligand 18 (pulmonary and activation-regulated) c-c motif chemokine 18-like	3.45776	4.50797	-2.21946	5.23 ^{E-09}	4.69 ^{E-07}
ADXC.2579.C1_at	ENS00000185745 OTTHUMG00000187112	3434	IFIT1	Interferon-induced protein with tetratricopeptide repeats 1	6.0444	7.19206	-2.21553	2.41 ^{E-13}	4.28 ^{E-11}
ADXCINTD.7500_s_at	ENS00000183508 OTTHUMG0000013703	54855	FAM46C	Family with sequence similarity 46, member C	4.45451	5.6004	-2.21281	3.23 ^{E-09}	3.04 ^{E-07}
ADXCADA.8176_s_at	ENS00000143297 OTTHUMG0000017481	83416	FORL5	Fc receptor-like 5	2.68437	3.82785	-2.20913	5.30 ^{E-12}	7.53 ^{E-10}
ADXCAD.3333_s_at	ENS00000172578 OTTHUMG00000148673	89857	KLHL6	Kelch-like family member 6	5.65926	6.80124	-2.20684	5.45 ^{E-10}	5.85 ^{E-08}
ADXC.5316.C1_at	ENS000000091490 OTTHUMG00000160331	23231	SELL13	Sell-1 suppressor of lin-12-like 3 (<i>Caenorhabditis elegans</i>)	4.82771	5.96955	-2.20663	2.66 ^{E-11}	3.43 ^{E-09}
ADXC.10461.C2_s_at	ENS000000093072 OTTHUMG00000030726	51816	CECR1	Cat eye syndrome chromosome region, candidate 1	7.51241	8.65084	-2.20141	2.27 ^{E-24}	2.55 ^{E-21}
ADXCCEMUTR.1465_x_at	ENS00000211644 OTTHUMG00000151035	96610	LOC96610	BMS1 homolog, ribosome assembly protein (yeast) pseudogene	3.62654	4.76068	-2.19487	6.50 ^{E-12}	9.11 ^{E-10}
ADXCADA.11548_at	ENS00000117091 OTTHUMG00000024009	962	CD48	CD48 molecule	3.50369	4.6368	-2.19332	9.80 ^{E-15}	2.16 ^{E-12}
ADXC.2957.C3_s_at	ENS000000204261 ENS000000206232 ENS000000206296 ENS000000231591 ENS000000233089 ENS000000233140 ENS000000234365 ENS000000235540 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}
ADXC.20447.C1-a_s_at	ENS000000023445 OTTHUMG00000167324	330	BIRC3	Baculoviral IAP repeat containing 3	3.40406	4.53881	-2.19125	2.54 ^{E-14}	5.30 ^{E-12}
ADXC.23036.C1_at	ENS00000100368 OTTHUMG00000150646	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.01822.X_at	ENS000000211677	3537	CYAT1	Immunoglobulin lambda light chain-like	11.2062	12.335	-2.18683	2.04 ^{E-12}	3.05 ^{E-10}
ADXLCEC.01823.X_at	ENS000000211679	28823	IGLC1	Immunoglobulin lambda constant 1 (Meg marker)					
ADXLCEC.01824.X_at	OTT-HUMG00000151214	100290481	IGLV1-44	Immunoglobulin lambda variable 1-44					
ADXLCEC.01825.X_at	OTT-HUMG00000151217								
ADXLCEC.01826.X_at	—	10964	IFI44L	Interferon-induced protein 44-like	5.06796	6.19457	-2.18345	5.23 ^{E-19}	2.52 ^{E-16}
ADXLCEC.01827.X_at	ENS000000137478	9873	FCHSD2	FCH and double SH3 domains 2	3.81617	4.94217	-2.18252	5.95 ^{E-08}	4.29 ^{E-05}
ADXLCEC.01828.X_at	ENS000000140379	597	BCL2A1	BCL2-related protein A1	2.5889	3.71381	-2.18088	2.11 ^{E-12}	3.15 ^{E-10}
ADXLCEC.01829.X_at	OTT-HUMG00000144173								
ADXLCEC.01830.X_at	ENS000000211677	—	IGLC2	Immunoglobulin lambda constant 2 (Kern-Oz- marker)	11.0423	12.167	-2.18061	1.80 ^{E-12}	2.74 ^{E-10}
ADXLCEC.01831.X_at	ENS000000211679		IGLC2	NULL					
ADXLCEC.01832.X_at	OTT-HUMG00000151214		IGLC3	Immunoglobulin lambda constant 3 (Kern-Oz+ marker)					
ADXLCEC.01833.X_at	OTT-HUMG00000151217		IGLC3	NULL					
ADXLCEC.01834.X_at	—	—	—	—	3.6222	4.74672	-2.18029	1.79 ^{E-19}	9.41 ^{E-17}
ADXLCEC.01835.X_at	ADXLCEC.19216.C2_s_at	3126	HUA-DRB4	Major histocompatibility complex, class II, DR beta 4	5.69655	6.82106	-2.18028	2.20 ^{E-06}	0.000107268
ADXLCEC.01836.X_at	ADXLCEC.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}
ADXLCEC.01837.X_at	ADXLCEC.30953.C1_at	10673	TNFSF13B	Tumor necrosis factor (ligand) superfamily, member 13b	5.62904	6.74879	-2.17309	4.43 ^{E-22}	3.29 ^{E-19}
ADXLCEC.01838.X_at	ADXLCEC.1300.S_at	80830	APOL6	Apolipoprotein L 6	5.35421	6.47237	-2.17107	2.08 ^{E-22}	1.62 ^{E-19}
ADXLCEC.01839.X_at	ADXLCEC.000000211899	3507	IGHM	Immunoglobulin heavy constant mu	4.73354	5.85014	-2.16835	3.14 ^{E-12}	4.55 ^{E-10}
ADXLCEC.01840.X_at	OTT-HUMG00000152452								
ADXLCEC.01841.X_at	ENS000000211896	3500	IGHG1	Immunoglobulin heavy constant gamma 1 (G1m marker)	8.87316	9.9897	-2.16827	9.52 ^{E-12}	1.29 ^{E-09}
ADXLCEC.01842.X_at	ENS000000211897	3502	IGHG3	Immunoglobulin heavy constant gamma 3 (G3m marker)					
ADXLCEC.01843.X_at	ENS000000253755	3507	IGHM	Immunoglobulin heavy constant mu					
ADXLCEC.01844.X_at	OTT-HUMG00000152493	28396	IGHV4-31	Immunoglobulin heavy variable 4-31					
ADXLCEC.01845.X_at	OTT-HUMG00000152495								
ADXLCEC.01846.X_at	OTT-HUMG00000152539								
ADXLCEC.01847.X_at	ENS000000115415	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}
ADXLCEC.01848.X_at	OTT-HUMG00000132699	—	—	—	4.29584	5.41019	-2.16498	3.53 ^{E-18}	1.49 ^{E-15}
ADXLCEC.01849.X_at	ADXLCEC.31757.C1_at	—	—	—	8.15647	9.27056	-2.16459	4.25 ^{E-34}	2.43 ^{E-30}
ADXLCEC.01850.X_at	ENS000000115415	6772	STAT1	Signal transducer and activator of transcription 1, 91 kDa					
ADXLCEC.01851.X_at	OTT-HUMG00000132699								
ADXLCEC.01852.X_at	ENS000000090382	4069	LIZ	Lysozyme	5.3106	6.42111	-2.15923	4.31 ^{E-14}	8.53 ^{E-12}
ADXLCEC.01853.X_at	OTT-HUMG00000169342								
ADXLCEC.01854.X_at	—	713	C1QB	Complement component 1, q subcomponent, B chain	6.5435	7.65048	-2.15394	9.94 ^{E-20}	5.54 ^{E-17}
ADXLCEC.01855.X_at	ENS000000140105	7453	WARS	Tryptophanyl-tRNA synthetase	5.25167	6.35776	-2.15261	1.89 ^{E-23}	1.84 ^{E-20}
ADXLCEC.01856.X_at	OTT-HUMG00000171572								
ADXLCEC.01857.X_at	ENS000000133106	94240	EPSTI1	Epithelial stromal interaction 1 (breast)	4.24474	5.34976	-2.15102	2.23 ^{E-22}	1.70 ^{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)
ADXC0C.7134.C2_at	ENS00000135899 OTTNUMG00000133204	3431	<i>SP110</i>	SP110 nuclear body protein	3.11184	4.2007	-2.12706	5.05 ^{E-11}	6.30 ^{E-09}
ADXC.2862.C1_s_at	ENS00000130208 OTTNUMG00000180844	341	<i>APOC1</i>	Apolipoprotein C-I	5.86174	6.94731	-2.12222	8.12 ^{E-13}	1.32 ^{E-10}
ADXCAD.7838_s_at	ENS00000117228 OTTNUMG00000106114	2633	<i>GBP1</i>	Guanylate binding protein 1, interferon-inducible	4.0349	5.11936	-2.12059	6.33 ^{E-23}	5.46 ^{E-20}
ADXC.23904.C1-a_s_at	ENS00000043462 OTTNUMG00000163121	3937	<i>LCP2</i>	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}
ADXC.1189.C19_x_at	ENS00000211677 ENS00000211679 ENS00000211685 OTTNUMG00000151017 OTTNUMG00000151214 OTTNUMG00000151217	28823	<i>IGLV1-44</i>	Immunoglobulin lambda variable 1-44	9.07779	10.1582	-2.1147	4.73 ^{E-12}	6.79 ^{E-10}
Adx-Hs-IGF3A-400-3_s_at	ENS00000115415 OTTNUMG00000132699	6772	<i>STAT1</i>	Signal transducer and activator of transcription 1, 91 kDa	8.20415	9.28303	-2.11238	4.84 ^{E-36}	3.99 ^{E-32}
ADXC.15732.C1_x_at	ENS00000156219 OTTNUMG00000130110	419	<i>ART3</i>	ADP-ribosyltransferase 3	2.56034	3.63707	-2.10926	7.42 ^{E-07}	4.12 ^{E-05}
ADXC.2450.C1-a_s_at	ENS00000002549 OTTNUMG00000048214	51056	<i>LAP3</i>	Leucine aminopeptidase 3	3.83898	4.91353	-2.10606	2.74 ^{E-18}	1.19 ^{E-15}
ADXC.30483.C1_s_at	ENS000000075884	55843	<i>ARHGAP15</i>	Rho GTPase activating protein 15	3.83529	4.90887	-2.10465	4.44 ^{E-15}	1.04 ^{E-12}
ADXC.119.C51_x_at	ENS00000204642 ENS00000206509 ENS00000229698 ENS00000235220 ENS00000237508 OTTNUMG00000004783 OTTNUMG00000031156 OTTNUMG00000031438 OTTNUMG00000041181 OTTNUMG00000148884 OTTNUMG00000149164	3134	<i>HLA-F</i>	Major histocompatibility complex, class I, F	4.1243	5.19787	-2.10464	2.72 ^{E-09}	2.60 ^{E-07}
ADXC.25108.C1_x_at	—	—	—	—	2.92115	3.99222	-2.10099	1.74 ^{E-14}	3.71 ^{E-12}
ADXCAD.8178_at	—	—	—	—	8.2885	9.35821	-2.09902	1.18 ^{E-27}	2.09 ^{E-24}
ADXCNTDJ.1535_s_at	ENS00000110777 OTTNUMG00000166659	5450	<i>POU2F1</i>	POU class 2 associating factor 1	5.20316	6.26877	-2.09306	9.88 ^{E-07}	5.30 ^{E-05}
ADXC.21778.C1_s_at	ENS00000102524 OTTNUMG0000017329	10673	<i>TNFSF13B</i>	Tumor necrosis factor (ligand) superfamily, member 13b	7.26037	8.32465	-2.09113	1.62 ^{E-22}	1.31 ^{E-19}
ADXC.42251_s_at	ENS00000115419 OTTNUMG00000132701	2744	<i>GLS</i>	Glutaminase	6.64437	7.70659	-2.08814	1.12 ^{E-26}	1.77 ^{E-23}
AFFX-HUMISGF3M/97935_3_at	ENS00000115415	6772	<i>STAT1</i>	Signal transducer and activator of transcription 1, 91 kDa	5.09163	6.15122	-2.08433	5.88 ^{E-30}	1.50 ^{E-26}
ADXCADA.20256_s_at	ENS00000206337 ENS00000227429 ENS00000230389 ENS00000237105 OTTNUMG00000031282 OTTNUMG00000031580 OTTNUMG00000037036 OTTNUMG00000149480	10866	<i>HCP5</i>	HLA complex P5 (nonprotein coding)	5.51305	6.57186	-2.08322	1.91 ^{E-19}	9.95 ^{E-17}
ADXC.11833.C1_at	ENS00000130487	113730	<i>KLHDC7B</i>	Kelch domain containing 7B	6.27113	7.32699	-2.07897	4.72 ^{E-14}	9.28 ^{E-12}
ADXCNTDJ.8070_at	ENS00000132530 OTTNUMG00000177908	54739	<i>XAF1</i>	XAP associated factor 1	4.78528	5.83886	-2.07567	2.31 ^{E-19}	1.17 ^{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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADDEC4833.C1_at	ENS00000168421 OTTHUMG00000099373	399	RHOH	Ras homolog family member H	3.05072	4.10067	-2.07046	5.97 ^{E-13}	9.99 ^{E-11}
ADDEC6372.C1_at	ENS00000188820 OTTHUMG0000015438	441168	FAM26F	Family with sequence similarity 26, member F	3.63479	4.68217	-2.06678	4.20 ^{E-16}	1.15 ^{E-13}
ADDEC8794.C1_at	ENS00000143119 OTTHUMG00000048020	963	CD53	CD53 molecule	4.38497	5.43159	-2.06568	5.17 ^{E-16}	1.40 ^{E-13}
ADDEC11065.C1_s_at	ENS00000117215 OTTHUMG00000002701	26279	PLA2G2D	Phospholipase A2, group IID	4.50062	5.54596	-2.06385	1.29 ^{E-22}	1.07 ^{E-19}
ADDEC6133.C8_s_at	ENS00000186818 ENS00000026397 ENS000000263061 ENS000000263108 OTTHUMG00000065879	11006	IL1RB4	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}
ADDECINTDJ.7501_at	ENS00000183508 OTTHUMG0000013703	54855	FAM46C	Family with sequence similarity 46, member C	4.19588	5.23636	-2.0569	3.08 ^{E-11}	3.94 ^{E-09}
ADDECADA.19485_at	ENS000000269215	2533	FYB	FYN binding protein	4.80313	5.841	-2.05318	1.22 ^{E-27}	2.10 ^{E-24}
ADDEC541.C5_x_at	ENS000000211893 ENS000000211896 ENS000000253755 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}
ADDEC8794.C1_x_at	ENS00000143119 OTTHUMG00000048020	963	CD53	CD53 molecule	4.17601	5.21112	-2.04927	1.49 ^{E-15}	3.72 ^{E-13}
ADDEC11578.C1_at	ENS000000086300 OTTHUMG00000023650	29887	SNX10	Sorting nexin 10	4.65828	5.69142	-2.04648	6.49 ^{E-18}	2.48 ^{E-15}
ADDEC15732.C1_at	ENS00000156219 OTTHUMG00000130110	419	ART3	ADP-ribosyltransferase 3	2.70328	3.73454	-2.04381	1.39 ^{E-06}	7.23 ^{E-05}
ADDEC19339.C1_at	ENS000000106560 OTTHUMG00000157488	26157	GIMAP2	GTPase, IMAP family member 2	4.28574	5.3153	-2.0414	3.89 ^{E-18}	1.62 ^{E-15}
ADDEC3103.C1_s_at	ENS00000162645 OTTHUMG0000010662	2634	GBP2	Guanylate binding protein 2, interferon-inducible	4.65938	5.68258	-2.03243	2.09 ^{E-15}	5.11 ^{E-13}
Adx-Hs-IGF3A-600-3_s_at	ENS00000115415 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}
ADDECINTDJ.1455_x_at	—	4069	LYZ	Lysozyme	4.96057	5.97843	-2.02492	2.04 ^{E-16}	5.95 ^{E-14}
ADDEC5570.C2-a_s_at	ENS00000188313 OTTHUMG00000159427	5359	PLSCR1	phospholipid scramblase 1	4.86584	5.88307	-2.02404	1.03 ^{E-10}	1.23 ^{E-08}
ADDECAD.2658_s_at	ENS00000153064 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}
ADDECADA.22193_s_at	ENS00000183508 OTTHUMG0000013703	54855	FAM46C	Family with sequence similarity 46, member C	4.54856	5.56483	-2.02268	6.63 ^{E-12}	9.27 ^{E-10}
ADDEC14394.C3_x_at	ENS00000179750 ENS000000262156 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}
ADDEC20389.C1_s_at	ENS00000101347 OTTHUMG00000032402	25939	SAMHD1	SAM domain and HD domain 1	6.06735	7.08152	-2.01973	2.06 ^{E-22}	1.62 ^{E-19}
ADDEC6156.C1_s_at	ENS00000163131 OTTHUMG00000035010	1520	CTSS	Cathepsin S	7.96887	8.98165	-2.0178	1.51 ^{E-25}	2.08 ^{E-22}
ADDEC5795.C1_s_at	ENS00000100865 OTTHUMG00000150648	4689	NCF4	Neutrophil cytosolic factor 4, 40 kDa	5.92178	6.93332	-2.01607	6.84 ^{E-15}	1.55 ^{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)
ADXC.119.C51_at	ENS00000137403 ENS00000204642 ENS00000206509 ENS00000229698 ENS00000235220 ENS00000237508 OTTTHUMG00000004783 OTTTHUMG000000031156 OTTTHUMG000000031438 OTTTHUMG000000041181 OTTTHUMG00000148884 OTTTHUMG00000149164	3134	<i>HLA-F</i>	Major histocompatibility complex, class I, F	3.37679	4.38739	-2.01476	2.13 ^{E-06}	0.00104487
ADXC.3131.C1_at	ENS00000165168 ENS00000268765 OTTTHUMG000000033175	1536	<i>CYBB</i>	Cytochrome b-245, beta polypeptide	5.99847	7.00346	-2.00693	8.74 ^{E-16}	2.27 ^{E-13}
ADXC.12744.C1_at	ENS00000133321 OTTTHUMG00000167850	5920	<i>RARRES3</i>	Retinot acid receptor responder (tazarotene induced) 3	5.9758	6.98021	-2.00612	5.15 ^{E-18}	2.09 ^{E-15}
ADXC.9547.C1_at	ENS00000137959	10964	<i>IFI44L</i>	Interferon-induced protein 44-like	2.11351	3.11667	-2.00438	4.94 ^{E-22}	3.59 ^{E-19}
ADXC.16385.C1_at	ENS00000183508 OTTTHUMG000000013703	54855	<i>FAM46C</i>	Family with sequence similarity 46, member C	4.76232	5.76384	-2.0021	1.68 ^{E-11}	2.23 ^{E-09}
ADXC.1189.CB7_x_at	—	28823	<i>IGLV1-44</i>	Immunoglobulin lambda variable 1-44	11.2452	12.2464	-2.00168	2.17 ^{E-11}	2.83 ^{E-09}
ADXC.1366.C1_s_at	—	2634	<i>GBP2</i>	Guanylate binding protein 2, interferon-inducible	2.72719	3.72838	-2.00165	4.06 ^{E-13}	7.03 ^{E-11}
AFFX-HUMISGF3A/M97935_MA_at	—	6772	<i>STAT1</i>	Signal transducer and activator of transcription 1, 91 kDa	5.77671	6.77741	-2.00096	5.80 ^{E-26}	6.94 ^{E-22}
ADXC.22969.C1_at	ENS00000132274 OTTTHUMG00000066904	10346	<i>TRIM22</i>	Tripartite motif containing 22	5.78822	6.78695	-1.99825	7.64 ^{E-10}	8.05 ^{E-08}
ADXCAD.9691_at	ENS00000162654 OTTTHUMG00000010663	115361	<i>GBP4</i>	Guanylate binding protein 4	1.77173	2.77034	-1.99808	1.29 ^{E-23}	1.32 ^{E-20}
ADXCAD.7172_at	ENS00000234883 OTTTHUMG00000078367	114614 406947	<i>MIR155</i> <i>MIR155HG</i>	MicroRNA 155 MIR155 host gene (nonprotein coding)	3.22787	4.22545	-1.99665	1.53 ^{E-13}	2.79 ^{E-11}
ADXC.21884.C1_s_at	ENS00000237988	—	<i>OR21JP</i>	Olfactory receptor, family 2, subfamily 1, member 1 pseudogene	3.15508	4.15086	-1.99417	7.81 ^{E-18}	2.96 ^{E-15}
ADXC.20447.C1_at	ENS00000234445 OTTTHUMG00000167324	330	<i>BIRC3</i>	Baculoviral IAP repeat containing 3	6.24381	7.23896	-1.99328	3.36 ^{E-14}	6.85 ^{E-12}
ADXC.1022.C5_x_at	—	3514	<i>IGKC</i>	Immunoglobulin kappa constant	11.5101	12.5026	-1.98861	1.36 ^{E-13}	2.50 ^{E-11}
ADXC.11868.C1_at	ENS00000115419 OTTTHUMG00000132701	2744	<i>GLS</i>	Glutaminase	5.78789	6.78018	-1.98933	5.99 ^{E-18}	2.35 ^{E-15}
Adx-Hs-IGSF3A-400-S_s_at	ENS00000115415 OTTTHUMG00000132699	6772	<i>STAT1</i>	Signal transducer and activator of transcription 1, 91 kDa	5.53875	6.53059	-1.98872	1.01 ^{E-15}	2.58 ^{E-13}
ADXC.29969.C1_at	ENS00000161570 OTTTHUMG00000132949	6352	<i>CCL5</i>	Chemokine (C-C motif) ligand 5	6.05079	7.04037	-1.9856	6.36 ^{E-09}	1.31 ^{E-26}
ADXC.17347.C1_at	ENS00000169403 OTTTHUMG00000003953	5724	<i>PTAFR</i>	Platelet-activating factor receptor	6.35869	7.34639	-1.98303	5.60 ^{E-18}	2.21 ^{E-15}
ADXC.18072.C1_at	ENS00000105369 OTTTHUMG00000182678	973	<i>CD79A</i>	CD79a molecule, immunoglobulin-associated alpha	5.90346	6.8906	-1.98224	2.16 ^{E-17}	7.79 ^{E-15}
ADXCINTD1.199_s_at	ENS00000263303	3903	<i>LAIR1</i>	Leukocyte-associated immunoglobulin-like receptor 1	6.55886	7.54492	-1.98077	2.74 ^{E-19}	1.37 ^{E-16}
ADXC.13342.C1_x_at	ENS00000173821 OTTTHUMG00000161415	57674	<i>RNF213</i>	Ring finger protein 213	4.95659	5.942	-1.97987	6.63 ^{E-17}	2.21 ^{E-14}
ADXCAD.20607_s_at	ENS00000122862 OTTTHUMG0000018369	5552	<i>SRGN</i>	Serglycin	4.6923	5.67651	-1.97823	6.18 ^{E-08}	4.44 ^{E-06}
ADXCINTD1.4796_s_at	ENS00000163840 OTTTHUMG00000159524	151636	<i>DTX3L</i>	Dextx 3-like (<i>Drosophila</i>)	4.4377	5.42031	-1.97604	1.77 ^{E-16}	5.31 ^{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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.11420.C1_at	ENS00000133574 OTTTHUMG00000157475	55303	GIMAP4	GTPase, IMAP family member 4	7.18136	8.16348	-1.97537	1.31 ^{E-18}	5.97 ^{E-16}
ADXC.26389.C1_at	ENS00000205413 OTTTHUMG00000155809	54809	SAMD9	Sterile alpha motif domain containing 9	3.47663	4.45837	-1.97485	9.00 ^{E-15}	2.01 ^{E-12}
ADXC.12489.C2_s_at	—	—	—	—	3.8722	4.8528	-1.97329	5.15 ^{E-08}	3.76 ^{E-06}
ADXC.14394.C3_at	ENS00000179750 ENS00000262156 OTTTHUMG00000151085 OTTTHUMG00000175305	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}
ADXC.2450.C1_x_at	ENS00000002549 OTTTHUMG00000048214	51056	LAP3	Leucine aminopeptidase 3	8.48908	9.46772	-1.97061	2.57 ^{E-29}	5.97 ^{E-26}
ADXC.20430_s_at	ENS00000079081 OTTTHUMG00000158387	27074	LAMP3	Lysosomal-associated membrane protein 3	3.06374	4.04108	-1.96883	1.83 ^{E-14}	3.89 ^{E-12}
ADXC.21063.C1_at	ENS00000139646 OTTTHUMG00000130953	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}
ADXC.2823_s_at	ENS00000245164 OTTTHUMG00000165025	100130231	LINC00861	Long intergenic nonprotein coding RNA 861	4.77971	5.75671	-1.96837	2.05 ^{E-11}	2.68 ^{E-09}
ADXC.1477.C4_x_at	ENS00000111801 OTTTHUMG00000114451	10384	BTN3A3	Butyrophilin, subfamily 3, member A3	5.22694	6.20287	-1.9669	1.67 ^{E-19}	8.88 ^{E-17}
ADXC.31890_s_at	ENS00000163568 OTTTHUMG0000037183	9447	AIM2	Absent in melanoma 2	2.50387	3.47943	-1.9664	3.44 ^{E-16}	9.63 ^{E-14}
ADXC.2833.C1_at	—	712	C10A	Complement component 1, q subcomponent, A chain	3.73388	4.70939	-1.96634	5.55 ^{E-14}	1.06 ^{E-11}
Adx-Hs-IGSF3A-300-5_s_at	ENS00000115415 OTTTHUMG00000132699	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}
ADXCAD.2691_x_at	—	—	—	—	3.97774	4.94794	-1.95911	5.50 ^{E-16}	1.47 ^{E-13}
ADXCNTDJ.4447_at	ENS00000101342 OTTTHUMG0000032400	140711	TLOC2	TBC1LysM-associated domain containing 2	5.75767	6.72696	-1.95788	4.65 ^{E-22}	3.42 ^{E-19}
ADXC.1601.C1_at	—	—	—	—	5.09814	6.06504	-1.95599	7.39 ^{E-17}	2.42 ^{E-14}
ADXCNTDJ.1455_at	—	4069	LIZ	Lysozyme	4.94589	5.91312	-1.95508	1.28 ^{E-16}	4.00 ^{E-14}
ADXC.9663.C1_at	ENS00000162692 OTTTHUMG0000010982	7412	VCAM1	Vascular cell adhesion molecule 1	3.70716	4.67313	-1.95337	1.83 ^{E-11}	2.42 ^{E-09}
ADXC.491.C4_at	ENS00000105193 ENS00000178715 OTTTHUMG00000003169 OTTTHUMG00000182972	6217	RPS16	Ribosomal protein S16	6.18983	7.15443	-1.95152	2.53 ^{E-17}	9.04 ^{E-15}
ADXCAD.20132_s_at	ENS00000140105 OTTTHUMG00000171572	7453	WARS	Tryptophanyl-tRNA synthetase	4.34256	5.30585	-1.94975	6.27 ^{E-17}	2.11 ^{E-14}
ADXCADA.10514_s_at	ENS00000101347 OTTTHUMG0000032402	29599	SAMHD1	SAM domain and HD domain 1	7.37239	8.33516	-1.94904	5.50 ^{E-16}	1.47 ^{E-13}
ADXC.442.C10_x_at	ENS00000197249 OTTTHUMG00000150355	5265	SERPINA1	Serpin peptidase inhibitor, clade A (alpha-1 antitrypsin), member 1	5.39938	6.35786	-1.94327	1.09 ^{E-08}	1.12 ^{E-09}
ADXCADA.24441_x_at	ENS00000163131 OTTTHUMG0000035010	1520	CTSS	Cathepsin S	3.93734	4.89444	-1.94141	1.25 ^{E-34}	7.70 ^{E-31}

(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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.21173.C1_at	ENS00000160326 ENS00000261768 OTTNUMG0000020874 OTTNUMG00000174705	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}
ADXC.20029.C1_s_at	ENS00000121858 OTTNUMG00000156917	8743	TNFSF10	Tumor necrosis factor (ligand) superfamily, member 10	3.98266	4.93882	-1.94014	3.90 ^{E-08}	2.92 ^{E-08}
ADXC.24.C2_s_at	ENS00000173221 OTTNUMG00000121167	2745	GLRX	Glutaredoxin (thioltransferase)	6.25789	7.21178	-1.9371	2.37 ^{E-13}	4.23 ^{E-11}
ADXC.119.C32_x_at	ENS000000206435 ENS000000206452 ENS000000282839 ENS000000237022 OTTNUMG00000037240 OTTNUMG00000148565 OTTNUMG00000149248 OTTNUMG00000149943	3107	HLA-C	Major histocompatibility complex, class I, C	7.76696	8.7127	-1.92617	1.52 ^{E-06}	0.000882559
ADXC.6MUTR.6000_at	ENS000000242472 OTTNUMG00000152461	3492 3493	IGH IGHA1	Immunoglobulin heavy locus Immunoglobulin heavy constant alpha 1	5.22548	6.17118	-1.92612	3.25 ^{E-14}	6.66 ^{E-12}
ADXC.11171.C1_s_at	ENS00000128284 OTTNUMG00000150632	3494 3500	IGHA2 IGHG1	Immunoglobulin heavy constant alpha 2 (A2m marker) Immunoglobulin heavy constant gamma 1 (G1m marker)	5.22548	6.17118	-1.92612	3.25 ^{E-14}	6.66 ^{E-12}
ADXC.1399.C10_s_at	ENS000000234745 OTTNUMG00000031153 OTTNUMG00000031435	3501 3502	IGHG2 IGHG3	Immunoglobulin heavy constant gamma 2 (G2m marker) Immunoglobulin heavy constant gamma 3 (G3m marker)	5.22548	6.17118	-1.92612	3.25 ^{E-14}	6.66 ^{E-12}
ADXC.18072.C1_x_at	ENS00000100342 OTTNUMG00000030427	3507 28396	IGHM IGHV4-31	Immunoglobulin heavy constant mu Immunoglobulin heavy variable 4-31	5.22548	6.17118	-1.92612	3.25 ^{E-14}	6.66 ^{E-12}
ADXC.28008_at	ENS000000269404 OTTNUMG00000183039	6689	SPB	Spi-B transcription factor (Spi-1/PU.1 related)	3.71992	4.66557	-1.92606	8.64 ^{E-10}	9.01 ^{E-08}
ADXC.11171.C1_s_at	ENS00000128284 OTTNUMG00000150632	80833	APOL3	Apolipoprotein L, 3	3.52894	4.47392	-1.92516	5.20 ^{E-23}	4.59 ^{E-20}
ADXC.26628_x_at	ENS000000223532 ENS000000234745 OTTNUMG00000031153 OTTNUMG00000031435	3106	HLA-B	Major histocompatibility complex, class I, B	7.22469	8.16834	-1.92339	4.62 ^{E-16}	1.26 ^{E-13}
ADXC.11171.C2_s_at	ENS00000100342 OTTNUMG00000030427	8542	APOL1	Apolipoprotein L, 1	6.08461	7.02758	-1.92248	3.63 ^{E-21}	2.43 ^{E-18}
ADXC.1399.C10_s_at	ENS000000067066 OTTNUMG00000133203	6672	SP100	SP100 nuclear antigen	5.1586	6.09961	-1.91987	4.49 ^{E-18}	1.85 ^{E-15}
ADXC.18072.C1_x_at	ENS00000105369 OTTNUMG00000182678	973	CD79A	CD79a molecule, immunoglobulin-associated alpha	5.78645	6.72733	-1.91971	1.53 ^{E-16}	4.73 ^{E-14}
ADXC.23005.C1_s_at	ENS00000140749 OTTNUMG00000090709	10261	IGSF6	Immunoglobulin superfamily, member 6	4.85054	5.78927	-1.91684	6.79 ^{E-16}	1.78 ^{E-13}
ADXC.6MUTR.1034_s_at	ENS000000019582 OTTNUMG00000163559	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}
ADXC.2450.C1_at	ENS000000002549 OTTNUMG00000048214	51066	LAP3	Leucine aminopeptidase 3	8.88245	9.8206	-1.91606	5.97 ^{E-23}	2.76 ^{E-20}
ADXC.21884.C2_s_at	ENS000000237988 OTTNUMG00000048214	—	OR21P	Olfactory receptor, family 2, subfamily I, member 1 pseudogene	3.52434	4.46026	-1.9131	2.42 ^{E-16}	6.92 ^{E-14}
ADXC.442.C81_s_at	ENS000000197249 OTTNUMG00000150355	5265	SERPINA1	Serpin peptidase inhibitor, clade A (alpha-1 antitrypsin), member 1	7.18407	8.11831	-1.91089	4.21 ^{E-11}	5.30 ^{E-09}
ADXC.23121.C1_at	ENS000000096996 OTTNUMG00000183417	3594	IL12RB1	Interleukin 12 receptor, beta 1	4.3219	5.25573	-1.91035	4.91 ^{E-13}	8.36 ^{E-11}
ADXC.24300_s_at	ENS000000082074 OTTNUMG00000162071	2533	FYB	FYB binding protein	4.73156	5.66522	-1.91011	9.98 ^{E-17}	3.23 ^{E-14}
ADXC.19547.C1_at	ENS00000118308 OTTNUMG00000170192	4033	LAMP	Lymphoid-restricted membrane protein	3.23827	4.17037	-1.90804	1.99 ^{E-06}	9.85 ^{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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.1056.C7_s_at	ENS00000112096 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}
ADXC.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}
ADXC.4039.C1_s_at	ENS00000168961 OTTHUMG00000179831	3965	LGALS9	Lectin, galactoside-binding, soluble, 9	7.04399	7.9738	-1.90503	6.33 ^{E-33}	2.76 ^{E-29}
ADXC.6996.C1_s_at	ENS00000115415 OTTHUMG00000132659	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}
ADXCADA.1441_at	—	—	—	—	7.08276	8.01069	-1.90254	2.09 ^{E-19}	1.07 ^{E-16}
ADXC.3314.C2_s_at	ENS00000211899 OTTHUMG00000152452	3507	IGHM	Immunoglobulin heavy constant mu	6.14428	7.07132	-1.90136	1.93 ^{E-12}	2.91 ^{E-10}
ADXC.541.C13_x_at	ENS00000211896 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}
ADXC.1189.C34_x_at	ENS00000211677 ENS00000211679 OTTHUMG00000151214 OTTHUMG00000151217	3537 28823 100230481	CIAT1 IGLC1 IGLV1-44	Immunoglobulin lambda light chain-like Immunoglobulin lambda constant 1 (M κ g marker) Immunoglobulin lambda variable 1-44	10.2689	11.1942	-1.89902	2.83 ^{E-12}	4.12 ^{E-10}
ADXC.25652_x_at	—	3126	H1A-DRB4	Major histocompatibility complex, class II, DR beta 4	3.64057	4.56574	-1.89891	2.24 ^{E-26}	1.78 ^{E-25}
ADXC.1255.C3_s_at	ENS00000179604 OTTHUMG00000178419	23580	CDC42EP4	CDC42 effector protein (Rho GTPase binding) 4	6.28595	7.21075	-1.89842	1.72 ^{E-26}	8.72 ^{E-25}
ADXC.1946.C1_at	ENS00000185507 OTTHUMG00000132019	3665	IRF7	Interferon regulatory factor 7	7.47335	8.39771	-1.89785	5.82 ^{E-21}	3.72 ^{E-18}
ADXC.NTIDJ.2849_at	ENS00000156234 OTTHUMG00000130201	10563	CXCL13	Chemokine (C-X-C motif) ligand 13	2.67528	3.59922	-1.89729	1.28 ^{E-13}	2.35 ^{E-11}
ADXC.2989.C6_at	—	—	—	—	7.37413	8.29266	-1.89019	7.47 ^{E-19}	3.45 ^{E-16}
ADXC.4829.C1_at	ENS00000134326 OTTHUMG00000151629	129607	CMPK2	Cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial	3.70994	4.62847	-1.89019	6.08 ^{E-16}	1.62 ^{E-13}
ADXC.32772.C1_x_at	—	567	B2M	Beta-2-microglobulin	7.22223	8.13872	-1.88751	1.74 ^{E-21}	1.21 ^{E-18}
ADXC.6996.C1_at	ENS00000115415 OTTHUMG00000132659	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}
ADXC.3160.C1_s_at	ENS00000159189 OTTHUMG00000002891	714	CIQC	Complement component 1, q subcomponent, C chain	7.47719	8.38887	-1.88123	5.76 ^{E-13}	9.67 ^{E-11}
ADXC.1644.C1_at	ENS00000140105 OTTHUMG00000171572	7453	WARS	Tryptophanyl-tRNA synthetase	5.66183	6.57072	-1.8776	2.93 ^{E-25}	3.63 ^{E-22}
ADXC.6664.C1_at	ENS00000111335 OTTHUMG00000169802	4939	OAS2	2'-5'-Oligoadenylate synthetase 2, 6971 kDa	6.30073	7.20879	-1.87652	2.38 ^{E-16}	6.88 ^{E-14}
ADXC.8819.C1_s_at	ENS00000182179 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}
ADXC.4610.C1_at	ENS00000130775 OTTHUMG00000003735	9473	THYMIS2	Thymocyte selection associated family member 2	6.00382	6.90893	-1.87269	1.52 ^{E-11}	2.03 ^{E-09}
ADXC.5068.C1_at	ENS00000140853 OTTHUMG00000133470	84166	NLR05	NLR family, CARD domain containing 5	6.32653	7.23065	-1.8714	8.35 ^{E-24}	8.72 ^{E-21}
ADXC.16064.C1_s_at	ENS00000158714 OTTHUMG0000035433	56833	SLAMF8	SLAM family member 8	5.47736	6.3812	-1.87104	3.33 ^{E-15}	7.93 ^{E-13}
ADXC.6133.C7_x_at	ENS00000131042 ENS00000263222 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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.119.C44_x_at	ENS00000206503 ENS00000224320 ENS00000227715 ENS00000229215 ENS00000235657 ENS00000265434 OTT000000031434 OTT000000030501 OTT000000048721 OTT000000048897 OTT000000049428	3105	HLA-A	Major histocompatibility complex, class I, A	9.71936	10.619	-1.86554	3.74 ^{E-14}	7.52 ^{E-12}
ADXC.2268.C2_s_at	ENS000000089127 OTT000000069792	4938	OAS1	2'-5'-Oligoadenylate synthetase 1, 40/46 kDa	4.78577	5.6848	-1.86481	2.79 ^{E-09}	2.66 ^{E-07}
ADXC.4124.C1_at	—	—	—	—	4.14319	5.04177	-1.86423	5.37 ^{E-06}	0.00172007
ADXC.6260.868_at	ENS00000151283 OTT0000000159275	10225	CD96	CD96 molecule	3.45049	4.34858	-1.86361	7.99 ^{E-11}	9.66 ^{E-09}
ADXC.20410.C1_s_at	ENS000000136250 OTT000000023566	313	AOAH	Acylowacyl hydrolase (neutrophil)	4.19376	5.09018	-1.86145	5.86 ^{E-17}	1.98 ^{E-14}
ADXC.29811.C1_at	ENS00000177409 OTT0000000155807	219285	SAMD9L	Sterile alpha motif domain containing 9-like	5.19945	6.09458	-1.85978	6.28 ^{E-20}	3.59 ^{E-17}
ADXC.23424.C1_at	ENS000000167984	197358	NLR3	NLR family, CARD domain containing 3	3.94205	4.8354	-1.85749	1.92 ^{E-16}	5.68 ^{E-14}
ADXP.624.C2_at	—	—	—	—	9.99479	10.8875	-1.85668	2.92 ^{E-03}	1.45 ^{E-09}
ADXC.23076.C1_at	ENS00000110324 OTT0000000166523	3587	IL10RA	Interleukin 10 receptor, alpha	4.26567	5.15825	-1.85649	2.61 ^{E-12}	3.83 ^{E-10}
ADXC.7250.C1-a_s_at	ENS00000189862 OTT000000032869	2124	EV2B	Ecdotropic viral integration site 2B	6.82529	7.71771	-1.8563	4.80 ^{E-15}	1.11 ^{E-12}
ADXC.6891.C7_s_at	ENS00000162645 OTT000000010662	2634	GBP2	Guanylate binding protein 2, interferon-inducible	6.18324	7.07492	-1.85533	2.53 ^{E-15}	6.14 ^{E-13}
ADXC.23400.C1_x_at	ENS00000165168 ENS00000268765 OTT000000033175	1536	CYBB	Cytochrome b-245, beta polypeptide	8.02986	8.92038	-1.85384	2.52 ^{E-09}	5.97 ^{E-06}
ADXC.32125.C1_s_at	ENS00000179583 OTT0000000129753	4261	CIITA	Class II, major histocompatibility complex, transactivator	5.81095	6.70097	-1.8532	2.71 ^{E-18}	1.18 ^{E-15}
ADXC.1022.C20_x_at	ENS00000211592 ENS00000211597 ENS00000231486 OTT0000000151679 OTT0000000151684 OTT0000000151686	3514 50802	IGK IGKC	Immunoglobulin kappa locus Immunoglobulin kappa constant	11.1112	11.9999	-1.85154	5.18 ^{E-13}	8.78 ^{E-11}
ADXCAD.23435_s_at	ENS000000204287 ENS00000206308 ENS00000226260 ENS00000227993 ENS00000228887 ENS00000230726 ENS00000234794 OTT000000012742 OTT000000031269 OTT000000031567 OTT000000038993 OTT000000049060 OTT000000049327 OTT000000049575	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	1.80 ^{E-11}	2.37 ^{E-09}
ADXC.29978.C1_at	ENS00000135074	8728	ADAM19	ADAM metalloproteinase domain 19	4.25382	5.13983	-1.84806	2.57 ^{E-10}	2.89 ^{E-08}
ADXC.18098.C1_at	ENS00000181381 OTT0000000161412	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)
ADXCADA.23690_at	ENS000000107201 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}
ADXC.111.CB14_s_at	ENS00000019582 OTTHUMG000000163559	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}
ADXC.21503.C1_at	—	643977	FLJ32255	Uncharacterized LOC643977	5.91144	6.78986	-1.83836	1.87 ^{E-06}	9.32 ^{E-05}
ADXC.33669.C1_at	ENS000000180353 OTTHUMG000000159409	3059	HCLS1	Hematopoietic cell-specific Lyn substrate 1	5.75531	6.63314	-1.8376	1.35 ^{E-18}	6.11 ^{E-16}
ADXC.13342.C1_at	ENS000000173821 OTTHUMG000000161415	57674	RNF213	Ring finger protein 213	4.89181	5.76874	-1.83647	1.70 ^{E-15}	4.24 ^{E-13}
ADXC.522.C10_s_at	ENS000000230708 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}
ADXC.EMUTR.3751_at	ENS000000074621 OTTHUMG000000167960	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}
ADXC.RS.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}
ADXC.20850.C1_at	ENS000000096956 OTTHUMG000000183417	3594	IL12RB1	Interleukin 12 receptor, beta 1	4.31818	5.19112	-1.8314	7.11 ^{E-09}	1.39 ^{E-05}
ADXC.22978.C1_at	ENS000000104951 OTTHUMG000000183377	259307	IL4I1	Interleukin 4 induced 1	7.53672	8.40808	-1.83339	1.14 ^{E-25}	1.59 ^{E-22}
ADXC.23126.C1_at	ENS000000197471 OTTHUMG000000097765	6693	SPN	Sialoprotein	4.04033	4.91072	-1.82816	8.59 ^{E-21}	5.26 ^{E-18}
ADXC.614.C1_s_at	ENS000000185215 OTTHUMG000000171890	7127	TNFAIP2	Tumor necrosis factor, alpha-induced protein 2	6.31803	7.18561	-1.82461	3.84 ^{E-18}	1.61 ^{E-15}
ADXC.28662.C1-a_s_at	ENS000000100219 OTTHUMG000000151094	7494	XBP1	X-box binding protein 1	6.33766	7.2045	-1.82367	2.06 ^{E-10}	2.34 ^{E-08}
ADXC.12905.C1_at	ENS000000101017 OTTHUMG00000033053	958	CD40	CD40 molecule, TNF receptor superfamily member 5	4.51541	5.37919	-1.8198	6.44 ^{E-18}	2.48 ^{E-15}
ADXC.30763.C1_at	ENS000000196533 ENS000000026361 OTTHUMG00000036122	440712	C1orf186	Chromosome 1 open reading frame 186	2.9401	3.80215	-1.81762	1.10 ^{E-05}	0.000440588
ADXC.1799.C2_s_at	ENS000000122862 OTTHUMG00000018369	5552	SRGN	Serglycin	6.441	7.30301	-1.81758	8.27 ^{E-20}	4.68 ^{E-17}
ADXC.6543.C1_at	ENS000000172724 OTTHUMG00000019833	6363	CCL19	Chemokine (C-C motif) ligand 19	9.53124	10.3927	-1.81692	2.15 ^{E-12}	3.20 ^{E-10}
ADXC.24209.C1_at	—	91526	ANKRD44	Ankyrin repeat domain 44	3.78144	4.64259	-1.81648	4.51 ^{E-09}	4.08 ^{E-07}
ADXC.4610.C1_x_at	ENS000000130775 OTTHUMG00000003735	9473	THEMIS2	Thymocyte selection associated family member 2	6.13146	6.99197	-1.81569	4.17 ^{E-14}	8.29 ^{E-12}
ADXC.23258.C1_s_at	ENS000000123329 OTTHUMG000000150147	64333	ARHGAP9	Rho GTPase activating protein 9	5.66483	6.52534	-1.81568	1.09 ^{E-20}	6.48 ^{E-18}
ADXC.119.C6_x_at	ENS000000204525 ENS000000233841 OTTHUMG00000031154 OTTHUMG00000031436	3107	HLA-C	Major histocompatibility complex, class I, C	3.83277	4.68936	-1.81076	0.000169184	0.00436472
ADXC.12456.C1_at	ENS000000167208 OTTHUMG000000133173	124460	SNX20	Sorting nexin 20	4.86056	5.71707	-1.81065	1.53 ^{E-22}	1.24 ^{E-19}
ADXC.7134.C2_x_at	ENS000000138959 OTTHUMG000000133204	3431	SP110	SP110 nuclear body protein	3.56998	4.42589	-1.80991	4.22 ^{E-13}	7.25 ^{E-11}
ADXC.EMUTR.4413_at	—	4237	KMT2A	Lysine (K)-specific methyltransferase 2A	4.74173	5.59339	-1.80458	4.05 ^{E-10}	4.46 ^{E-08}
ADXC.138.CB2-a_s_at	ENS000000166710 OTTHUMG000000131247	567	B2M	Beta-2-microglobulin	9.1405	9.99155	-1.80381	1.82 ^{E-21}	1.25 ^{E-18}
ADXCAD.17266_at	—	50615	IL21R	Interleukin 21 receptor	4.30745	5.15488	-1.79953	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)
ADXC.14799.C1_at	ENS00000132109 OTTHUMG00000165701	6737	TRIM21	Tripartite motif containing 21	5.59049	6.4379	-1.79927	2.88 ^{E-15}	6.93 ^{E-13}
ADXCAD.19551_x_at	ENS00000164308 OTTHUMG00000128718	64167	ERAP2	Endoplasmic reticulum aminopeptidase 2	3.05316	3.89998	-1.79854	3.90 ^{E-09}	3.59 ^{E-07}
ADXC.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}
ADXC.23126.C1_x_at	ENS00000197471 OTTHUMG0000097765	6693	SPW	Sialophorin	4.064	4.91002	-1.79753	1.90 ^{E-22}	1.52 ^{E-19}
ADXCADA.22526_s_at	ENS00000128335 OTTHUMG00000150634	23780	APOL2	Apolipoprotein L, 2	7.1849	8.03055	-1.79707	4.91 ^{E-12}	7.04 ^{E-10}
ADXC.26495.C1_at	ENS00000204359 ENS00000239754 ENS00000241253 ENS00000241534 ENS00000242335 ENS00000243570 ENS00000243649 OTTHUMG0000004992 OTTHUMG00000311198 OTTHUMG00000314999 OTTHUMG00000377485 OTTHUMG00000149098 OTTHUMG00000149355 OTTHUMG00000149616	629	CFB	Complement factor B	3.58233	4.42709	-1.79597	3.06 ^{E-05}	0.001063
ADXC.14860.C1_at	ENS00000117091 OTTHUMG0000024009	962	CD48	CD48 molecule	4.4973	5.34157	-1.79535	2.43 ^{E-19}	1.23 ^{E-16}
ADXC.25003.C1_x_at	ENS00000163665 OTTHUMG0000037108	3428	IFI16	Interferon, gamma-inducible protein 16	5.31042	6.15418	-1.79471	2.25 ^{E-14}	4.75 ^{E-12}
ADXC.16763.C1_at	ENS00000169442 OTTHUMG0000003491	1043	CD52	CD52 molecule	6.7482	7.59189	-1.79463	1.02 ^{E-18}	4.71 ^{E-16}
ADXC.3092.C1_s_at	ENS00000141574 OTTHUMG00000178668	6398	SECTM1	Secreted and transmembrane 1	6.99145	7.83433	-1.79363	1.15 ^{E-12}	1.83 ^{E-10}
ADXCNTD1.2864_at	ENS00000156587 OTTHUMG00000167047	9246	UBE2L6	Ubiquitin-conjugating enzyme E2L 6	4.62271	5.46538	-1.79337	2.01 ^{E-08}	1.62 ^{E-06}
ADXC.22834.C1-s_s_at	ENS00000138899 OTTHUMG00000133204	3431	SP110	SP110 nuclear body protein	6.75412	7.59472	-1.7908	1.54 ^{E-23}	1.54 ^{E-20}
ADXC.20342.C1_at	ENS00000203747 OTTHUMG0000034466	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}
ADXCAD.14444_at	ENS00000143119 OTTHUMG0000048020	963	CD53	CD53 molecule	6.28922	7.12866	-1.78935	9.59 ^{E-16}	2.45 ^{E-13}
ADXC.4039.C1_at	ENS00000168961 OTTHUMG00000179831	3965	LGALS9	Lectin, galactoside-binding, soluble, 9	7.14925	7.98822	-1.78877	5.97 ^{E-29}	1.26 ^{E-26}
ADXCNTD1.5195_at	ENS00000205413 OTTHUMG00000155809	54809	SAMD9	Sterile alpha motif domain containing 9	4.1157	4.95436	-1.78839	3.25 ^{E-08}	2.49 ^{E-06}
ADXC.8192.C1_at	ENS00000158869 OTTHUMG0000034343	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}
ADXCCE.9547.C1_x_at	ENS00000105193 ENS00000178715 OTTHUMG0000003169 OTTHUMG00000182972	10964	IFI44L	Interferon-induced protein 44-like	2.1474	2.98491	-1.78696	2.64 ^{E-18}	1.16 ^{E-15}
ADXC.491.04_x_at	—	6217	RPS16	Ribosomal protein S16	4.59747	5.43387	-1.78558	3.27 ^{E-18}	1.39 ^{E-15}
ADXCADA.729_at	ENS00000115267 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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.6543.C1_s_at	ENS00000172724 OTTNUMG0000019833	6363	CCL19	Chemokine (C-C motif) ligand 19	8.20563	9.04171	-1.7852	1.39 ^{E-12}	2.17 ^{E-10}
ADXCAD.24530_s_at	ENS00000111331 OTTNUMG00000169795	4940	OAS3	2'-5'-Oligoadenylate synthetase 3, 100 kDa	4.01416	4.84966	-1.78448	8.30 ^{E-11}	1.00 ^{E-08}
ADXCERS.658_s_at	ENS00000161405 OTTNUMG00000133250	22806	IKZF3	IKAROS family zinc finger 3 (Aldos)	4.35629	5.19154	-1.78418	4.95 ^{E-14}	9.65 ^{E-12}
ADXC.7824.C1_s_at	—	—	—	—	5.08317	5.91814	-1.78383	8.65 ^{E-10}	9.01 ^{E-08}
ADXC.1201.C2_s_at	ENS00000067066 OTTNUMG00000133203	6672	SP100	SP100 nuclear antigen	4.81948	5.65431	-1.78364	7.59 ^{E-15}	1.71 ^{E-12}
ADXC.5437.C3_s_at	ENS00000025434 OTTNUMG00000150628	10062	NRIH3	Nuclear receptor subfamily 1, group H, member 3	9.59495	10.4292	-1.78299	3.16 ^{E-14}	6.50 ^{E-12}
ADXCCEMUTR.3658_at	ENS00000179583 OTTNUMG00000129753	4261	CIITA	Class II, major histocompatibility complex, transactivator	5.37491	6.20887	-1.78257	1.89 ^{E-16}	5.64 ^{E-14}
ADXC.18.C1_s_at	ENS000001185201 ENS00000118585 OTTNUMG00000165357 OTTNUMG00000165359	8519 10581	IFITM1 IFITM2	Interferon induced transmembrane protein 1 Interferon induced transmembrane protein 2	4.44194	5.27298	-1.77897	1.88 ^{E-08}	0.000704483
ADXC.23400.C1_s_at	ENS00000165168 ENS00000068765 OTTNUMG00000033175	1536	CYBB	Cytochrome b-245, beta polypeptide	6.27862	7.10952	-1.7788	1.89 ^{E-04}	2.15 ^{E-21}
ADXCADA.11632_x_at	—	—	—	—	6.98307	7.81184	-1.77617	1.13 ^{E-14}	2.46 ^{E-12}
ADXC.9349.C1_s_at	ENS00000239836 ENS00000240065 ENS00000240118 ENS00000240508 ENS00000242711 ENS00000243067 ENS00000243594 ENS00000243958 OTTNUMG0000012781 OTTNUMG00000131287 OTTNUMG00000131585 OTTNUMG00000140189 OTTNUMG00000148833 OTTNUMG00000149102 OTTNUMG00000149359 OTTNUMG00000149620	5698	PSMB9	Proteasome (prosome, macropain) subunit, beta type, 9	4.22869	5.05714	-1.77578	2.45 ^{E-08}	4.65 ^{E-26}
ADXC.11295.C2_s_at	ENS00000226264 ENS00000234154 ENS00000239329 ENS00000241296 ENS00000241674 ENS00000242092 ENS00000242386 ENS00000242574 OTTNUMG0000012587 OTTNUMG00000131176 OTTNUMG00000131467 OTTNUMG00000140192 OTTNUMG00000148834 OTTNUMG00000149103 OTTNUMG00000149360 OTTNUMG00000149621	3109	HLA-DMB	Major histocompatibility complex, class II, DM beta	5.12108	5.94912	-1.77527	2.59 ^{E-20}	1.50 ^{E-17}
ADXCERS.39931_s_at	ENS00000101347 OTTNUMG00000132402	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	Entrez Gene	Gene Symbol	Gene Title	DDRD Negative (mean)	DDRD Positive (mean)	Fold Change (DDRD Negative/DDRD Positive)	P	P (FDR)
ADCECMUTR.2840_x_at	445347 ENS000000211697 ENS000000211699 ENS000000211701 ENS000000228668 OTTHUMG00000155095 OTTHUMG00000155097 OTTHUMG00000155101 OTTHUMG00000155102	TARP	TCR gamma alternate reading frame protein	2.81003	3.63662	-1.77349	7.96 ^{E-13}	1.30 ^{E-10}
ADDEC.9016.C1_at	1230 ENS00000163823 OTTHUMG00000133451	CCR1	Chemokine (C-C motif) receptor 1	7.00396	7.82817	-1.77056	5.59 ^{E-19}	2.66 ^{E-16}
ADDEC.814.C1_at	151636 ENS00000163840 OTTHUMG00000159524	DTX3L	Deltek 3-like (<i>Drosophila</i>)	7.24319	8.06684	-1.76988	2.66 ^{E-15}	6.43 ^{E-13}
ADPCC.106.C30_s_at	972 ENS00000019582 OTTHUMG00000163559	CD74	CD74 molecule, major histocompatibility complex class II invariant chain	9.07606	9.89307	-1.76909	3.15 ^{E-21}	2.12 ^{E-18}
ADDEC.RS.31462_at	—	APOL6	Apolipoprotein L, 6	6.71464	7.53749	-1.7689	6.08 ^{E-18}	2.37 ^{E-15}
ADDECAD.21101_s_at	1520 ENS00000163131 OTTHUMG00000035010	CTSS	Cathepsin S	2.44801	3.27022	-1.76811	3.97 ^{E-14}	7.94 ^{E-12}
ADDEC.2862.C3_s_at	341 ENS00000130208 OTTHUMG00000180844	APOC1	Apolipoprotein C-I	7.04481	7.86552	-1.76627	2.95 ^{E-17}	1.04 ^{E-14}
ADDEC.RS.31462_x_at	—	APOL6	Apolipoprotein L, 6	6.84801	7.66806	-1.76546	7.03 ^{E-19}	3.28 ^{E-16}
ADDEC.9748.C1_at	5918 ENS00000118849 OTTHUMG00000158834	RARRES1	Retinoic acid receptor responder (tazarotene induced) 1	5.07118	5.88794	-1.76145	0.000759497	0.0137901
ADDECNTDJ.37_s_at	3507 ENS000000211859 OTTHUMG00000152452	IGHM	Immunoglobulin heavy constant mu	6.0843	6.90051	-1.76077	5.63 ^{E-12}	7.97 ^{E-10}
ADDEC.32309.C1_at	4261 ENS00000179583 OTTHUMG00000129753	CIITA	Class II, major histocompatibility complex, transactivator	5.12128	5.93527	-1.75807	3.56 ^{E-16}	9.90 ^{E-14}
ADDEC.6543.C1_s_at	6363 ENS00000172724 OTTHUMG00000119833	CCL19	Chemokine (C-C motif) ligand 19	5.6098	6.42377	-1.75804	7.28 ^{E-08}	5.16 ^{E-06}
ADDECNTDJ.7597_s_at	2568 ENS000000094755 OTTHUMG00000130443	GABRP	GABA A receptor, pi	5.66244	6.47615	-1.75772	5.42 ^{E-06}	0.00173231
ADDEC.6806.C1_at	57823 ENS00000026751 OTTHUMG0000024008	SLAMF7	SLAM family member 7	4.09631	4.90839	-1.75574	1.26 ^{E-15}	3.18 ^{E-13}
ADDEC.138.CB1_x_at	567 ENS00000166710 OTTHUMG00000131247	B2M	Beta-2-microglobulin	9.88478	10.6962	-1.75493	6.68 ^{E-29}	1.34 ^{E-26}
ADDEC.31841.C1_x_at	3580 ENS000000229754 OTTHUMG00000155244	CXCR2P1	Chemokine (C-X-C motif) receptor 2 pseudogene 1	2.11029	2.92029	-1.75321	9.75 ^{E-20}	5.48 ^{E-17}
ADDECNTDJ.8069_at	54739 ENS00000132530 OTTHUMG00000177908	XAF1	XAP associated factor 1	4.10298	4.9119	-1.7519	1.54 ^{E-16}	4.73 ^{E-14}
ADDEC.15017.C1-a_s_at	140691 ENS00000188880 OTTHUMG00000131246	TRIM69	Tripartite motif containing 69	4.94644	5.75336	-1.74948	1.66 ^{E-10}	1.91 ^{E-08}
ADDECAD.23434_s_at	3936 ENS00000136167 OTTHUMG0000016864	LOP1	Lymphocyte cytosolic protein 1 (L-plastin)	6.75131	7.55742	-1.7485	6.45 ^{E-07}	3.64 ^{E-05}
ADDEC.138.C10_x_at	567 ENS00000166710 OTTHUMG00000131247	B2M	Beta-2-microglobulin	9.72991	10.5354	-1.7478	1.29 ^{E-31}	4.37 ^{E-28}
ADDEC.16910.C1_s_at	64926 ENS00000105122 OTTHUMG00000182450	RASAL3	RAS protein activator like 3	6.50352	7.30808	-1.74661	2.64 ^{E-18}	1.16 ^{E-15}
ADDEC.21347.C1_at	84868 ENS00000135077 OTTHUMG00000130249	HAICR2	Hepatitis A virus cellular receptor 2	3.6652	4.469	-1.74569	1.15 ^{E-12}	1.82 ^{E-10}
ADDEC.5349.C2_at	—	—	—	3.86482	4.66736	-1.74417	1.73 ^{E-16}	5.23 ^{E-14}
ADDECNTDJ.5191_at	91543 ENS00000134321 OTTHUMG00000090352	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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.1022.C6_x_at	ENS00000211632 ENS00000224041 ENS00000224437 OTTTHUMG00000151563 OTTTHUMG00000151568 OTTTHUMG00000151563	50802	IGK	Immunoglobulin kappa locus	9.33937	10.1414	-1.74362	5.11 ^{E-12}	7.29 ^{E-10}
ADXCADA.2653_at	ENS00000254838 OTTTHUMG00000165506	387151	GMNP1	GTPase, very large interferon inducible pseudogene 1	3.14214	3.94362	-1.74289	1.47 ^{E-12}	2.28 ^{E-10}
ADXCADA.23711_s_at	ENS00000136514 OTTTHUMG00000156459	64108	RTP4	Receptor (chemosensory) transporter protein 4	3.28222	4.0832	-1.74229	4.89 ^{E-13}	8.35 ^{E-11}
ADXC.20449.C1_at	ENS00000100453 OTTTHUMG0000029369	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}
ADXC.2268.C3_s_at	ENS000000089127 OTTTHUMG00000169792	4938	OAS1	2'-5'-Oligoadenylate synthetase 1, 40/46 kDa	4.8887	5.6889	-1.74133	3.37 ^{E-10}	3.74 ^{E-08}
ADXC.11420.C1-a_s_at	ENS00000133574 OTTTHUMG00000157475	55303	GIMAP4	GTPase, IMAP family member 4	4.86265	5.66213	-1.74047	6.71 ^{E-14}	1.28 ^{E-11}
ADXC.23016.C1_at	ENS00000006658 OTTTHUMG0000020578	7185	TRAF1	TNF receptor-associated factor 1	6.38931	7.18694	-1.73824	3.02 ^{E-13}	5.29 ^{E-11}
ADXC.60.C3_at	ENS00000116701 OTTTHUMG0000035329	4688	NCF2	Neutrophil cytosolic factor 2	4.24989	5.04734	-1.73803	1.05 ^{E-08}	9.03 ^{E-07}
ADXC.3331.C1_s_at	ENS000000077420 OTTTHUMG0000017841	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}
ADXC.119.C55_x_at	ENS00000204525 ENS00000206435 ENS00000206450 ENS00000206452 ENS00000224608 ENS00000225691 ENS00000228399 ENS00000228664 ENS00000232126 ENS00000233841 ENS00000237022 OTTTHUMG0000031154 OTTTHUMG0000031436 OTTTHUMG0000036662 OTTTHUMG0000037240 OTTTHUMG0000048965 OTTTHUMG0000049247 OTTTHUMG0000049248 OTTTHUMG0000049478 OTTTHUMG0000049479 OTTTHUMG0000049943 OTTTHUMG0000049955	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
ADXC.11578.C1-a_s_at	ENS000000086300 OTTTHUMG0000023650	29887	SNX10	Sorting nexin 10	3.69216	4.486	-1.73368	1.66 ^{E-13}	3.02 ^{E-11}
ADXC.6664.C1-a_s_at	ENS00000111335 OTTTHUMG00000169802	4939	OAS2	2'-5'-Oligoadenylate synthetase 2, 69/71 kDa	6.01398	6.807	-1.7327	3.55 ^{E-15}	8.41 ^{E-13}
ADXC.13126.C1_at	ENS00000107742 OTTTHUMG0000018430	9806	SPOCK2	Sparc/osteonectin, ovcv and kazai-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/DDR Positive)	P	P (FDR)
ADXC.481.C10_x_at	ENS00000204287 ENS00000206308 ENS00000226260 ENS00000227993 ENS00000228987 ENS00000230726 ENS00000234794 OTT000000012742 OTT0000000031269 OTT0000000031567 OTT0000000038993 OTT0000000049060 OTT0000000049327 OTT0000000049575	3122	<i>HLA-DRA</i>	Major histocompatibility complex, class II, DR alpha	3.23936	4.02826	-1.72776	4.48 ^{E-07}	2.63 ^{E-05}
ADXC.23215.C1_at	ENS00000168384 ENS00000206391 ENS00000224103 ENS00000228163 ENS00000229685 ENS00000231389 ENS00000235844 ENS00000236177 OTT0000000012625 OTT0000000031058 OTT0000000031328 OTT0000000040241 OTT0000000048836 OTT0000000049106 OTT0000000049363 OTT0000000049624	3113	<i>HLA-DPA1</i>	Major histocompatibility complex, class II, DP alpha 1	5.27933	6.06704	-1.72633	1.42 ^{E-12}	2.21 ^{E-10}
ADXC.11619.C1_at	ENS000000205744 OTT0000000080853	79958	<i>DENND1C</i>	DENND1C domain containing 1C	5.76573	6.5534	-1.72628	3.17 ^{E-17}	1.11 ^{E-14}
ADXCADA.4972_s_at	ENS000000090600 OTT0000000014576	2289	<i>FKBP5</i>	FKBP5 binding protein 5	5.19855	5.98618	-1.72624	7.47 ^{E-09}	6.56 ^{E-07}
ADXCAD.18269_s_at	ENS000000163644 OTT0000000030952	152926	<i>PPM1K</i>	Protein phosphatase, Mg2+/Mn2+ dependent, 1K	5.53487	6.32132	-1.72482	4.53 ^{E-14}	8.93 ^{E-12}
ADXCAD.19551_at	ENS000000164308 OTT00000000128718	64167	<i>ERAP2</i>	Endoplasmic reticulum aminopeptidase 2	2.77361	3.55941	-1.72405	6.93 ^{E-07}	3.88 ^{E-05}
ADXC.119.C46_x_at	ENS000000206435 ENS00000206452 ENS00000228299 ENS00000237022 OTT0000000037240 OTT0000000048965 OTT0000000049248 OTT0000000049943	3107	<i>HLA-C</i>	Major histocompatibility complex, class I, C	8.85475	9.63905	-1.72225	4.54 ^{E-19}	2.21 ^{E-16}
ADXC.25003.C1_at	ENS000000163565 OTT0000000037108	3428	<i>IFI16</i>	Interferon, gamma-inducible protein 16	6.05229	6.83562	-1.7211	2.67 ^{E-13}	4.71 ^{E-11}
ADXC.6133.C1_s_at	ENS000000104972	10859	<i>LILRB1</i>	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}
ADXC.22822.C1_at	—	—	—	—	3.0604	3.84193	-1.71895	1.01 ^{E-12}	1.62 ^{E-10}
ADXLCEC.5698.C1_s_at	—	441108	<i>C5orf56</i>	Chromosome 5 open reading frame 56	2.07313	2.85451	-1.71877	1.32 ^{E-14}	2.85 ^{E-12}
ADXC.12823.C1_at	ENS000000125354 OTT0000000022280	23157	<i>OSG1</i>	Septin 6	6.87795	7.65908	-1.71847	2.09 ^{E-09}	2.03 ^{E-07}
ADXC.119.CB1_x_at	ENS000000223532 ENS00000234745 OTT0000000031153 OTT0000000031435	3106	<i>HLA-B</i>	Major histocompatibility complex, class I, B	10.6643	11.4452	-1.71822	1.88 ^{E-15}	4.63 ^{E-13}

(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)
ADXCERS.23469_s_at	ENS00000187912 OTTTHUMG00000169312	388512	QLEC17A	C-type lectin domain family 17, member A	2.83234	3.61306	-1.71799	1.11 ^{E-08}	9.54 ^{E-07}
ADXC.224.C14_x_at	ENS00000225890 ENS00000228284 ENS00000236418 OTTTHUMG00000149069 OTTTHUMG00000149336 OTTTHUMG00000149584	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
ADXC.20449.C1_x_at	ENS00000100453 OTTTHUMG0000029369	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}
ADXCERS.7275_at	ENS00000263304 OTTTHUMG00000179762	284021	MILR1	Mast cell immunoglobulin-like receptor 1	4.42634	5.20419	-1.71458	7.10 ^{E-07}	3.95 ^{E-05}
ADXC.29145.C1_s_at	ENS00000173821 OTTTHUMG00000161415	57674	RNF213	Ring finger protein 213	6.24023	7.01767	-1.71408	9.72 ^{E-18}	3.62 ^{E-15}
ADXC.31791.C1_at	ENS00000115085	7535	ZAP70	Zeta-chain (TCR) associated protein kinase 70 kDa	2.15729	2.93396	-1.71317	6.65 ^{E-13}	1.10 ^{E-10}
ADXPCC.1278C1_s_at	ENS00000160255 OTTTHUMG0000090257	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}
ADXCNTD1.8224_at	—	—	—	—	6.843	7.61693	-1.70993	2.25 ^{E-07}	1.43 ^{E-05}
ADXPCC.10579.C1_at	ENS00000197536 OTTTHUMG0000059493	441108	C5orf56	Chromosome 5 open reading frame 56	3.85537	4.60709	-1.7073	5.32 ^{E-19}	2.54 ^{E-16}
ADXC.24212.C1_at	ENS00000267349 OTTTHUMG00000179901	—	OTTTHUMG00000179901 RPI1-68022.9	NULL NULL	3.32581	4.09584	-1.7053	4.73 ^{E-14}	9.29 ^{E-12}
ADXC.541.C10_x_at	ENS00000253755 OTTTHUMG00000152493	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}
ADXC.2602.C1_s_at	ENS00000130489 OTTTHUMG00000150251	9997	SCD2	SCD2 cytochrome c oxidase assembly protein	5.29079	6.05941	-1.70364	1.01 ^{E-16}	3.27 ^{E-14}
ADXC.20525.C1_s_at	ENS00000204482 ENS00000206433 ENS00000223465 ENS00000226182 ENS00000230791 ENS00000231048 ENS00000234514 ENS00000235915 OTTTHUMG0000031264 OTTTHUMG0000031562 OTTTHUMG0000040404 OTTTHUMG00000148785 OTTTHUMG00000148999 OTTTHUMG00000149282 OTTTHUMG00000149513 OTTTHUMG00000149937	7940	LST1	Leukocyte-specific transcript 1	6.65738	7.42487	-1.70231	9.25 ^{E-11}	1.11 ^{E-08}
ADXC.3295.C1_s_at	ENS00000162892 OTTTHUMG0000036459	11009	IL24	Interleukin 24	2.80988	3.57697	-1.70183	2.26 ^{E-08}	2.19 ^{E-07}
ADXC.32733.C1_s_at	—	100129399	LOC100129399	Uncharacterized LOC100129399	7.06652	7.83359	-1.70181	1.45 ^{E-07}	9.64 ^{E-05}
ADXCAD.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}
ADXC.22939.C1_s_at	ENS00000056558 OTTTHUMG0000020578	7185	TRAF1	TNF receptor-associated factor 1	5.2202	5.98677	-1.70122	9.39 ^{E-15}	2.08 ^{E-12}
ADXCNTD1.82_s_at	ENS00000082074 OTTTHUMG00000162071	2533	FYB	FYB binding protein	4.66331	5.42955	-1.70082	2.56 ^{E-18}	1.14 ^{E-15}
ADXC.8090.C1-a_s_at	ENS00000127951 OTTTHUMG00000130681	10875	FGI2	Fibrinogen-like 2	2.66694	3.43259	-1.70014	6.38 ^{E-10}	6.81 ^{E-08}
ADXC.3276.C1_at	ENS00000109861 OTTTHUMG00000167290	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)
ADXCADA.20312_at	ENS00000105851 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}
ADXC.15017.C1_at	ENS00000118580 OTTHUMG00000131246	140691	TRIM69	Tripartite motif containing 69	6.13944	6.90401	-1.69887	3.18 ^{E-18}	1.37 ^{E-15}
ADXC.10021.C3_s_at	ENS00000105185 ENS00000255909 OTTHUMG00000168907 OTTHUMG00000180224	9141	PDCD5	Programmed cell death 5	6.43487	7.19883	-1.69815	5.86 ^{E-05}	0.00183997
ADXC.22688.C1_at	ENS00000264198 OTTHUMG00000179517	22806	IKZF3	IKAROS family zinc finger 3 (Aiolos)	4.68827	5.49888	-1.69538	1.66 ^{E-19}	8.88 ^{E-17}
ADXC.29271.C1_s_at	ENS00000069493 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}
ADXC.11760.C1_at	ENS00000153563 OTTHUMG00000130265	925	CD8A	CD8a molecule	4.57498	5.3352	-1.69375	3.96 ^{E-15}	9.32 ^{E-13}
ADXC.31359.C1_s_at	ENS00000111335 OTTHUMG00000169802	4939	OAS2	2'-5'-Oligoadenylate synthetase 2, 6971 kDa	5.30529	6.06499	-1.69313	2.43 ^{E-12}	3.58 ^{E-10}
ADXC.1432.X_at	ENS00000242534 ENS00000244116 OTTHUMG00000151616 OTTHUMG00000151652	3514	IGKC	Immunoglobulin kappa constant	2.8024	3.56167	-1.69263	2.09 ^{E-09}	2.03 ^{E-07}
ADXC.10067_s_at	—	—	—	—	5.44549	6.20457	-1.6924	2.39 ^{E-13}	4.24 ^{E-11}
ADXC.10067_s_at	ENS00000153563 OTTHUMG00000130265	925	CD8A	CD8a molecule	4.73213	5.48974	-1.69069	8.34 ^{E-15}	1.87 ^{E-12}
ADXC.23683.C1_x_at	ENS00000169508 OTTHUMG0000017263	1880	GPR183	G protein-coupled receptor 183	4.41737	5.17368	-1.68917	1.18 ^{E-11}	1.59 ^{E-09}
ADXC.10067_s_at	ENS00000172243 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}
ADXC.10067_s_at	ENS00000108679 OTTHUMG00000177572	3959	LGALS3BP	Lectin, galactoside-binding, soluble, 3 binding protein	7.59942	8.35544	-1.68883	4.16 ^{E-09}	3.80 ^{E-07}
ADXC.16046_at	ENS00000196329 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}
ADXC.6368.C1_s_at	ENS00000124256 OTTHUMG0000032824	81030	ZBP1	Z-DNA-binding protein 1	3.12472	3.88008	-1.68804	2.30 ^{E-15}	5.60 ^{E-13}
ADXC.12783_at	—	—	—	—	4.05381	4.80889	-1.68773	2.29 ^{E-06}	0.000111145
ADXC.12920.C1_at	ENS00000110934	51411	BIN2	Bridging integrator 2	7.72358	8.47725	-1.68607	1.80 ^{E-15}	4.46 ^{E-13}
ADXC.27278.C1_s_at	ENS00000094755 OTTHUMG00000130443	2568	GABRP	GABA A receptor, pi	6.99519	7.7482	-1.68531	0.000336945	0.00751633
ADXC.33505.C1_at	—	—	—	—	3.17411	3.92701	-1.68518	5.82 ^{E-11}	7.15 ^{E-09}
ADXC.481.C4_s_at	ENS00000204287 ENS00000206308 ENS00000226260 ENS00000227993 ENS00000228987 ENS00000230726 ENS00000234794 OTTHUMG0000012742 OTTHUMG0000031269 OTTHUMG0000031567 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	ENS000000206505 ENS000000223980 ENS000000227715 ENS000000231834 ENS000000233567 OTTTHUMG00000004793 OTTTHUMG000000044844 OTTTHUMG000000148897 OTTTHUMG000000149177 OTTTHUMG000000149428	3105	HLA-A	Major histocompatibility complex, class I, A	11.1624	11.9137	-1.68328	2.31 ^{E-14}	4.86 ^{E-12}
ADXCAD.24372_x_at	ENS000000206450 ENS000000223532 ENS000000224608 ENS000000228964 ENS000000232126 ENS000000234745 OTTTHUMG000000311153 OTTTHUMG00000031435 OTTTHUMG00000036662 OTTTHUMG000000149247 OTTTHUMG000000149478 OTTTHUMG000000149555	3106	HLA-B	Major histocompatibility complex, class I, B	5.91097	6.66222	-1.68325	3.98 ^{E-15}	9.33 ^{E-13}
ADXC.119.C28_x_at	ENS000000206505 ENS000000223980 ENS000000231834 OTTTHUMG00000004793 OTTTHUMG000000044844 OTTTHUMG000000148897 OTTTHUMG000000149177	3105	HLA-A	Major histocompatibility complex, class I, A	10.8214	11.5721	-1.68254	7.71 ^{E-16}	2.01 ^{E-13}
ADXC.23683.C1_at	ENS000000169508 OTTTHUMG00000017263	1880	GPR183	G protein-coupled receptor 183	4.01164	4.76207	-1.6823	1.50 ^{E-10}	1.75 ^{E-08}
ADXCADA.20351_at	ENS000000162676 OTTTHUMG00000010897	2672	GFI1	Growth factor independent 1 transcription repressor	3.00246	3.75172	-1.68093	7.24 ^{E-11}	8.78 ^{E-09}
ADXC.2026.C1_s_at	ENS000000155629 OTTTHUMG00000018838	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}
ADXC.7237.C1_s_at	ENS00000005844 OTTTHUMG000000176964	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}
ADXC.16819.C1_at	ENS000000126353 OTTTHUMG000000133375	1236	CCR7	Chemokine (C-C motif) receptor 7	4.54962	5.29553	-1.67703	5.45 ^{E-13}	9.19 ^{E-11}
ADXC.3276.C1_x_at	ENS000000109861 OTTTHUMG000000167290	1075	CTSC	Cathepsin C	5.75073	6.4956	-1.67583	3.96 ^{E-14}	7.94 ^{E-12}
ADXCADA.16167_at	—	—	—	—	2.78587	3.53074	-1.67582	1.73 ^{E-08}	1.42 ^{E-06}
ADXLCEC.128.C4_x_at	ENS000000166710 OTTTHUMG000000131247	567	B2M	Beta-2-microglobulin	5.59575	6.34013	-1.67525	7.36 ^{E-08}	1.33 ^{E-04}
ADXCERS.41932_x_at	ENS000000172243 OTTTHUMG000000133597	64581	CLEC7A	C-type lectin domain family 7, member A	4.03904	4.78328	-1.6751	3.92 ^{E-07}	2.94 ^{E-05}
ADXC.21503.C1_x_at	—	643977	FLJ32255	Uncharacterized LOC643977	5.297	6.04118	-1.67502	1.40 ^{E-06}	7.30 ^{E-05}
ADXCAD.15721_at	ENS000000197813 OTTTHUMG000000184009	—	CTC-30107.4 OTTTHUMG000000184009	NULL NULL	7.43896	8.18136	-1.67296	1.49 ^{E-14}	3.19 ^{E-12}
ADXC.22574.C1_at	ENS000000163219 OTTTHUMG000000152621	9938	ARHGAP25	Rho GTPase activating protein 25	5.26468	6.00707	-1.67294	1.75 ^{E-16}	5.28 ^{E-14}
ADXCAD.12444_s_at	ENS000000107059 OTTTHUMG00000078789	81704	DOCK8	Dedicator of cytokinesis 8	5.30217	6.04289	-1.671	1.19 ^{E-14}	2.58 ^{E-12}
ADXC.10461.C2_s_at	ENS000000093072 OTTTHUMG00000030726	51816	CECR1	Cell 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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDR Positive)	P	P (FDR)
ADXC.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}
ADXCAD.2691_at	—	—	—	—	3.68679	4.42491	-1.66801	3.40 ^{E-10}	3.77 ^{E-08}
ADXCCEMUTR.868_x_at	ENS00000153283 OTTTHUMG00000159275	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}
ADXC.119.C14_x_at	ENS00000206450 ENS00000223532 ENS00000234745 OTTTHUMG0000031153 OTTTHUMG0000031435 OTTTHUMG00000149955	3106	HLA-B	Major histocompatibility complex, class I, B	10.7923	11.529	-1.66539	1.81 ^{E-17}	6.62 ^{E-15}
ADXCADA.22573_s_at	ENS00000117020 OTTTHUMG0000039994	10000	AKT3	V-akt murine thymoma viral oncogene homolog 3 (protein kinase B, gamma)	4.41658	5.15234	-1.66527	3.69 ^{E-06}	0.00125105
ADXCAD.20735_at	ENS00000048740 OTTTHUMG0000017668	10659	CEL22	CUGBP, Elav-like family member 2	6.51308	7.24863	-1.66504	9.86 ^{E-12}	1.33 ^{E-09}
ADXC.2988.C2_s_at	ENS00000166384 ENS00000206291 ENS00000224103 ENS00000228163 ENS00000225665 ENS00000231389 ENS00000235844 ENS00000236177 OTTTHUMG0000012625 OTTTHUMG0000031058 OTTTHUMG0000031328 OTTTHUMG00000140241 OTTTHUMG00000148836 OTTTHUMG00000149106 OTTTHUMG00000149363 OTTTHUMG00000149624	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}
ADXPCC.13546.C1_at	—	—	—	—	2.14138	2.87606	-1.66403	1.19 ^{E-12}	1.88 ^{E-10}
ADXC.541.CB1_x_at	ENS00000211896 ENS00000253755 OTTTHUMG00000152493 OTTTHUMG00000152495	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}
ADXC.17029.C1_s_at	ENS00000098827 OTTTHUMG0000031757	6614	SIGLEC1	Sialic acid binding Ig-like lectin 1, sialoadhesin	6.97946	7.71339	-1.66316	5.49 ^{E-17}	1.88 ^{E-14}
ADXC.12685.C1_at	ENS00000162511 OTTTHUMG00000303707	7805	LAPTM5	Lysosomal protein transmembrane 5	5.59234	6.32373	-1.66024	8.57 ^{E-11}	1.03 ^{E-08}
ADXC.22235.C1_at	ENS00000066923 ENS00000213413 OTTTHUMG00000155183 OTTTHUMG00000156798	10734 79037	PIRIG STAG3	Pdlovirus receptor related immunoglobulin domain containing Stromal antigen 3	7.03191	7.76299	-1.65988	5.50 ^{E-07}	3.16 ^{E-06}
ADXCAD.19914_at	—	—	—	—	4.94455	5.67542	-1.65964	1.28 ^{E-19}	6.98 ^{E-17}
ADXC.28931.C1_at	ENS00000154642 OTTTHUMG0000074509	54149	C21orf91	Chromosome 21, open reading frame 91	4.42579	5.15635	-1.65928	7.05 ^{E-06}	0.00215033
ADXCNTD1.3401_x_at	—	10730	YME1L1	YME1-like 1 ATPase	3.83972	4.57019	-1.65918	4.10 ^{E-07}	2.43 ^{E-06}
ADXC.541.C7_x_at	ENS00000211897 ENS00000253755 OTTTHUMG00000152493 OTTTHUMG00000152639	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	-1.65903	9.96 ^{E-10}	1.03 ^{E-07}
ADXC.9502.C1_at	ENS00000101336 OTTTHUMG0000032204	3055	HCK	Hemopoietic cell kinase	4.32305	5.05102	-1.65663	2.98 ^{E-08}	2.29 ^{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)
ADXCERS.24793_x_at	ENS00000146192 OTTHUMG00000014616	221472	FGD2	FYVE, RhoGEF and PH domain containing 2	5.56511	6.29239	-1.65552	4.07 ^{E-21}	2.69 ^{E-18}
ADXCAD.26949_s_at	ENS00000179583 OTTHUMG00000129753	4261	CIITA	Class II, major histocompatibility complex, transactivator	6.0737	6.79841	-1.65257	2.09 ^{E-17}	7.61 ^{E-15}
ADXCAD.8106_s_at	—	—	—	—	5.37813	6.10276	-1.65248	5.10 ^{E-06}	0.000225069
ADXC.20433.C1_at	ENS00000197943 OTTHUMG00000176532	5336	PLCG2	Phospholipase C, gamma 2 (phosphatidylinositol-specific)	6.85967	7.58421	-1.65238	3.61 ^{E-09}	3.36 ^{E-07}
ADXCERS.44768_at	—	6672	SP100	SP100 nuclear antigen	4.66189	5.3862	-1.65211	1.37 ^{E-06}	7.16 ^{E-05}
ADXPCC.4821.05_x_at	ENS000000211892 ENS000000211893 ENS000000211896 ENS000000211897 ENS000000253755 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}
ADXC.3942.C3_s_at	ENS00000145267 OTTHUMG00000130294	51316	PLA2G8	Placenta-specific 8	2.42296	3.14667	-1.65143	3.28 ^{E-07}	2.00 ^{E-05}
ADXCERS.408_x_at	ENS00000243811 OTTHUMG00000151084	140564	AP0BEC3D	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3D	7.71732	8.44046	-1.65077	1.14 ^{E-19}	6.26 ^{E-17}
ADXC.21620.C1_at	ENS00000113088 OTTHUMG00000097009	3003	GZMK	Granzyme K (granzyme 3; tryptase II)	3.7909	4.51378	-1.65047	1.28 ^{E-12}	2.02 ^{E-10}
ADXC.23834.C1_x_at	ENS000000187474 OTTHUMG00000183502	2399	FPR3	Formyl peptide receptor 3	5.22514	5.94792	-1.65036	4.95 ^{E-17}	1.71 ^{E-14}
ADXC.18764.C1_at	ENS000000171488 OTTHUMG00000103005	84230	LRC8C	Leucine rich repeat containing 8 family, member C	3.51196	4.23407	-1.6496	3.21 ^{E-08}	2.46 ^{E-06}
ADXCAD.8513_at	—	—	—	—	4.67953	5.401	-1.64885	5.59 ^{E-09}	5.00 ^{E-07}
ADXC.1477.C3_x_at	ENS000000026950 OTTHUMG00000114449	11119	BTN3A1	Butyrophilin, subfamily 3, member A1	6.24846	6.96905	-1.64786	4.48 ^{E-17}	1.57 ^{E-14}
ADXC.19534.C1_at	ENS000000145088 OTTHUMG00000159424	55840	EAF2	ELL associated factor 2	3.72901	4.44912	-1.64731	2.68 ^{E-07}	1.66 ^{E-05}
ADXC.8829.C1_at	ENS000000094755 OTTHUMG00000130443	2568	GABRP	GABA A receptor, pi	8.83282	9.5523	-1.64659	0.00213074	0.0287375
ADXC.1924.C10_s_at	ENS000000165949 OTTHUMG00000171303	3429	IFI27	Interferon, alpha-inducible protein 27	5.31612	6.03363	-1.64434	8.65 ^{E-12}	1.18 ^{E-09}
ADXC.3238.C1_at	ENS000000138959 OTTHUMG00000133204	3431	SP110	SP110 nuclear body protein	4.50099	5.21798	-1.64375	1.78 ^{E-09}	1.77 ^{E-07}
ADXC.12837.C1_at	ENS000000069424 OTTHUMG00000007095	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}
ADXC.4600.C1_s_at	ENS000000160255 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}
ADXCNTD1.1662_s_at	ENS000000124103 ENS000000213714 OTTHUMG0000032799 OTTHUMG0000032800	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
ADXCAD.16416_at	—	—	—	—	4.41088	5.12481	-1.64026	9.56 ^{E-17}	3.11 ^{E-14}
ADXCNTD1.403_s_at	ENS00000211866 OTTHUMG00000170944	—	TBAU23 TBAU23	T-cell receptor alpha joining 23 NULL	3.68809	4.4018	-1.64002	9.88 ^{E-07}	5.30 ^{E-05}
ADXCADA.8117_at	—	—	—	—	5.2212	5.93466	-1.63974	1.37 ^{E-10}	1.61 ^{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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.119.C1_x.at	ENS00000206505 ENS00000223960 ENS00000227715 ENS00000231834 ENS00000235657 OTTTHUMG0000004793 OTTTHUMG00000044844 OTTTHUMG00000148897 OTTTHUMG00000149177 OTTTHUMG00000149428	3105	HLA-A	Major histocompatibility complex, class I, A	10.77	11.4832	-1.63939	3.72 ^{E-16}	1.02 ^{E-13}
ADXCAD.28491_s.at	ENS00000111537 OTTTHUMG00000169113	3458	IFNG	Interferon, gamma	3.08809	3.77123	-1.63937	1.99 ^{E-06}	1.61 ^{E-06}
ADXCADA.15927.at	ENS00000081189	4208	MEF2C	Myocyte enhancer factor 2C	4.78083	5.49317	-1.63845	9.49 ^{E-07}	5.11 ^{E-06}
ADXC.7531.C1-a_s.at	ENS00000041357 OTTTHUMG00000143859	5685	PSMA4	Proteasome (prosome, macropain) subunit, alpha type, 4	4.17648	4.88949	-1.63808	7.11 ^{E-06}	0.000300514
ADXC.13340.C1.at	ENS000000187239 OTTTHUMG0000020800	23048	FNBP1	Formin binding protein 1	5.8032	6.51513	-1.638	5.94 ^{E-14}	1.13 ^{E-11}
ADXC.7250.C1.at	ENS00000188862 OTTTHUMG00000132869	2124	EIV2B	Ecotropic viral integration site 2B	4.48687	5.19875	-1.63793	6.12 ^{E-18}	2.38 ^{E-15}
ADXC.6635.C2_s.at	ENS00000138642 OTTTHUMG00000160983	5508	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}
ADXCAD.14647_s.at	—	—	—	—	2.93491	3.6466	-1.63772	4.13 ^{E-07}	2.45 ^{E-06}
ADXC.4208.C1.at	ENS00000154124 OTTTHUMG00000161762	9028	FAM106B	Family with sequence similarity 105, member B	5.82468	6.53511	-1.6363	0.00225727	0.00550193
ADXC.25371.C1.at	ENS00000166750 OTTTHUMG00000179858	162394	SLFN5	Schlafen family member 5	5.51958	6.22996	-1.63623	1.41 ^{E-07}	9.45 ^{E-06}
ADXC.8396.C1.at	ENS00000026751 OTTTHUMG0000024008	57823	SLAMF7	SLAM family member 7	3.4482	4.1577	-1.63523	5.37 ^{E-18}	2.15 ^{E-15}
ADXC.11734.C1.at	ENS000000184979 OTTTHUMG00000150104	11274	USP18	Ubiquitin-specific peptidase 18	3.46738	4.17678	-1.63512	4.20 ^{E-11}	5.30 ^{E-09}
ADXC.2739.C1.at	ENS000000157873 OTTTHUMG0000000792	8764	TNFRSF14	Tumor necrosis factor receptor superfamily, member 14	7.48352	8.19223	-1.63434	1.59 ^{E-13}	2.89 ^{E-11}
ADXCAD.15016.at	ENS000000083799 OTTTHUMG00000173404	1540	CYLD	Cylindromatosis (turban tumor syndrome)	4.32179	5.03021	-1.63401	0.000623068	0.0118496
ADXC.26661.C1.at	—	—	—	—	4.6549	5.36179	-1.63228	3.62 ^{E-09}	3.36 ^{E-07}
ADXC.18764.C1_x.at	ENS000000171488 OTTTHUMG00000103005	84230	LRC8C	Leucine-rich repeat containing 8 family, member C	4.41917	5.12604	-1.63226	6.84 ^{E-06}	4.88 ^{E-06}
ADXC.6664.C1_x.at	ENS000000111335 OTTTHUMG00000169802	4939	OAS2	2'-5'-Oligoadenylate synthetase 2, 6971 kDa	6.08279	6.789	-1.63152	9.68 ^{E-13}	1.57 ^{E-10}
ADXC.4004.C1.at	ENS000000110042 OTTTHUMG00000167336	23220	DTX4	Detlex homolog 4 (<i>Drosophila</i>)	3.6627	4.36837	-1.63089	3.12 ^{E-12}	4.53 ^{E-10}
ADXC.3768.C2_x.at	ENS000000140379 OTTTHUMG00000144173	597	BCL2A1	BCL2-related protein A1	4.13156	4.83718	-1.63084	3.49 ^{E-08}	2.64 ^{E-06}
ADXC.32000.C1.at	ENS000000231578	—	—	—	2.31383	3.01942	-1.6308	3.53 ^{E-14}	7.12 ^{E-12}
ADXC.1732.C2_s.at	ENS000000113845 OTTTHUMG00000159388	51300	TIMMDC1	Translocase of inner mitochondrial membrane domain containing 1	4.78788	5.49329	-1.63061	1.23 ^{E-07}	8.30 ^{E-06}
ADXC.12372.C1_s.at	ENS000000119922 OTTTHUMG0000018707	3433	IFT2	Interferon-induced protein with tetratricopeptide repeats 2	5.39497	6.10023	-1.63044	1.84 ^{E-12}	2.79 ^{E-10}
ADXCADA.10962_s.at	ENS000000070190 OTTTHUMG00000160974	27071	DAPPI	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)
ADXCAD.2593_at	ENS00000171488 OTTHUMG00000010305	84230	LRRRC8C	Leucine-rich repeat containing 8 family, member C	3.49226	4.19648	-1.62926	2.05 ^{E-08}	1.65 ^{E-06}
ADXC.5286.C3_s_at	ENS00000196954 OTTHUMG00000166078	837	CASP4	Caspase 4, apoptosis-related cysteine peptidase	6.66916	7.37203	-1.62773	1.58 ^{E-08}	1.31 ^{E-06}
ADXCCEMUTR.6361_at	—	51561	IL23A	Interleukin 23, alpha subunit p19	4.97263	5.67548	-1.62772	2.43 ^{E-14}	5.08 ^{E-12}
ADXC.6891.C1_at	ENS00000117228 OTTHUMG00000106114	2633	GBP1	Guanylate-binding protein 1, interferon-inducible	3.87662	4.57937	-1.62761	9.72 ^{E-13}	1.57 ^{E-10}
ADXC.7351.C1_s_at	ENS000001165140 OTTHUMG0000020268	2203	FBP1	Fructose-1,6-bisphosphatase 1	4.5942	5.29571	-1.6262	6.91 ^{E-05}	0.00211391
ADXC.19605.C1_s_at	ENS00000105967 OTTHUMG0000023518	22797	TREC	Transcription factor EC	2.63795	3.33881	-1.62548	3.49 ^{E-14}	7.05 ^{E-12}
ADXCAD.12222_at	—	—	IGKV1-17	Immunoglobulin kappa variable 1-17	3.53459	4.23584	-1.62547	1.37 ^{E-10}	1.61 ^{E-08}
ADXC.8312.C1_s_at	ENS00000163565 OTTHUMG0000037108	3428	IFI16	Interferon, gamma-inducible protein 16	3.72553	4.42639	-1.62547	4.24 ^{E-09}	3.87 ^{E-07}
ADXC.603.C3_x_at	ENS00000116701 OTTHUMG0000035329	4688	NCF2	Neutrophil cytosolic factor 2	4.80958	5.51009	-1.62463	1.22 ^{E-08}	1.03 ^{E-06}
ADXC.20554.C1_at	ENS00000115935 OTTHUMG00000132334	7456	WIPF1	WAS/WASL interacting protein family, member 1	5.76956	6.46999	-1.62454	9.02 ^{E-13}	1.46 ^{E-10}
ADXC.119.C16_at	—	—	—	—	7.47993	8.17945	-1.62396	2.95 ^{E-19}	1.47 ^{E-16}
ADXCAD.11127_s_at	ENS00000131876 ENS00000144158 OTTHUMG00000149871 OTTHUMG00000153382	6627	SNRPA1	Small nuclear ribonucleoprotein polypeptide A'	5.41283	6.11186	-1.62341	0.000534555	0.0105676
ADXC.13347.C1_at	ENS00000131018 OTTHUMG00000115841	23345	SYNE1	Spectrin repeat containing, nuclear envelope 1	3.95741	4.85643	-1.6234	1.73 ^{E-06}	8.75 ^{E-05}
ADXC.27278.C2_at	ENS000000094755 OTTHUMG00000130443	2568	GABRP	GABA A receptor, pi	6.10812	6.8071	-1.62336	0.00305297	0.0364148
ADXC.22834.C1_x_at	ENS00000139899 OTTHUMG00000133204	3431	SP110	SP110 nuclear body protein	4.27294	4.97079	-1.62209	1.15 ^{E-14}	2.50 ^{E-12}
ADXCAD.12181_s_at	ENS00000137265 OTTHUMG00000162394	3662	IRF4	Interferon regulatory factor 4	4.51658	5.21336	-1.62087	1.30 ^{E-10}	1.53 ^{E-08}
ADXC.4829.C1-a_s_at	ENS00000134326 OTTHUMG00000151629	129607	CMPK2	Cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial	3.49544	4.19217	-1.62083	1.51 ^{E-15}	3.77 ^{E-13}
ADXCADA.20532_s_at	ENS00000174946 OTTHUMG00000159861	29909	GPR171	G protein-coupled receptor 171	4.21846	4.915	-1.62062	1.14 ^{E-07}	7.75 ^{E-06}
ADXPCC.12456.C1_at	—	—	—	—	4.12043	4.81675	-1.62037	2.85 ^{E-08}	2.21 ^{E-06}
ADXCNTD1.4119_s_at	ENS00000070190 OTTHUMG00000160974	27071	DAPP1	Dual adaptor of phosphotyrosine and 3-phosphoinositides	5.81361	6.50874	-1.61903	8.80 ^{E-11}	1.06 ^{E-08}
ADXC.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}
ADXC.7199.C1_s_at	ENS00000112862 OTTHUMG0000018369	5552	SRGN	Slycin	2.45511	3.14957	-1.61828	1.36 ^{E-08}	1.14 ^{E-06}
ADXC.23398.C1_s_at	ENS00000177272 OTTHUMG0000034493	3738	KCNMA3	Potassium voltage-gated channel, shaker-related subfamily, member 3	2.34049	3.03453	-1.61781	5.82 ^{E-09}	5.20 ^{E-07}
ADXC.3982.C1_s_at	ENS00000137752 ENS00000204397 OTTHUMG0000048072 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}
ADXC.22709.C1_at	ENS00000145779 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)
ADXC.17999.C1_at	ENS00000154016 OTTHUMG00000059436	10750	GRAP	GRB2-related adaptor protein	4.63945	5.33188	-1.616	0.00088263	0.0166782
ADXCERS.41932_s_at	ENS00000172243 OTTHUMG00000133597	64581	CLEC7A	C-type lectin domain family 7, member A	3.84526	4.5375	-1.6158	0.000569599	0.00629412
ADXCERS.41599_s_at	ENS00000170085 OTTHUMG00000130663	202181 375484	LOC202181 SIMC1	SUMO-interacting motifs containing 1 pseudogene SUMO-interacting motifs containing 1	4.23808	4.92373	-1.61513	0.00270521	0.0335997
ADXC.18303.C1_at	—	55824	PAG1	Phosphoprotein associated with glycosphingolipid microdomains 1	3.20927	3.90075	-1.61493	6.17 ^{E-07}	3.49 ^{E-06}
ADXCERS.12890_s_at	ENS000000089012 OTTHUMG00000031680	55423	SIRPG	Signal-regulatory protein gamma	5.03622	5.72749	-1.61471	1.45 ^{E-15}	3.66 ^{E-13}
ADXC.10461.C2_x_at	ENS000000093072	51816	GEOR1	Cat eye syndrome chromosome region, candidate 1	6.97203	7.66112	-1.61226	2.35 ^{E-23}	2.24 ^{E-20}
ADXC.9663.C1-a_s_at	ENS00000162692 OTTHUMG0000010982	7412	VCAM1	Vascular cell adhesion molecule 1	2.70338	3.39233	-1.61212	6.10 ^{E-10}	6.53 ^{E-08}
ADXC.19287.C1_s_at	ENS00000164691 OTTHUMG0000015923	117289	TAGAP	T-cell activation RhoGTPase activating protein	2.77176	3.46069	-1.61209	8.39 ^{E-18}	3.14 ^{E-15}
ADXCAD.15016_x_at	ENS000000083799 OTTHUMG00000173404	1540	CYLD	Cylindromatosis (turban tumor syndrome)	3.6816	4.37047	-1.61203	0.000151166	0.00399578
ADXCAD.4629_at	—	—	—	—	3.86072	4.54902	-1.61138	1.71 ^{E-10}	1.96 ^{E-08}
ADXC.6180.C1_at	ENS00000204673 OTTHUMG00000150246	84335	AKT1S1	AKT1 substrate 1 (proline-rich)	5.33689	6.02417	-1.61025	5.18 ^{E-06}	0.000227521
ADXCERS.29144_at	ENS00000204267 ENS00000206235 ENS00000206299 ENS00000223481 ENS00000225967 ENS00000228582 ENS00000232326 ENS00000237599 OTTHUMG0000012641 OTTHUMG0000031068 OTTHUMG0000031338 OTTHUMG0000041555 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}
ADXC.745.C1_s_at	ENS00000010030 OTTHUMG0000014594	51513	ETV7	Ets variant 7	6.17561	6.86263	-1.60996	3.83 ^{E-05}	4.85 ^{E-28}
ADXC.26927.C1_s_at	ENS00000107742 OTTHUMG0000018430	9806	SPOCK2	Sparc/osteonectin, ovcv and kazal-like domains proteoglycan (testican) 2	4.95745	5.64364	-1.60903	6.13 ^{E-08}	4.41 ^{E-06}
ADXCAD.23758_s_at	ENS00000067066 OTTHUMG00000133203	6672	SP100	SP100 nuclear antigen	4.27392	4.95989	-1.60879	7.03 ^{E-07}	3.92 ^{E-05}
ADXCADA.22526_x_at	ENS00000128335 OTTHUMG00000150634	23780	APOL2	Apolipoprotein L 2	8.35313	9.03886	-1.60851	1.74 ^{E-23}	1.73 ^{E-20}
ADXCERS.38610_s_at	ENS00000135838 OTTHUMG0000035321	80896	NPL	N-acetylneuraminic pyruvate lyase (dihydrodipicolinate synthase)	4.75083	5.43627	-1.60819	1.15 ^{E-07}	7.83 ^{E-06}
ADXCAD.18205_at	ENS00000260655 OTTHUMG00000172730	—	CTA-250D10.23 OTTHUMG00000172730	NULL NULL	3.09747	3.78225	-1.60745	1.56 ^{E-07}	1.04 ^{E-05}
ADXC.32510.C1_x_at	ENS00000196684 OTTHUMG00000182256	84941	HSH2D	Hematopoietic SH2 domain containing	4.36801	5.0526	-1.60724	3.47 ^{E-15}	8.25 ^{E-13}
ADXC.583.C2_s_at	ENS00000173369 OTTHUMG0000002896	713	C1QB	Complement component 1, q subcomponent, B chain	6.54826	7.23195	-1.60624	1.85 ^{E-09}	1.82 ^{E-07}
ADXC.3847.C3_s_at	ENS00000100906 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}

(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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.5183.C1_s_at	ENS00000173821 OTTHUMG00000161415	57674	RNF213	Ring finger protein 213	5.1164	5.79786	-1.60376	1.96 ^{E-13}	3.52 ^{E-11}
ADXC.481.C13_x_at	ENS00000204287 ENS00000206308 ENS00000226260 ENS00000227993 ENS00000228987 ENS00000230726 ENS00000234794 OTTHUMG0000012742 OTTHUMG0000031269 OTTHUMG0000031567 OTTHUMG0000031893 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}
ADXC.EMUTR.1413_x_at	ENS00000211666 ENS00000211674 ENS00000254709 OTTHUMG00000151225 OTTHUMG00000151235 OTTHUMG00000165670	100423062	IGLL5	Immunoglobulin lambda-like polypeptide 5	4.93804	5.61492	-1.59868	1.66 ^{E-12}	2.54 ^{E-10}
ADXC.617.C1_s_at	ENS00000111275 OTTHUMG00000169603	217	ALDH2	Aldehyde dehydrogenase 2 family (mitochondrial)	8.92411	9.60035	-1.59797	3.20 ^{E-11}	4.08 ^{E-09}
ADXC.1111.C193_s_at	ENS00000211890 ENS00000211895 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
ADXCADA.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}
ADXCAD.17927_at	ENS00000173821 OTTHUMG00000161415	57674	RNF213	Ring finger protein 213	6.57402	7.24963	-1.59727	5.35 ^{E-17}	1.84 ^{E-14}
ADXC.22266_x_at	ENS00000206505 OTTHUMG0000004793	3105	HLA-A	Major histocompatibility complex, class I, A	6.60567	7.27982	-1.59566	5.79 ^{E-12}	8.18 ^{E-10}
ADXC.1056.C4_s_at	ENS00000112096 OTTHUMG00000159440	6648 100129518	LOC100129518 SOD2	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	7.67752	8.35143	-1.59554	1.12 ^{E-08}	9.59 ^{E-07}
ADXCADA.20312_x_at	ENS00000109851 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}
ADXC.17610_s_at	ENS00000169554 OTTHUMG00000131834	9839	ZEB2	Zinc finger E-box binding homeobox 2	4.39199	5.0652	-1.59462	5.08 ^{E-08}	3.71 ^{E-06}
ADXCAD.7800_s_at	ENS00000197872 OTTHUMG00000090615	81553	FAM49A	Family with sequence similarity 49, member A	5.0179	5.69003	-1.59343	0.000234641	0.0056689
ADXC.7301.C1_at	ENS00000116824 OTTHUMG0000022750	914	CD2	CD2 molecule	5.8015	6.47345	-1.59323	6.75 ^{E-18}	2.57 ^{E-15}
ADXCNTD1.5601_at	ENS00000189404 OTTHUMG0000034809	6402	SELL	Selectin L	4.6303	5.30188	-1.59282	1.87 ^{E-15}	4.61 ^{E-13}
ADXC.23091.C1_at	ENS00000135905 OTTHUMG00000153428	55619	DOCK10	Dedicator of cytokinesis 10	3.70869	4.37957	-1.59205	6.43 ^{E-15}	1.47 ^{E-12}
ADXC.6734_at	—	729230	COR2	Chemokine (C-C motif) receptor 2	4.86222	5.53265	-1.59154	2.82 ^{E-14}	5.82 ^{E-12}
ADXC.1428.C1_at	ENS00000213809 ENS00000255819 OTTHUMG00000168631 OTTHUMG00000168674	22914 100528032	KLRK4-KLRK1 KLRK1	KLRK4-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}
ADXC.15.C10_at	ENS00000184371 OTTHUMG0000011646	1435	CSF1	Colony stimulating factor 1 (macrophage)	4.59879	5.26742	-1.58956	1.14 ^{E-08}	9.77 ^{E-07}

(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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADDEC.8692.C1_s_at	ENS00000125730 OTTHUMG00000150335	718	C3	Complement component 3	8.8893	9.55751	-1.58952	7.94 ^{E-08}	5.60 ⁻⁰⁶
ADDEC.22991.C1_at	ENS00000161921 OTTHUMG00000090761	58191	CXCL16	Chemokine (C-X-C motif) ligand 16	7.41762	8.08605	-1.58934	1.961 ^{E-05}	0.000727973
ADDEC.6719.C1_s_at	ENS00000163131 OTTHUMG00000035010	1520	CTSS	Cathepsin S	3.26889	3.93622	-1.58812	1.251 ^{E-10}	1.48E-08
ADDEC.5662.C1_at	ENS00000120637	10866	HCP5	HLA complex P5 (nonprotein coding)	2.45072	3.11636	-1.58627	4.551 ^{E-10}	4.93 ⁻⁰⁸
ADDECADA.18168_at	ENS00000163131	1520	CTSS	Cathepsin S	5.32749	5.99281	-1.58591	1.101 ^{E-15}	2.80 ⁻¹³
ADDEC.15.C10_x_at	ENS00000184371 OTTHUMG0000011646	1435	CSF1	Colony stimulating factor 1 (macrophage)	5.15363	5.81883	-1.58579	1.531 ^{E-08}	1.27 ⁻⁰⁶
ADDEC.11542.C2_s_at	ENS00000073331 OTTHUMG00000132911	80216	ALPK1	Alpha-kinase 1	5.44374	6.10819	-1.58497	7.321 ^{E-12}	1.02 ⁻⁰⁹
ADDEC.23396.C1_at	ENS00000112096 OTTHUMG0000015940	6648	LOC100129518 SOD2	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	3.43963	4.10135	-1.58197	2.811 ^{E-05}	0.000988428
ADDEC.12905.C1_x_at	ENS00000101017 OTTHUMG00000033053	958	CD40	MD40 molecule, TNF receptor superfamily member 5	5.01986	5.68138	-1.58176	2.121 ^{E-16}	6.18 ⁻¹⁴
ADDEC.22339.C1_s_s_at	ENS00000056558 OTTHUMG00000020578	7185	TRAF1	TNF receptor-associated factor 1	4.23635	4.89705	-1.58084	4.791 ^{E-07}	2.80 ⁻⁰⁵
ADDEC.26430.C1_at	—	—	—	—	6.1926	6.85284	-1.58035	4.931 ^{E-14}	9.62 ⁻¹²
ADDEC.25169.C1_at	OTTHUMG00000184118	15901.3	Ckorf38	Chromosome X open reading frame 38	4.6659	5.32544	-1.57958	9.481 ^{E-08}	6.55 ⁻⁰⁶
369890_at	ENS00000006547	3735	KARS	Lysyl-tRNA synthetase	2.40414	3.06349	-1.57937	4.851 ^{E-06}	0.000215687
ADDEC.2863.C3_s_at	ENS00000010610 ENS00000026879 OTTHUMG00000168514	920	CD4	CD4 molecule	6.94849	7.60756	-1.57905	1.201 ^{E-09}	1.22 ⁻⁰⁷
ADDEC.13057.C1_at	ENS00000009039 OTTHUMG00000180403	3383	ICAM1	Intercellular adhesion molecule 1	7.14534	7.8043	-1.57894	1.581 ^{E-10}	1.83 ⁻⁰⁸
ADDECAD.12819_s_at	—	—	—	—	5.52739	6.18588	-1.57843	1.271 ^{E-07}	8.60 ⁻⁰⁶
ADDEC.22551.C1_at	—	—	—	—	5.01662	5.67447	-1.57773	2.351 ^{E-07}	1.48 ⁻⁰⁵
ADXPCC.5488.C1_s_at	ENS000000111679 ENS00000026894 OTTHUMG00000168518	5777	PTPN6	Protein tyrosine phosphatase, nonreceptor type 6	6.90145	7.55881	-1.5772	1.471 ^{E-06}	7.61 ⁻⁰⁵
ADDEC.119.C12_x_at	ENS000000204592 ENS000000206493 ENS000000225201 ENS000000229252 ENS000000230254 ENS000000233904 ENS000000236632 OTTHUMG00000004820 OTTHUMG000000311155 OTTHUMG00000031437 OTTHUMG00000132983 OTTHUMG00000148925 OTTHUMG00000149205 OTTHUMG00000149447	3133	HLA-E	Major histocompatibility complex, class I, E	5.76228	6.41883	-1.57631	2.171 ^{E-23}	2.09 ⁻²⁰
ADDECAD.15087_s_at	ENS00000166750 OTTHUMG00000179858	162394	SLFN5	Schlafen family member 5	4.79517	5.45147	-1.57604	3.661 ^{E-11}	4.63 ⁻⁰⁹
ADDECADA.2898_at	—	—	—	—	2.70671	3.3625	-1.57548	1.931 ^{E-13}	3.49 ⁻¹¹
ADDEC.2633.C2_x_at	ENS00000115523 OTTHUMG00000130179	10578	GNLY	Granulysin	4.55366	5.20911	-1.5751	7.151 ^{E-11}	8.69 ⁻⁰⁹
ADDEC.15758.C1_at	—	—	—	—	6.11037	6.76488	-1.57408	8.531 ^{E-09}	7.40 ⁻⁰⁷

(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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXCADA.20383_s_at	ENS00000134545 ENS00000205809 OTTTHUMG00000168532 OTTTHUMG00000168584	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 ^{±07}	1.74 ^{±05}
ADXC.23287.C1_s_at	ENS00000186407 OTTTHUMG00000067605	342510	CD300E	CD300e molecule	3.58824	4.21165	-1.57289	0.007405655	0.0135284
ADXCADA.94_at	ENS00000130487 OTTTHUMG00000150250	113730	KLHDC7B	Kelch domain containing 7B	4.98823	5.61127	-1.57248	2.89 ^{±11}	3.71 ^{±09}
ADXC.13225.C1_at	ENS00000143390 OTTTHUMG00000112495	5993	RFX5	Regulatory factor X, 5 (influences HLA class II expression)	4.19662	4.84931	-1.5721	3.79 ^{±09}	3.50 ^{±07}
ADXCAD.28806_s_at	ENS00000107551 OTTTHUMG0000018060	83937	RASSF4	Ras association (RalGDS/AF-6) domain family member 4	3.89503	4.5461	-1.57033	8.31 ^{±10}	8.69 ^{±08}
ADXC.19598.C1_s_at	ENS00000110077 OTTTHUMG00000167241	64231	MS4A6A	Membrane-spanning 4-domains, subfamily A, member 6A	4.68995	5.34078	-1.57007	1.37 ^{±08}	1.15 ^{±06}
ADXC.242.C9_s_at	ENS000000094755 OTTTHUMG00000130443	2568	GABRP	GABA A receptor, pi	5.51708	6.16773	-1.56988	0.000167176	0.00432948
ADXC.22822.C1_x_at	—	—	—	—	6.37127	7.02184	-1.56979	1.47 ^{±07}	9.77 ^{±06}
ADXCAD.23576_s_at	ENS00000115165 OTTTHUMG00000154651	9595	CYTP	Cytoshesin 1 interacting protein	3.70863	4.35822	-1.56873	2.10 ^{±08}	1.69 ^{±06}
ADXCADA.7015_at	ENS00000115985	56990	CDCA2SE2	CDCA2 small effector 2	7.5615	8.21038	-1.56795	4.27 ^{±14}	8.47 ^{±12}
ADXC.6335_s_at	ENS00000009790 OTTTHUMG0000036480	80342	TRAF3IP3	TRAF3 interacting protein 3	4.26387	4.90128	-1.56635	1.73 ^{±06}	8.73 ^{±05}
ADXC.5919.C2_s_at	ENS00000008617 ENS00000025261 OTTTHUMG00000167498	9235	IL32	Interleukin 32	7.06257	7.70988	-1.56625	3.58 ^{±08}	2.70 ^{±06}
ADXC.126.C9_x_at	ENS00000215048 ENS000000223865 ENS00000226826 ENS00000225935 ENS00000230708 ENS00000230763 ENS00000236693 ENS00000237710 OTTTHUMG0000012659 OTTTHUMG0000031076 OTTTHUMG0000031346 OTTTHUMG00000140240 OTTTHUMG00000148842 OTTTHUMG00000149113 OTTTHUMG00000149370 OTTTHUMG00000149629	3115	HLA-DPB1	Major histocompatibility complex, class II, DP beta 1	5.30857	5.95532	-1.56564	3.79 ^{±08}	2.84 ^{±06}
ADXC.EMUTR.4394_at	ENS00000244682 OTTTHUMG00000174101	2212	FCGR2A	Fc fragment of IgG, low affinity Ila, receptor (CD32)	7.12069	7.76725	-1.56543	4.94 ^{±07}	2.87 ^{±05}
ADXCADA.2098_s_at	ENS00000173931 OTTTHUMG00000168527	4973	OLRI	Oxidized low density lipoprotein (lectin-like) receptor 1	5.45033	6.09655	-1.56506	3.76 ^{±06}	0.00017101
ADXC.7293.C1_at	ENS00000134324 OTTTHUMG00000119082	23175	LPIN1	Lipin 1	4.94776	5.59349	-1.56454	2.73 ^{±07}	1.70 ^{±06}
ADXC.8757_at	ENS00000134028 OTTTHUMG00000097858	27299	ADAMDEC1	ADAM-like, decayin 1	2.83489	3.48009	-1.56395	1.24 ^{±09}	1.26 ^{±07}
ADXC.3925.C1_at	—	—	—	—	4.04171	4.68658	-1.56359	9.88 ^{±08}	6.77 ^{±06}
ADXC.4338_at	ENS00000163664 OTTTHUMG0000037109	149628	PHYHI1	Pyrin and HIN domain family, member 1	5.83906	6.48315	-1.56275	1.15 ^{±14}	2.49 ^{±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)
ADCECMUTR.2694_s_at	ENS000000065413 OTTHUMG00000154411	91526	ANKRD44	Ankyrin repeat domain 44	2.38841	3.03249	-1.56273	6.29 ^{E-07}	3.56 ^{E-05}
ADXECAD.6399_at	ENS000000166750 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}
ADXECNTD1.2722_s_at	ENS000000081237 ENS000000262418 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	ENS000000172349 OTTHUMG00000144186	3603	IL16	Interleukin 16	5.15747	5.79877	-1.55974	2.48 ^{E-11}	3.21 ^{E-09}
ADXEC.1477.C3_at	ENS000000026950 OTTHUMG00000144449	11119	BTN3A1	Butyrophilin, subfamily 3, member A1	6.38856	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	ENS000000267369 OTTHUMG00000179903	—	OTTHUMG00000179903 RPI1-1094M14.8	NULL NULL	2.28655	2.92892	-1.55754	2.59 ^{E-12}	3.81 ^{E-10}
ADXEC.16157.C1_s_at	ENS000000012779 ENS000000262552 OTTHUMG0000018081 OTTHUMG00000174846	240	ALOX5	Acyl oxidase 5-lipoxygenase	5.83744	6.47636	-1.55716	2.46 ^{E-09}	2.36 ^{E-07}
ADXEC.8964.C2_s_at	ENS000000083799 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	ENS000000155962 ENS000000268943 OTTHUMG0000022660	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}
ADCECMUTR.6354_at	—	—	—	—	4.37614	5.01444	-1.5565	6.94 ^{E-13}	1.15 ^{E-10}
ADXEC.11663.C1_s_at	ENS000000185811 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	ENS000000187474 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	ENS000000114013 OTTHUMG00000159482	942	CD86	CD86 molecule	2.71726	3.35515	-1.55605	5.27 ^{E-14}	1.02 ^{E-11}
ADXEC.28199.C1_at	ENS000000163545 OTTHUMG0000037196	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	ENS000000254838 OTTHUMG00000161306	387751	GMMP1	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	ENS000000106798 OTTHUMG00000161306	51225	ABI3	ABI family, member 3	7.19284	7.82845	-1.55359	1.03 ^{E-16}	3.29 ^{E-14}
ADXEC.59191.C1_s_at	ENS00000008517 OTTHUMG00000167498	9235	IL32	Interleukin 32	10.2236	10.8592	-1.55354	2.40 ^{E-14}	5.02 ^{E-12}
ADXEC.22774.C1_x_at	ENS000000105639 OTTHUMG00000165648	3718	JAK3	Janus kinase 3	6.80387	7.439	-1.55308	2.06 ^{E-13}	3.70 ^{E-11}
ADXEC.22911.C1_at	ENS000000171310 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	ENS000000166710 OTTHUMG00000131247	567	B2M	Beta-2-microglobulin	9.38774	10.0221	-1.55228	4.48 ^{E-09}	9.77 ^{E-06}
ADXEC.1136.C2_s_at	ENS000000092010 OTTHUMG0000028795	5720	PSME1	Proteasome (prosome, macropro) activator subunit 1 (PA28 alpa)	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)
ADXCERS.27824_s_at	—	—	—	TAP binding protein (tapasin)	5.39007	6.02228	-1.54954	2.29 ^{E-08}	1.81 ^{E-06}
ADXCAD.5238_s_at	—	—	—	—	4.31148	4.94357	-1.54981	3.35 ^{E-09}	3.14 ^{E-07}
ADXCADA.13013_at	—	—	—	—	2.823	3.45378	-1.5484	1.02 ^{E-07}	6.95 ^{E-06}
ADXC.19082.C1_x_at	—	—	—	—	4.46771	5.0982	-1.5481	1.64 ^{E-17}	6.03 ^{E-15}
ADXCAD.27653_at	ENS000000254087 OTTTHUMG00000044345	4067	LYN	V-yes-1 Yamaguchi sarcoma viral related oncogene homolog	4.85263	5.48307	-1.54803	2.72 ^{E-06}	0.000129988
ADXCNTD1.9875_x_at	—	10730	YME1L1	YME1-like 1 ATPase	4.24633	4.87662	-1.54788	4.60 ^{E-13}	7.88 ^{E-11}
ADXC.12647.C2_at	ENS00000005810 OTTTHUMG00000017105	23077	MYCBP2	MYC binding protein 2, E3 ubiquitin protein ligase	5.83426	6.46318	-1.5464	1.84 ^{E-06}	9.22 ^{E-05}
ADXCAD.1752_at	ENS000000114127 OTTTHUMG000000159251	54464	XRN1	5'-3' Exoribonuclease 1	4.21768	4.84656	-1.54637	5.76 ^{E-07}	3.29 ^{E-05}
ADXC.16953.C1_at	ENS000000010810 OTTTHUMG00000016305	2534	FYN	FYN oncogene related to SRC, FGR, YES	4.22615	4.85471	-1.54603	1.17 ^{E-06}	6.18 ^{E-05}
ADXC.8622.C1_at	ENS00000018811 OTTTHUMG000000155907	10320	IKZF1	IKAROS family zinc finger 1 (Ikaros)	3.30977	3.93819	-1.54586	4.07 ^{E-09}	3.73 ^{E-07}
ADXCENMUTR.6379_at	—	203328	SUSO3	Sushi domain containing 3	4.93919	5.56738	-1.54563	2.93 ^{E-05}	0.00102496
ADXC.14205.C1_at	ENS000000130813 OTTTHUMG000000180393	55337	C19orf66	Chromosome 19 open reading frame 66	6.43463	7.06272	-1.54553	3.43 ^{E-09}	3.21 ^{E-07}
ADXCNTD1.8064_at	ENS0000000141682 OTTTHUMG000000132765	5366	PMAIP1	Phorbol-12-myristate-13-acetate-induced protein 1	5.3069	5.93451	-1.54499	2.23 ^{E-05}	0.000813419
ADXCADA.19962_s_at	ENS000000055332 OTTTHUMG000000100962	5610	EIF2AK2	Eukaryotic translation initiation factor 2-alpha kinase 2	6.52976	7.15607	-1.54361	5.64 ^{E-11}	6.93 ^{E-09}
ADXC.25226.C1_at	—	—	—	—	3.57675	4.20285	-1.54339	7.41 ^{E-13}	1.22 ^{E-10}
ADXC.7155.C3-a_s_at	ENS000000152926 ENS000000213462 OTTTHUMG000000156631 OTTTHUMG000000165023	2086 51351	ERV3-1 ZNF117	Endogenous retrovirus group 3, member 1 Zinc finger protein 117	4.36238	4.98858	-1.54286	2.09 ^{E-12}	3.13 ^{E-10}
ADXC.2579.C1_s_at	ENS000000185745 OTTTHUMG00000018712	3434	IFIT1	Interferon-induced protein with tetratricopeptide repeats 1	4.27239	4.89764	-1.54248	2.43 ^{E-06}	0.000116874
ADXC.21558.C1_x_at	—	—	—	—	5.02231	5.64751	-1.54243	1.46 ^{E-06}	7.58 ^{E-05}
ADXC.20916.C1_at	ENS000000174718 OTTTHUMG000000128501	55196	KIAA1551	KIAA1551	6.06968	6.69461	-1.54213	4.34 ^{E-09}	3.95 ^{E-07}
ADXCAD.13559_at	—	—	—	—	5.33761	5.9624	-1.54199	1.85 ^{E-06}	1.51 ^{E-05}
ADXCERS.7275_x_at	ENS000000263304 OTTTHUMG000000179762	284021	MILR1	Mast cell immunoglobulin-like receptor 1	4.74695	5.37166	-1.54191	4.16 ^{E-06}	0.000188287
ADXC.20716.C1_at	—	—	—	—	3.4593	4.08356	-1.54143	3.74 ^{E-09}	3.45 ^{E-07}
ADXCADA.15896_at	ENS000000004468	952	CD38	CD38 molecule	2.21364	2.83788	-1.54139	2.30 ^{E-12}	3.41 ^{E-10}
ADXCAD.21664_s_at	ENS000000137265 OTTTHUMG00000016294	3662	IRF4	Interferon regulatory factor 4	4.38537	5.00915	-1.54091	5.06 ^{E-13}	8.59 ^{E-11}
ADXC.4130.C1_s_at	ENS000000172183 OTTTHUMG000000148679	3669	ISG20	Interferon stimulated exonuclease gene 20 kDa	6.22322	6.84621	-1.54007	7.18 ^{E-16}	1.88 ^{E-13}

(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)
ADXCNTDJ.4121_x_at	ENS00000070190 OTTHUMG00000160974	27071	DAPPI	Dual adaptor of phosphotyrosine and 3-phosphoinositides	2.67844	3.30102	-1.53963	7.81 ^{E-08}	5.51 ^{E-06}
ADXC.5570.C2_s_at	ENS000000188313 OTTHUMG00000159427	5359	PLSCR1	Phospholipid scramblase 1	4.77119	5.39321	-1.53903	5.55 ^{E-07}	3.18 ^{E-06}
ADXCADA.7888_s_at	—	—	—	—	7.36578	7.98877	-1.53899	2.78 ^{E-16}	7.91 ^{E-14}
ADXC.7382.C1_at	ENS000000110777 OTTHUMG00000166559	5450	POU2AF1	POU class 2 associating factor 1	2.88859	3.51018	-1.53856	4.37 ^{E-08}	3.24 ^{E-06}
ADXC.1056.C3_s_at	ENS000000112096 OTTHUMG0000015940	6648	LOC100129518 SOD2	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	6.78248	7.40386	-1.53835	1.41 ^{E-07}	9.43 ^{E-06}
ADXC.17460.C1_s_at	ENS000000167286 OTTHUMG00000166970	915	COD3	COD3 molecule, delta (COD3-TCR complex)	5.74558	6.36491	-1.53617	8.88 ^{E-17}	2.90 ^{E-14}
ADXCAD.25972_s_at	ENS000000185811 OTTHUMG00000155907	10320	IKZF1	IKAROS family zinc finger 1 (Ikaros)	5.7925	6.41146	-1.53577	2.73 ^{E-13}	4.81 ^{E-11}
ADXC.15393.C1_at	ENS000000198759 OTTHUMG0000021155	25975	EGF6	EGF-like domain, multiple 6	2.22312	2.84132	-1.53496	9.11 ^{E-07}	4.93 ^{E-06}
ADXCERS.30295_s_at	ENS000000205045 OTTHUMG00000167707	100566736	SLFN1ZL	Schlafen family member 12-like	2.57006	3.18823	-1.53493	1.13 ^{E-08}	9.65 ^{E-07}
ADXCAD.27568_at	ENS000000162747 ENS000000203747 OTTHUMG00000034466 OTTHUMG00000174099	2215	FCGR3B	Fc fragment of IgG, low affinity IIb, receptor (CD16b)	6.14472	6.76204	-1.53402	1.91 ^{E-08}	1.54 ^{E-06}
ADXC.22774.C1_at	ENS000000105639 OTTHUMG00000165648	3718	JAK3	Janus kinase 3	6.88633	7.50261	-1.53292	7.92 ^{E-13}	1.29 ^{E-10}
ADXCADA.4101_at	ENS000000171488 OTTHUMG00000103005	84230	LRR6C	Leucine rich repeat containing 8 family, member C	3.75074	4.36688	-1.53277	7.62 ^{E-06}	0.000320119
ADXC.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
ADXC.6959.C2_at	ENS000000179456 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}
ADXC.1056.C2_s_at	ENS000000112096 OTTHUMG0000015940	6648	LOC100129518 SOD2	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	8.42621	9.04213	-1.53253	1.82 ^{E-09}	1.80 ^{E-07}
ADXC.932.C3_at	ENS000000101084 ENS000000259399 OTTHUMG00000032382 OTTHUMG00000032384	55969 100527943	C2orf24 TGIF2-C2orf24	Chromosome 20 open reading frame 24 TGIF2-C2orf24 readthrough	3.29697	3.91264	-1.53227	2.31 ^{E-07}	1.46 ^{E-06}
ADXPCC.12496.C1_at	ENS000000169085 OTTHUMG00000156998	254778	C8orf46	Chromosome 8 open reading frame 46	2.85924	3.4749	-1.53225	0.00055596	0.0108831
ADXCERS.15980_s_at	ENS000000134255 OTTHUMG0000012357	10390	CEP71	Choline/ethanolamine phosphotransferase 1	5.18895	5.80458	-1.53222	1.94 ^{E-10}	2.21 ^{E-08}
ADXC.3796.C2_at	ENS000000118503 OTTHUMG0000015664	7128	TNFAIP3	Tumor necrosis factor, alpha-induced protein 3	3.61964	4.23487	-1.53181	5.45 ^{E-14}	1.05 ^{E-11}
ADXC.24229.C1_s_at	ENS000000114127 OTTHUMG00000159251	54464	XRN1	5'-3' Exonuclease 1	3.31757	3.93266	-1.53166	0.000272754	0.00634382
ADXC.30934.C2_at	ENS000000055332 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}
ADXCAD.17520_x_at	ENS000000231486	—	—	—	4.0614	4.67577	-1.53089	6.00 ^{E-10}	6.43 ^{E-08}
ADXC.23107.C1_at	ENS000000188313 OTTHUMG00000159427	5359	PLSCR1	Phospholipid scramblase 1	4.28829	4.87237	-1.53058	7.75 ^{E-06}	0.00231628
ADXC.21052.C1_at	ENS000000168685 OTTHUMG00000090791	3575	IL7R	Interleukin 7 receptor	3.22746	3.84101	-1.53002	1.34 ^{E-09}	1.35 ^{E-07}
ADXC.EMUTR.213_s_at	—	—	—	—	4.11874	4.73218	-1.5299	0.00352643	0.0401472

(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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC.26133.C1_at	ENS00000055332 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}
ADXC.3377.C1_at	ENS000000163131 OTTHUMG00000035010	1520	CTSS	Cathepsin S	3.51899	4.13211	-1.52956	4.17 ^{E-05}	0.0013912
ADXC.31493.C3_s_at	ENS000000143110 OTTHUMG0000011750	128346	C1orf162	Chromosome 1 open reading frame 162	5.68688	6.29915	-1.52866	3.27 ^{E-10}	3.65 ^{E-08}
ADXC.30618.C1_s_at	ENS00000017821 OTTHUMG00000161415	57674	RNF213	Ring finger protein 213	6.41799	7.02964	-1.52801	3.27 ^{E-10}	3.65 ^{E-08}
ADXC.1131.CB4_s_at	ENS000000236943 ENS000000269601 OTTHUMG00000182426 OTTHUMG00000182668	727820 728855 728875	LINC006623 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}
ADXC.6959.C2_x_at	ENS000000179456 OTTHUMG00000040013	10472	ZBTB18	Zinc finger and BTB domain containing 18	7.49879	8.10919	-1.52668	1.90 ^{E-08}	1.54 ^{E-06}
ADXC.648.C9-a_s_at	ENS000000245105 OTTHUMG00000168289	144571	A2M-AS1	A2M antisense RNA 1	3.54624	4.15635	-1.52637	3.24 ^{E-06}	0.000151839
ADXC.42976_s_at	ENS000000178104 ENS000000264708 OTTHUMG00000013846	9659 728802 10096724	LOC100996724 LOC100996761 LOC101060291	Myomegalin-like Myomegalin-like Myomegalin-like	4.51357	5.12366	-1.52635	1.32 ^{E-08}	1.12 ^{E-06}
ADXC.27706_x_at	ENS000000188004 OTTHUMG00000035430	284677	C1orf204	Chromosome 1 open reading frame 204	5.39307	6.00292	-1.52611	2.68 ^{E-09}	2.57 ^{E-07}
ADXC.19998.C1_s_at	ENS000000171115 OTTHUMG00000158327	155038	GIMAP8	GTPase, IMAP family member 8	4.59579	5.2055	-1.52595	3.58 ^{E-05}	0.00121883
ADXC.111.C86_s_at	ENS000000130177 OTTHUMG0000017402	8881	CDC16	Cell division cycle 16	5.47636	6.08572	-1.52558	0.000254185	0.00502529
ADXC.ND1.7388_at	—	—	—	—	4.51185	5.12111	-1.52548	1.70 ^{E-08}	1.39 ^{E-05}
ADXCAD.19112_at	ENS000000135838 OTTHUMG00000035321	80896	NPL	N-acetylneuraminic pyruvate lyase (dihydrodipicolinate synthase)	3.60256	4.21174	-1.52539	8.41 ^{E-06}	0.000349319
ADXC.126.C9_at	ENS000000215048 ENS000000223865 ENS000000226826 ENS000000229295 ENS000000230708 ENS000000230763 ENS000000236693 ENS000000237710 OTTHUMG0000012659 OTTHUMG00000031076 OTTHUMG00000031346 OTTHUMG00000140240 OTTHUMG00000148842 OTTHUMG00000149113 OTTHUMG00000149370 OTTHUMG00000149629	3115	HUA-DPB1	Major histocompatibility complex, class II, DP beta 1	3.11036	3.71847	-1.52426	4.36 ^{E-05}	0.00144296
ADXC.548.C1_s_at	ENS000000164430 OTTHUMG0000015034	115004	MB21D1	Map-21 domain containing 1	2.93812	3.54558	-1.52357	2.91 ^{E-08}	2.25 ^{E-05}
ADXC.3599.C1_s_at	ENS000000025708 OTTHUMG00000150249	1890	TYMP	Thymidine phosphorylase	7.03706	7.64442	-1.52346	5.27 ^{E-11}	3.40 ^{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)
ADCECRS.9321_s_at	ENS000000171928 ENS000000175106 OTTTHUMG000000059052 OTTTHUMG000000171461	51030 201158	<i>TVP23B</i> <i>TVP23C</i>	Transgolgi network vesicle protein 23 homolog B (<i>Saccharomyces cerevisiae</i>) Transgolgi network vesicle protein 23 homolog C (<i>S cerevisiae</i>)	2.55371	3.15878	-1.52104	1.49 ^{E-05}	0.00057503
ADCECRS.7877_C1_at	ENS000000177409	219285	<i>SAMD9L</i>	Sterile alpha motif domain containing 9-like	4.83346	5.43828	-1.52078	2.13 ^{E-19}	1.09 ^{E-16}
ADCECRS.23107_C1_x_at	ENS000000188313 OTTTHUMG000000159427	5359	<i>PLSCR1</i>	Phospholipid scramblase 1	3.96772	4.57074	-1.51889	7.63 ^{E-06}	0.00228802
ADCECRS.21321_s_at	ENS000000101082 OTTTHUMG00000032293	84174	<i>SLA2</i>	Src-like adaptor 2	3.46651	4.06781	-1.51709	2.82 ^{E-12}	4.12 ^{E-10}
ADCECRS.1119_C2_s_at	ENS000000164104 OTTTHUMG000000160799	3148	<i>HMG82</i>	High mobility group box 2	4.00687	4.60817	-1.51708	0.00262967	0.0329469
ADCECRS.29962_s_at	ENS000000165178 ENS000000182487 ENS000000261919 ENS000000262960 ENS000000262984 OTTTHUMG000000149664 OTTTHUMG000000156804	653361 654816 654817	<i>NCF1</i> <i>NCF1B</i> <i>NCF1C</i>	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}
ADCECRS.1056_C2-a_s_at	ENS000000112096 OTTTHUMG00000015940	6648 100129518	<i>LOC100129518</i> <i>SOD2</i>	Uncharacterized LOC100129518 Superoxide dismutase 2, mitochondrial	6.64396	7.24261	-1.5143	2.67 ^{E-07}	1.66 ^{E-06}
ADCECRS.6447_C2_at	ENS000000175309 OTTTHUMG000000130892	85007	<i>PHYKPL</i>	5-Phosphohydroxy-L-lysine phosphatase	5.31662	5.91515	-1.51418	0.000180022	0.00459005
ADCECRS.22601_C1_at	ENS000000258588 ENS000000258659 OTTTHUMG00000066892 OTTTHUMG00000066899	53840 445372	<i>TRIM34</i> <i>TRIM6-TRIM34</i>	Tripartite motif containing 34 TRIM6-TRIM34 readthrough	2.81314	3.41133	-1.51381	4.68 ^{E-06}	3.44 ^{E-06}
ADCECRS.3438_C1_s_at	ENS000000216490 ENS000000268173 OTTTHUMG000000150640 OTTTHUMG000000183373	5296 10437	<i>IFI30</i> <i>PIK3R2</i>	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}
ADCECRS.7753_C1_s_at	ENS000000091490 OTTTHUMG000000160331	23231	<i>SEL1L3</i>	Sel-1 suppressor of lin-12-like 3 (<i>C. elegans</i>)	4.38858	4.98653	-1.51357	2.18 ^{E-07}	1.39 ^{E-05}
ADCECRS.13723_C1_s_at	ENS000000187754 OTTTHUMG00000020185	10507	<i>SEMA4D</i>	Sema domain, immunoglobulin domain (lg), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4D	5.2214	5.82003	-1.5135	2.96 ^{E-14}	6.09 ^{E-12}
ADCECRS.28662_C1_s_at	ENS000000100219 OTTTHUMG000000151094	7494	<i>XBP1</i>	X-box binding protein 1	4.17897	4.77664	-1.51327	3.13 ^{E-06}	0.00108381
ADCECRS.25981_C1_s_at	ENS000000227039 OTTTHUMG00000090253	10050746	<i>ITGB2-AS1</i>	ITGB2 antisense RNA 1	5.55908	6.15666	-1.51318	1.68 ^{E-12}	2.56 ^{E-10}
ADCECRS.17672_C1_at	ENS000000084154 OTTTHUMG00000090700	5026	<i>P2RX5</i>	Purinergic receptor P2X, ligand-gated ion channel, 5	3.43864	4.03608	-1.51303	3.50 ^{E-06}	3.26 ^{E-09}
ADCECRS.32046_C1_at	ENS000000132256 OTTTHUMG00000066893	85363	<i>TRIM5</i>	Tripartite motif containing 5	3.99695	4.59392	-1.51253	3.67 ^{E-07}	2.21 ^{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)
ADXC.17390.C1_at	ENS00000204252 ENS00000206292 ENS00000230141 ENS00000231558 ENS00000232957 ENS00000232962 ENS00000235744 OTTTHUMG00000112644 OTTTHUMG00000031211 OTTTHUMG00000031511 OTTTHUMG00000040242 OTTTHUMG00000149105 OTTTHUMG00000149362 OTTTHUMG00000149623	3111	HLA-DQA	Major histocompatibility complex, class II, DQ alpha	3.45379	4.05019	-1.51194	2.33 ^{E-07}	1.47 ^{E-05}
ADXC.138.C20-a_s_at	ENS000001166710 OTTTHUMG00000131247	567	B2M	Beta-2-microglobulin	3.64376	4.24012	-1.5119	2.40 ^{E-16}	6.90 ^{E-14}
ADXC.25371.C1-a_s_at	ENS000001166750 OTTTHUMG00000179858	162394	SLFN5	Schlafen family member 5	5.30949	5.90575	-1.5118	4.82 ^{E-08}	3.54 ^{E-06}
ADXC.14637.C1-a_s_at	ENS00000048740 OTTTHUMG0000017668	10659	CELF2	CUGBP, Elav-like family member 2	4.38021	4.97646	-1.51179	1.78 ^{E-09}	1.77 ^{E-07}
ADXC.409.C46_s_at	ENS000001159417 OTTTHUMG00000153242	9669	EIF5B	Eukaryotic translation initiation factor 5B	5.90573	6.50096	-1.51071	0.000519172	0.010375
ADXC.10433.C2_s_at	ENS00000050730 OTTTHUMG00000132969	79931	TNIP3	TNFAIP3 interacting protein 3	7.1813	7.77623	-1.51039	2.87 ^{E-09}	2.72 ^{E-07}
ADXCAD.24936_s_at	ENS000000103522 OTTTHUMG00000131675	50615	IL21R	Interleukin 21 receptor	3.41336	4.0078	-1.50988	7.20 ^{E-13}	1.19 ^{E-10}
ADXC.12444.C1_s_at	ENS000000107951 OTTTHUMG00000118960	83937	RASSF4	Ras association (RalGDS/AF-6) domain family member 4	5.58961	6.18946	-1.50926	1.19 ^{E-07}	8.04 ^{E-05}
ADXC.7439.C1_at	ENS000000116514 OTTTHUMG00000004013	127544	RNF19B	Ring finger protein 19B	6.97816	7.57176	-1.50901	8.83 ^{E-07}	4.82 ^{E-05}
ADXC.7875.C1_at	ENS000000204487 ENS000000206437 ENS000000223448 ENS000000227507 ENS000000231314 ENS000000236237 ENS000000236925 ENS000000238114 OTTTHUMG00000031136 OTTTHUMG00000031416 OTTTHUMG00000040405 OTTTHUMG00000148787 OTTTHUMG00000149004 OTTTHUMG00000149287 OTTTHUMG00000149518 OTTTHUMG00000149956	4050	LTB	Lymphotoxin beta (TNF superfamily, member 3)	5.83849	6.43183	-1.50874	9.10 ^{E-15}	2.02 ^{E-12}
ADXC.4210.C1_at	ENS000000110031 OTTTHUMG00000167466	9404	LPXN	Leupaxin	4.48465	5.07777	-1.5085	6.55 ^{E-11}	8.00 ^{E-09}
ADXC.22967.C1_at	ENS00000139899 OTTTHUMG00000171315	64386	CBLN3	Cerebellin 3 precursor	4.72925	5.32183	-1.50794	2.08 ^{E-09}	2.03 ^{E-07}
ADXC.10150.C1_at	—	—	—	—	2.63251	3.2245	-1.50733	2.87 ^{E-06}	0.000136481
ADXC.5919.C1_x_at	ENS00000008517 OTTTHUMG00000167498	9235	IL32	Interleukin 32	9.38765	9.97945	-1.50713	6.59 ^{E-15}	1.50 ^{E-12}
ADXL.CEC.9139.C1_at	ENS000001181631 OTTTHUMG00000155745	53829	P2RY13	Purinergic receptor P2Y, G-protein coupled, 13	4.94806	5.53975	-1.507	1.95 ^{E-09}	1.92 ^{E-07}

(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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADDEC.18512.C1_s_at	ENS00000127951 OTTHUMG00000130681	10875	<i>FGL2</i>	Fibrinogen-like 2	5.26164	5.8831	-1.50677	1.40 ^{E-10}	1.63 ^{E-08}
ADDEC.7439.C1_x_at	ENS00000116514 OTTHUMG00000004013	127544	<i>RNF19B</i>	Ring finger protein 19B	7.01813	7.60949	-1.50666	8.31 ^{E-07}	4.57 ^{E-05}
ADDEC.30545.C1_at	ENS00000146094 OTTHUMG00000130850	79930	<i>DOK3</i>	Docking protein 3	5.78388	6.37515	-1.50657	2.09 ^{E-10}	2.38 ^{E-08}
ADDEC.5050.C1_at	ENS00000164099 OTTHUMG00000161166	8492	<i>PRSS12</i>	Protease, serine, 12 (neutrypsin, motopsin)	3.19981	3.79105	-1.50654	0.00113347	0.018384
ADDEC.7295.C1_at	ENS00000254087 OTTHUMG0000044345	4067	<i>L1YN</i>	Vyee-1 Yamaguchi sarcoma viral related oncogene homolog	2.75076	3.34196	-1.5065	1.69 ^{E-08}	1.39 ^{E-06}
ADDECADA.3464_at	—	—	—	—	2.86157	3.45234	-1.50604	1.16 ^{E-13}	2.15 ^{E-11}
ADDEC.14159.C1_s_at	ENS00000106948	80709	<i>AKNA</i>	AT-hook transcription factor	4.17895	4.76946	-1.50578	0.00010569	0.00299432
ADXPCEC.161.C17_x_at	ENS00000206435 ENS00000206450 ENS00000206452 ENS00000223532 ENS00000224608 ENS00000228299 ENS00000228964 ENS00000232126 ENS00000234745 ENS00000237022 OTTHUMG00000311153 OTTHUMG00000314335 OTTHUMG00000365662 OTTHUMG0000037240 OTTHUMG0000048565 OTTHUMG0000049247 OTTHUMG0000049248 OTTHUMG0000049478 OTTHUMG0000049943 OTTHUMG0000049955	3106 3107	<i>HLA-B</i> <i>HLA-C</i>	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}
ADDEC.8403.C1_at	ENS0000012889 OTTHUMG00000102082	2185	<i>PTK2B</i>	Protein tyrosine kinase 2 beta	5.25717	5.84684	-1.5049	1.12 ^{E-16}	3.56 ^{E-14}
ADDECBS.19227_s_at	ENS00000181800 OTTHUMG0000017669	414196	<i>CEL2-AS1</i>	CEL2 antisense RNA 1	3.00391	3.593	-1.5043	6.86 ^{E-07}	3.85 ^{E-05}
ADDEC.7609.C5_s_at	ENS00000128951 OTTHUMG00000172155	1854	<i>DUT</i>	Deoxyuridine triphosphatase	7.14391	7.73186	-1.50311	0.000176311	0.00458895
ADDEC.28196.C1_at	ENS00000137403 ENS00000204642 ENS00000206509 ENS00000229698 ENS00000235220 ENS00000237508 OTTHUMG00000004783 OTTHUMG00000311156 OTTHUMG00000314338 OTTHUMG00000411181 OTTHUMG0000048884 OTTHUMG0000049164	3134	<i>HLA-F</i>	Major histocompatibility complex, class I, F	3.95414	4.54204	-1.50305	2.37 ^{E-08}	2.30 ^{E-07}
ADDECAD.15610_s_at	ENS00000157654 ENS00000241978 OTTHUMG00000156811 OTTHUMG00000156812	11217 445815	<i>AKAP2</i> <i>PALM2-AKAP2</i>	A kinase (PRKA) anchor protein 2 PALM2-AKAP2 readthrough	5.54727	6.13424	-1.5021	0.00360816	0.0407665
ADDECAD.14381_at	ENS00000170542 OTTHUMG0000014131	5272	<i>SERPINB9</i>	Serpin peptidase inhibitor, clade B (ovalbumin), member 9	6.06739	6.65417	-1.50189	7.28 ^{E-07}	4.05 ^{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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDR Positive)	P	P (FDR)
ADXCNTD1.8414_at	ENS00000140968 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	ENS00000108691 OTTHUMG00000132887	6347	CCL2	Chemokine (C-C motif) ligand 2	4.63688	5.22338	-1.5016	4.37 ^{E-10}	4.76 ^{E-08}
ADXEC.11189.C30_x_at	ENS00000211675 ENS00000254709 OTTHUMG00000151218 OTTHUMG00000165670	3537 100423062	IGLC1 IGLL5	Immunoglobulin lambda constant 1 (M α g marker) Immunoglobulin lambda-like polypeptide 5	4.7742	5.35981	-1.50067	1.73 ^{E-09}	1.73 ^{E-07}
ADXEC.3716.C1_s_at	ENS000000091483 OTTHUMG00000139597	2271	FH	Fumarate hydratase	4.36579	4.95095	-1.50021	6.46 ^{E-06}	0.00199852
ADXEC.20273.C1_s_at	ENS00000095585 ENS00000262509 OTTHUMG00000118827 OTTHUMG00000182227	29760	BLNK	B-cell linker	3.28069	3.86383	-1.50019	2.76 ^{E-07}	1.71 ^{E-06}
ADXEC.6547.C1_at	ENS00000198771 OTTHUMG00000135318	92241	RCS1	RCS1 domain containing 1	2.80294	3.38799	-1.5001	6.91 ^{E-08}	4.92 ^{E-06}
ADXEC.2639.C1_at	ENS00000130635 OTTHUMG00000120891	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	ENS00000130508 OTTHUMG00000159697	7837	PXDN	Peroxidase homolog (<i>Drosophila</i>)	7.16843	6.58114	1.50242	2.76 ^{E-07}	1.71 ^{E-06}
ADXEC.2115.C1_at	ENS00000162545 OTTHUMG00000102837	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	ENS00000038427 OTTHUMG00000131321	1462	VCAN	Versican	8.20478	7.51468	1.50535	1.66 ^{E-07}	1.08 ^{E-06}
ADXPCC.7986.C1_at	—	3164	NRAA1	Nuclear receptor subfamily 4, group A, member 1	7.8951	7.30449	1.50588	3.21 ^{E-06}	0.00015055
ADXEC.23162.C1_at	ENS00000137801 OTTHUMG00000133665	7057	THBS1	Thrombospondin 1	8.50406	7.91329	1.50605	1.36 ^{E-05}	0.000632503
ADXEC.2011.C1-a_s_at	ENS00000137801 OTTHUMG00000133665	7057	THBS1	Thrombospondin 1	7.04127	6.44387	1.50671	5.20 ^{E-06}	0.000228186
ADXEC.4452.C1_s_at	ENS00000166033 OTTHUMG0000019186	5654	HTRA1	HtrA serine peptidase 1	7.45788	6.86483	1.50843	4.21 ^{E-08}	3.13 ^{E-06}
ADXCNTD1.6318_at	ENS00000165474 OTTHUMG00000165113	2706	GJB2	Gap junction protein, beta 2, 26 kDa	6.39062	5.79744	1.50857	0.00107151	0.0176431
ADXEC.26082.C1_s_at	ENS00000099953 OTTHUMG00000150742	4320	MMP11	Matrix metalloproteinase 11 (stromelysin 3)	7.31721	6.72401	1.50859	0.000320306	0.00721671
ADXEC.823.C2_s_at	ENS000001186847 ENS00000226145 OTTHUMG00000159171 OTTHUMG00000133426	3861	KRT14	Keratin 14	6.44685	5.84772	1.5148	0.00134913	0.0208124
ADXEC.10326.C1_at	ENS00000147257 OTTHUMG00000122448	2719	GPC3	Glypican 3	3.34438	2.745	1.51507	3.74 ^{E-06}	0.0012648
ADXEC.3715.CB2_x_at	ENS00000108821 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	ENS00000147257 OTTHUMG00000122448	2719	GPC3	Glypican 3	3.32792	2.72295	1.52095	2.29 ^{E-06}	0.00083115
ADXCAD.6247_x_at	ENS00000131711 OTTHUMG00000100952	4131	MAP1B	Microtubule-associated protein 1B	4.4032	3.79709	1.52215	9.00 ^{E-07}	4.88 ^{E-06}
ADXEC.18311.C1_s_at	ENS00000187955 OTTHUMG00000149877	7373	COL1A1	Collagen, type XV, alpha 1	4.00066	3.39386	1.52288	1.06 ^{E-06}	5.66 ^{E-06}
ADXEC.2446.C1_s_at	ENS00000144063 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)
ADXC.5310.C1_s_at	ENS00000163359 OTTHUMG00000150020	1293	COL6A3	Collagen, type VI, alpha 3	6.60048	5.9926	1.52401	5.08 ^{E-05}	0.00164365
ADXC.679.C1_s_at	ENS000000081853 ENS0000000204956 ENS0000000240184 ENS0000000240764 ENS0000000242419 ENS0000000253159 ENS0000000253305 ENS0000000253485 ENS0000000253537 ENS0000000253731 ENS0000000253846 ENS0000000253910 ENS0000000259653 ENS0000000254122 ENS0000000254221 ENS0000000254245 ENS0000000261934 ENS0000000262209 ENS0000000262576 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-05}
ADXC.5091.C2_s_at	ENS000000118523 OTTHUMG00000115573	1490	CTGF	Connective tissue growth factor	9.30794	8.69914	1.52498	1.88 ^{E-05}	0.000702362
ADXC.8706.C1_s_at	ENS000000152288 ENS000000262655 OTTHUMG00000165751 OTTHUMG00000181576	10418	SPON1	Spondin 1, extracellular matrix protein	5.19453	4.58418	1.52662	1.11 ^{E-07}	7.56 ^{E-05}
ADXC.12292.C1_at	ENS000000156535 OTTHUMG00000115040	135228	CD109	CD109 molecule	4.52579	3.91504	1.52705	8.91 ^{E-07}	4.85 ^{E-05}
ADXCAD.21682_s_at	ENS000000038427 OTTHUMG00000131321	1462	VCAN	Versican	6.97476	6.36109	1.53014	1.70 ^{E-05}	0.000644035
ADXC.2446.C2_at	ENS000000144063 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
ADXC.10090.C1_at	ENS000000134909 OTTHUMG00000165774	9743	ARHGAP32	Rho GTPase activating protein 32	5.4659	4.85497	1.53148	1.46 ^{E-07}	9.74 ^{E-05}
ADXC.8092.C1_s_at	—	—	—	—	5.86387	5.2482	1.53227	2.19 ^{E-07}	1.40 ^{E-05}
ADXC.5091.C1_s_at	ENS000000118523 OTTHUMG00000115573	1490	CTGF	Connective tissue growth factor	6.90153	6.28471	1.53349	2.64 ^{E-05}	0.000939203

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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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADXC-4995.C1_s_at	—	—	—	—	9.25918	8.63663	1.53959	4.63 ^{E-07}	2.71 ^{E-05}
ADXC-1186.C3_at	—	—	—	—	9.0131	8.38755	1.5428	0.00386913	0.0428133
ADXC-31194.C1_s_at	ENS00000144810 OTTTHUMG00000148669	1295	COL8A1	Collagen, type VIII, alpha 1	6.84868	6.22181	1.54421	0.000411994	0.00872587
ADXC-2177.C5-a_s_at	ENS00000134775 OTTTHUMG00000182381	80206	FHOD3	Formin homology 2 domain containing 3	4.57732	3.94789	1.54696	0.00018306	0.00465789
ADXC-4573.C1-a_s_at	ENS00000050165 OTTTHUMG00000165709	27122	DKK3	Dickkopf WNT signaling pathway inhibitor 3	5.68713	5.05659	1.54814	4.98 ^{E-06}	0.000220209
ADXC-20484.C1_at	ENS00000140937	1009	CDH11	Cadherin 11, type 2, OB-cadherin (osteoblast)	6.26948	5.63778	1.54939	3.73 ^{E-08}	2.81 ^{E-06}
ADXC-716.C1_s_at	ENS00000115461 OTTTHUMG00000133058	3488	IGFBP5	Insulin-like growth factor binding protein 5	8.83455	8.20176	1.55055	1.76 ^{E-05}	0.000664677
ADXCAD.1745_s_at	ENS00000133110 OTTTHUMG0000016751	10631	POSTN	Perostin, osteoblast specific factor	7.68107	7.04816	1.55069	3.97 ^{E-06}	0.000180044
ADXC-4684.C1_at	ENS00000213190 OTTTHUMG00000035160	10962	MLLT11	Myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, <i>Drosophila</i>), translocated to, 11	6.60293	5.97001	1.5507	0.000166659	0.00432061
ADXC-14670.C3_at	ENS00000138162 OTTTHUMG0000019181	10579	TACC2	Transforming, acidic coiled-coil containing protein 2	8.77267	8.1328	1.55818	3.52 ^{E-08}	2.65 ^{E-05}
ADXC-14012.C1_s_at	ENS00000152377 OTTTHUMG00000129157	6695	SPOCK1	Spock/osteonectin, ovcv and kazal-like domains proteoglycan (testican) 1	4.6098	3.96766	1.56065	8.52 ^{E-07}	4.68 ^{E-05}
ADXC-9628.C1_at	—	—	—	—	7.96442	7.32116	1.56186	0.000205971	0.00512294
ADXCAD.17188_s_at	ENS00000038427 OTTTHUMG00000131321	1462	VCAN	Versican	7.49486	6.85147	1.562	5.26 ^{E-05}	0.00169081
ADXC-8730.C1_at	ENS00000113140 OTTTHUMG00000130122	6678	SPARC	Secreted protein, acidic, cysteine-rich (osteonectin)	5.33696	4.69116	1.5646	1.55 ^{E-05}	0.000594706
ADXC-5783.C3_at	ENS00000145423 OTTTHUMG00000161559	6423	SFRP2	Secreted frizzled-related protein 2	6.66635	6.01753	1.56789	1.42 ^{E-05}	0.000649962
ADXC-8089.C1_at	ENS00000154553	27295	PDLIM3	PDZ and LIM domain 3	3.75771	3.09976	1.57783	3.89 ^{E-08}	2.91 ^{E-05}
ADXC-2007.CB1_x_at	—	1278	COL1A2	Collagen, type I, alpha 2	10.5618	9.90281	1.57893	2.08 ^{E-08}	1.67 ^{E-05}
ADXC-2356_x_at	ENS00000188219 ENS00000196604 ENS00000250852 OTTTHUMG00000153536 OTTTHUMG00000153628	445582 728378	POTEE POTEF	POTE ankryrin domain family, member E POTE ankryrin domain family, member F	5.40113	4.73913	1.58228	0.00178296	0.0253904
ADXC-11777.C1_at	ENS00000156535 OTTTHUMG0000015040	135228	CD109	CD109 molecule	3.92596	3.26214	1.58428	3.83 ^{E-06}	0.000174204
ADXC-9153.C1_at	ENS00000106819 OTTTHUMG00000120227	54829	ASPN	Asporin	6.20075	5.53179	1.58993	8.94 ^{E-07}	4.86 ^{E-05}
ADXC-3805.C1_x_at	ENS00000013588 OTTTHUMG00000168710	9052	GPRC5A	G protein-coupled receptor, family C, group 5, member A	6.21978	5.54974	1.59111	6.01 ^{E-06}	0.000258989
ADXC-6819.C2_at	ENS00000185479 OTTTHUMG00000169593	3854	KRT6B	Keratin 6B	5.07303	4.4027	1.59144	0.000691341	0.0128258
ADXC-18997.C1_s_at	ENS00000176641 OTTTHUMG00000132774	220441	RNF152	Ring finger protein 152	5.1647	4.49194	1.59413	1.35 ^{E-06}	7.07 ^{E-05}
ADXC-34426.C1_x_at	ENS00000104490 OTTTHUMG00000164876	83988	NCALD	Neurocalcin delta	6.02504	5.3516	1.59487	0.00130069	0.0202718
ADXC-2007.CB1_at	—	1278	COL1A2	Collagen, type I, alpha 2	10.0905	9.41681	1.59517	7.06 ^{E-07}	3.93 ^{E-05}
ADXC-2011.C1_s_at	ENS00000137801 OTTTHUMG00000133665	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	DDIR Negative (mean)	DDIR Positive (mean)	Fold Change (DDIR Negative/DDIR Positive)	P	P (FDR)
ADDEC-3805.C1_at	ENS00000013588 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
ADDEC-8917.C1_s_at	ENS000000060718 OTTHUMG0000010872	1301	COL11A1	Collagen, type XI, alpha 1	5.51833	4.82141	1.62104	1.26 ^{E-05}	0.000497687
ADDEC-159.CB2_s_at	ENS000000163017 OTTHUMG00000129813	72	ACTG2	Actin, gamma 2, smooth muscle, enteric	8.25579	7.55284	1.62783	0.00336574	0.0389206
ADDEC-3426.C1_at	ENS000000104430 OTTHUMG00000164876	83988	NCALD	Neurocalcin delta	6.52002	5.81381	1.63151	0.00215697	0.028946
ADDECADA.15978.at	ENS000000133110 OTTHUMG0000016751	10631	POSTN	Perostin, osteoblast specific factor	4.175	3.46534	1.63542	2.05 ^{E-09}	2.01 ^{E-07}
ADDECAD.22446_s_at	ENS000000170577 OTTHUMG00000152421	10736	SKX2	SKX homeobox 2	7.12574	6.41207	1.63996	0.00203424	0.0278754
ADDEC-3415.C1_s_at	ENS000000133110 OTTHUMG0000016751	10631	POSTN	Perostin, osteoblast specific factor	6.81472	6.09846	1.64292	1.12 ^{E-06}	5.93 ^{E-05}
ADDEC-13772.C1_at	ENS000000184828 OTTHUMG00000180322	201501	ZBTB7C	Zinc finger and BTB domain containing 7C	5.52516	4.80225	1.6505	0.000335408	0.00750228
ADDECAD.17850.at	—	—	—	—	4.34139	3.61843	1.65056	0.000900326	0.0186206
ADDEC-21625.C1_s_at	ENS000000164692 OTTHUMG00000148675	1278	COL1A2	Collagen, type I, alpha 2	5.68957	4.95734	1.66167	1.66 ^{E-07}	1.08 ^{E-05}
ADDEC-298.C2_s_at	ENS000000167244 ENS000000240801 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}
ADDECAD.6687.at	—	—	—	—	6.89192	6.14456	1.67872	2.32 ^{E-08}	1.83 ^{E-05}
ADDEC-5080.C2_at	ENS000000144810 OTTHUMG00000148669	1295	COL8A1	Collagen, type VIII, alpha 1	5.59182	4.84394	1.67932	8.72 ^{E-08}	6.08 ^{E-05}
ADDEC-15995.C1_at	ENS000000152377 OTTHUMG00000129157	6695	SPOCK1	Sparc/osteonectin, ovcv and kazal-like domains proteoglycan (testican) 1	4.50347	3.75469	1.68037	3.75 ^{E-08}	2.82 ^{E-05}
ADDECCEMUTR.4185_s_at	ENS000000038427 OTTHUMG00000131321	1462	VCAN	Versican	7.74793	6.99775	1.68199	5.95 ^{E-05}	0.00186183
ADDEC-8917.C1_at	ENS000000060718 OTTHUMG0000010872	1301	COL11A1	Collagen, type XI, alpha 1	5.39171	4.64064	1.68304	0.000278483	0.00644271
ADDEC-9217.C1-a_s_at	—	—	—	—	7.37404	6.61365	1.69394	3.58 ^{E-06}	0.000164778
ADDEC-25223.C1_at	ENS000000137745 ENS000000262325 OTTHUMG00000165850	4322	MMP13	Matrix metalloproteinase 13 (collagenase 3)	5.5192	4.75493	1.69851	3.14 ^{E-05}	0.00108627
ADDEC-298.C3_s_at	ENS000000167244 ENS000000240801 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}
ADDEC-8579.C2_s_at	ENS000000197614 OTTHUMG00000168703	8076	MFAP5	Microfibrillar associated protein 5	7.31694	6.5356	1.71873	4.81 ^{E-05}	0.00157199
ADDEC-18200.C1_at	ENS000000197614 OTTHUMG00000168703	8076	MFAP5	Microfibrillar associated protein 5	7.63057	6.83318	1.73795	8.59 ^{E-06}	0.0003556
ADDEC-823.C1_s_at	ENS000000128422 ENS000000173801 OTTHUMG00000133505	3728 3872	JUP KRT17	Junction plakoglobin Keratin 17	9.83313	9.03249	1.74187	3.29 ^{E-05}	0.00113386
ADDEC-3014.C5_s_at	ENS000000149591 OTTHUMG00000167067	6876	TAGLN	Transgelin	8.43101	7.62493	1.74846	0.000167142	0.00432948
ADDECCEMUTR.5466_s_at	ENS000000176641 OTTHUMG00000132774	22041	RNF152	Ring finger protein 152	3.82722	3.01331	1.75797	1.71 ^{E-07}	1.11 ^{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.21861.C1_s_at	ENS000000167244 OTTTHUMG00000009395	3481 723961	IGF2 INS-IGF2	Insulin-like growth factor 2 (somatomedin A) INS-IGF2 readthrough	10.148	9.32616	1.76769	1.86 ^{±08}	1.51 ^{±06}
ADXECAD.20866_at	ENS000000129965 ENS000000167244 OTTTHUMG00000009395 OTTTHUMG000000166213	3481 723961	IGF2 INS-IGF2	Insulin-like growth factor 2 (somatomedin A) INS-IGF2 readthrough	7.78117	6.9562	1.7715	3.48 ^{±08}	2.63 ^{±06}
ADXECAD.20866_x_at	ENS000000129965 ENS000000167244 OTTTHUMG00000009395 OTTTHUMG000000166213	3481 723961	IGF2 INS-IGF2	Insulin-like growth factor 2 (somatomedin A) INS-IGF2 readthrough	7.84451	7.00865	1.78492	2.32 ^{±08}	1.83 ^{±06}
ADXEC.15009.C1_at	ENS000000164176 OTTTHUMG000000119047	10085	EDIL3	EGF-like repeats and discoidin I-like domains 3	3.66375	2.82545	1.78794	3.43 ^{±08}	2.60 ^{±06}
ADXEC.6924.C1_at	ENS000000169604 OTTTHUMG000000129575	84168	AMXR1	Anthrax toxin receptor 1	7.13904	6.29525	1.79476	1.80 ^{±07}	1.17 ^{±06}
ADXECNTD1.3932_s_at	ENS000000152377 OTTTHUMG000000129157	6695	SPOCK1	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 1	5.80313	4.92105	1.84304	1.56 ^{±07}	1.03 ^{±06}

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, PAGI, APOL1, C19orf66, KLK1, 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, SPI100, JAK2, COL1A2, IGHG1, GPR183, TNFAIP3, NRIH3, CD8A, CIITA, APOBEC3G, IGf2, LILRB1, XAF1, CCL2, BTN3A3, TRIM34, RAC2, COL1A1, LPXN, CXCL11, C1QB, STAT1, IFIH1, TRIM5, SECTM1, ADAMDEC1, TRIM21, TAPBP, SAMHD1, TRAC, NLRCS, TNFRSF14, ITGAL, APOBEC3B, B2M, HMGB2, APOBEC3A, IGKC, SEL, PIK3CG, PTPN6, TAP2, CCL19, PSME1, AIM2, IRF8, CCR7, CYLD, GBP2, FCGR3A, CD38, IGLL5, GF1, XBP1, SERPINB9, KLRC2, LAIR1, SLAMF7, IL18, CD79A, FCR15, 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, PAGI, APOL1, C19orf66, KLK1, 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, SPI100, GPR171, CD3E, JAK2, GPC3, SIRPG, IGHG1, COL1A2, TNFAIP3, HERC6, GPR183, NRIH3, 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, NLRCS, TNFRSF14, APOBEC3B, ITGAL, B2M, HMGB2, APOBEC3A, OLR1, SNX10, IGKC, SEL, PIK3CG, RASAL3, CD2, PTPN6, TAP2, CCL19, PSME1, IRF8, AIM2, CD48, CCR7, IL21R, CYLD, CD109, GBP2, FCGR3A, IGLL5, CD38, GF11, SERPINB9, XBP1, IKZF1, KCNAB2, KLRC2, LAIR1, SLAMF7, IL18, NLRCS, FCR15, CD79A, IGSF6, HLA-DOB, PSMB9, WIPF1, IFIT3, HCL1, 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, GBPL, 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, KLK1, 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, AOA1, ALOX5, JAK3, TRIM22, TAP1, CCR1, ALPK1, LYZ, HAVCR2, ZBP1, IRF7, LTF, CYBB, LYN, HLA-A, PMAIP1, THEMIS2, MB21D1, ISG20, CD86, IGHG4, DDX58, APOL3, CFB, SPI100, JAK2, IGHG1, TNFAIP3, CASP1, CD8A, NRIH3, CIITA, APOBEC3G, IGf2, LILRB1, XAF1, CCL2, TRIM34, CXCL11, SERPINA1, C1QB, STAT1, HTRA1, IFIH1, TRIM5, TRIM21, ORM2, SAMHD1, NLRCS, TNFRSF14, ITGAL, APOBEC3B, B2M, APOBEC3A, HMGB2, OLR1, IGKC, PIK3CG, PTPN6, P2RX1, CCL19, PSME1, IRF8, AIM2, CD48, CCR7, CYLD, GBP2, IGLL5, GF11, 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, KLK1, 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, PLOG2, FCGR3B, JAK3, TAP1, 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, NLRCS, TNFRSF14, ITGAL, B2M, HMGB2, IGKC, SEL, RASAL3, PTPN6, CD2, CCL19, PSME1, AIM2, CCR7, CYLD, FCGR3A, CD38, IGLL5, GF11, 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, NLRCS, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, C1QC, CD74, HMGB2, PLSCR1, IGKC, HLA-DRA, PAG1, SEL, PTPN6, KLK1, CCL19, PSME1, CD300E, AIM2, IFITM1, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, CCR2, IGLL5, CD38, CD4, SERPINB9, GF11, FYN, XBP1, ICAM1, IRF1, LAIR1, SPN, RBCK1, SLAMF7, CD40, CD79A, FCRL5, PSMB9, LGALS9, CLEC2D, WIPF1, PIK3AP1, HLA-B, IGHA1, MEF2C, CXCL13, PLOG2, 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, IGF2AK2, VCAM1, CD5, HLA-C, PTAFR, OAS3, HLA-DPB1, C1QB, STAT1, GBP5, IFIH1, IGHM, APOBEC3D, TRIM5, ITGB2, TRIM21, SAMHD1, OAS2, CTSS, NLRCS, RSAD2, NCF2, OAS1, IFI30, APOBEC3B, B2M, C1QC, APOBEC3A, MX1, HMGB2, PLSCR1, IGKC, HLA-DRA, PIK3CG, APOL1, PTPN6, C19orf66, KLK1, CCL19, CASP4, PSME1, CD300E, IRF8, AIM2, IFITM1, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, GBP2, IGLL5, SERPINB9, GF11, FYN, ICAM1, IRF1, PTK2B, CCL18, KLRC2, SLAMF7, PSMB9, LGALS9, PIK3AP1, HLA-B, CXCL16, IFIT3, IGHA1, IFIT2, GZMB, PLOG2, 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, NLRCS, LILRB2, RSAD2, TNFRSF14, B2M, CD3D, C1QC, CD74, HMGB2, PLSCR1, IGKC, HLA-DRA, PAG1, RASAL3, PTPN6, CD2, KLK1, CCL19, PSME1, AIM2, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, CCR2, IGLL5, CD38, CD4, GF11, FYN, XBP1, ICAM1, PIK3AP1, HLA-B, HCLS1, IGHA1, MEF2C, RBCK1, IL18, CD40, CD79A, FCRL5, PSMB9, LGALS9, WIPF1, PIK3AP1, HLA-B, HCLS1, IGHA1, MEF2C, CXCL13, PLOG2, 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, NLRCS, RSAD2, TNFRSF14, B2M, CD3D, C1QC, CD74, HMGB2, PLSCR1, IGKC, HLA-DRA, PAG1, PTPN6, KLK1, CCL19, PSME1, AIM2, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, CCR2, IGLL5, CD38, CD4, GF11, FYN, XBP1, RBCK1, CD40, CD79A, FCRL5, PSMB9, LGALS9, WIPF1, PIK3AP1, HLA-B, IGHA1, MEF2C, PLOG2, BIRC3, STAP1, JAK3, HLA-E, FCER1G, PTPRC, C3, LAX1, HLA-DMB, 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: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, OAS2, TNFRSF14, APOBEC3B, ITGAL, B2M, C1QC, CD74, APOBEC3A, MX1, PLSCR1, IGKC, PIK3CG, PTPN6, C19orf66, KLRK1, CCL19, AIM2, IFITM1, TRAF3, HLA-DRB1, FCGR3A, COR2, SERPINB9, FYN, XBP1, ICAM1, CXCL9, IRF1, PTK2B, KIRC2, SPN, SLAMF7, CD40, LGALS9, WIPF1, APBB1P, HLA-B, IFIT3, IFIT2, GZMB, PLOG2, 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, COR7, TRAF3, HLA-DRB1, COR2, IGLL5, CD4, SERPINB9, GFIL1, XBP1, ICAM1, CXCL9, IRF1, SPN, IL18, CD40, PSMB9, LGALS9, WIPF1, HLA-B, CXCL16, IFIT3, IGH1, MEF2C, IFIT2, CXCL13, PLOG2, 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, COR7, TRAF3, HLA-DRB1, COR2, IGLL5, CD4, SERPINB9, GFIL1, XBP1, ICAM1, CXCL9, IRF1, SPN, IL18, CD40, PSMB9, LGALS9, WIPF1, HLA-B, CXCL16, IFIT3, IGH1, MEF2C, IFIT2, CXCL13, PLOG2, 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, APBB1P, IGH1, MEF2C, DOCK8, PLOG2, 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, COR7, TRAF3, HLA-DRB1, COR2, IGLL5, CD4, SERPINB9, GFIL1, XBP1, ICAM1, CXCL9, IRF1, CCL18, SPN, IL18, CD40, PSMB9, LGALS9, WIPF1, HLA-B, CXCL16, IFIT3, IGH1, MEF2C, IFIT2, CXCL13, PLOG2, 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, IL12RB1, CCL2, IGLC2, VCAM1, IDO1, RAC2, CCL5, PTAFA, HLA-DPB1, IGHM, ITGB2, TRAC, IL12RB2, RSAD2, TNFRSF14, OAS1, ITGAL, B2M, CD3D, CD74, PLSOR1, IGKC, HLA-DRA, PIK3CG, PAG1, RASAL3, PTPN6, CD2, KLK1, CCL19, MS4A1, CCR7, HLA-DPA1, IL21R, CYLD, HLA-DRB1, CCR2, IGL5, CD38, CD4, XBP1, FYN, IKZF1, ICAM1, IRF1, PTK2B, RHOH, BANK1, THBS1, SPN, SLAMF7, NLRC3, IL18, CD40, CD79A, BCL11B, LGALS9, APBB1IP, IGHAI1, MEF2C, DOCK8, PLOG2, 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, SPI100, JAK2, CSF1, IL12RB1, CCL8, TNFSF13B, SIRPG, IGHG1, BLNK, GPR183, TNFAIP3, CD8A, IGF2, IL12RB1, CCL2, IGLC2, VCAM1, IDO1, RAC2, CCL5, HLA-DPB1, IGHM, ITGB2, TRAC, IL12RB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, IGKC, HLA-DRA, PIK3CG, PAG1, RASAL3, PTPN6, CD2, KLK1, CCL19, MS4A1, CCR7, HLA-DPA1, IL21R, CYLD, HLA-DRB1, CCR2, IGL5, CD38, CD4, XBP1, FYN, IKZF1, ICAM1, IRF1, PTK2B, RHOH, BANK1, SPN, SLAMF7, NLRC3, IL18, CD40, CD79A, BCL11B, LGALS9, APBB1IP, IGHAI1, MEF2C, DOCK8, PLOG2, JAK3, PLA2G2D, HLA-E, FCER1G, PTPRC, ATM, HLA-DOA, LAX1, HLA-DMB, IKZF3, HAVCR2
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, IL12RB1, CCL2, IGLC2, VCAM1, IDO1, RAC2, CCL5, HLA-DPB1, IGHM, ITGB2, TRAC, IL12RB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, IGKC, HLA-DRA, PIK3CG, PAG1, RASAL3, PTPN6, CD2, KLK1, CCL19, MS4A1, CCR7, HLA-DPA1, IL21R, CYLD, HLA-DRB1, CCR2, IGL5, CD38, CD4, XBP1, FYN, IKZF1, ICAM1, IRF1, PTK2B, RHOH, BANK1, SPN, SLAMF7, NLRC3, IL18, CD40, CD79A, BCL11B, LGALS9, APBB1IP, IGHAI1, MEF2C, DOCK8, PLOG2, 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, SPI100, JAK2, CSF1, IL12RB1, CCL8, TNFSF13B, IL10RA, TNFAIP3, NRIH3, C1QA, IGHG1, LCP2, TNFAIP3, NRIH3, KLHL6, IGLC2, EIF2AK2, VCAM1, TRAF1, COL1A1, CCL5, HLA-C, CXCL11, POSTN, PTAFA, IL24, OAS3, HLA-DPB1, STAT1, GBP5, TRIM5, PXDN, TRIM21, SAMHD1, OAS2, NLRC5, RSAD2, OAS1, TNFRSF14, IFI30, B2M, CD74, MX1, PLSOR1, HLA-DRA, PTPN6, C19orf66, CSF2RB, CCL19, PSMEL, 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, SPI100, JAK2, CSF1, IL12RB1, CCL8, TNFSF13B, IL10RA, TNFAIP3, NRIH3, C1QA, IGHG1, LCP2, TNFAIP3, NRIH3, KLHL6, IGLC2, COL1A1, CCL5, HLA-C, CXCL11, POSTN, PTAFA, IL24, OAS3, HLA-DPB1, STAT1, GBP5, TRIM5, PXDN, TRIM21, SAMHD1, OAS2, NLRC5, RSAD2, TNFRSF14, OAS1, IFI30, B2M, CD74, MX1, HLA-DRA, PTPN6, CSF2RB, CCL19, PSMEL, 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, NRIH3, KLHL6, IGLC2, LPXN, HLA-DPB1, C1QB, IFI1, IGHM, TRIM5, ITGB2, CTSS, TRAC, RSAD2, CD3D, C1QC, IGKC, PLSOR1, HLA-DRA, PAG1, PTPN6, KLK1, RBC1, PSMEL, AIM2, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYB, FCGR3A, IGL5, CD38, CD4, FYN, NKG2A, FCRL5, CD79A, LGALS9, PSMB9, WIPF1, PIK3AP1, IGHAI1, MEF2C, PLOG2, 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, IFG2, IL1RB1, CCL2, IGLC2, VCAM1, IDO1, CCL5, RAC2, PTAFR, HLA-DPB1, IGHM, TRAC, IL1RB2, 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, XBPI, IRF1, BANK1, THBS1, SPN, IL18, CD40, LGALS9, IGHAI, 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, IFG2, IL1RB1, CCL2, IGLC2, VCAM1, IDO1, CCL5, RAC2, PTAFR, HLA-DPB1, IGHM, TRAC, IL1RB2, TNFRSF14, CD3D, CD74, IGKC, PLSCR1, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, IGLL5, CD38, CD4, FYN, XBPI, IRF1, BANK1, THBS1, SPN, IL18, CD40, LGALS9, IGHAI, MEF2C, STAP1, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, ATM, HLA-DOA, LAX1, IKZF3, HLA-DMB, 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, IL1RB1, KLHL6, IGLC2, LPXN, HLA-DPB1, IFIH1, IGHM, TRIM5, ITGB2, CTSS, TRAC, IL1RB2, RSAD2, CD3D, IGKC, PLSCR1, HLA-DRA, PAG1, PTPN6, KLRK1, PSMEL, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYN, FCGR3A, IGLL5, CD38, CD4, FYN, GF11, RBCK1, CD40, FCRL5, CD79A, LGALS9, PSMB9, PIK3AP1, WIPF1, IGHAI, MEF2C, PLOC2, 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, PSMEL, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, FYN, FCGR3A, IGLL5, CD38, CD4, FYN, GF11, RBCK1, FCRL5, CD79A, LGALS9, PSMB9, PIK3AP1, WIPF1, IGHAI, MEF2C, PLOC2, 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, IFG2, IL1RB1, CCL2, IGLC2, VCAM1, IDO1, CCL5, RAC2, HLA-DPB1, IGHM, TRAC, IL1RB2, TNFRSF14, CD3D, CD74, IGKC, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, CD38, CD4, IGLL5, FYN, XBPI, IRF1, BANK1, SPN, IL18, CD40, LGALS9, IGHAI, 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, IL1RB2, NCF2, MLT11, RSAD2, OAS1, IFI30, CD3D, MX1, CD74, PLSCR1, HLA-DRA, PAG1, CHST11, KLRK1, P2RX5, IFITM1, HLA-DPA1, TRAF3, HLA-DRB1, FYN, CCR2, CD4, SEMA4D, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, THBS1, RBCK1, SPN, CD40, CLEC2D, HLA-B, IGHAI, CXCL13, PLOC2, JAK3, PLEK, TRIM22, LTB, CCR1, LAX1, IRF7, CYBB, LTF, LYN, HLA-A, PMAIP1, THEMIS2, ISG20, IGHG4, PRKCB, SPI00, CD3E, GPR171, JAK2, GPC3, IGHG1, COL1A2, CD53, TNFAIP3, NR1H3, CD8A, CIITA, IGFBP5, SAMHD1, TRAC, NLRCS, TNFRSF14, COL1A1, CXCL11, POSTN, STAT1, HTRA1, TRIM5, TRIM21, IGF2, IL1RB1, XAF1, CCL2, TRIM34, TRAF1, DKK3, LPXN, ITGAL, CTGF, B2M, HMGB2, IGKC, CD2, PTPN6, CSF2RB, P2RX1, PSMEL, AIM2, IRF8, GPRCSA, CCR7, IL21R, CYLD, ZEB2, GBP2, CD109, BCL2A1, FCGR3A, IGLL5, CD38, GF11, XBPI, 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, NLRCS, 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, C1TS, 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, IGHAI, GZMB, CXCL13, PLCG2, JAK3, TRIM22, CCRI, 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, NRIH3, IGF2, LILRB1, CCL2, RAC2, COL1A1, LPXN, PDCD5, CXCL11, GRAP, C1QB, IFIH1, TRIM5, SECTM1, IGFBP5, TRAC, NLRCS, TNFRSF14, CTGF, B2M, HMGB2, IGKC, PIK3CG, PTPNG, CCL19, PSME1, AIM2, CCR7, CYLD, ZEB2, FCGR3A, CD38, IGLL5, GF11, XBPI, FGD2, IL18, CD79A, FCRL5, PSMB9, WIPF1, HCLSI, 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, PTPNG, CD2, KLRK1, CCL19, ZAP70, IFNG, CD86, IGHG4, CCR7, CD3E, JAK2, IL12RB1, HLA-DPA1, TNFSF13B, HLA-DRB1, SIRPG, IGHG1, CCR2, IGLL5, CD4, CD38, XBPI, FYN, GPR183, THBS1, IGF2, SPN, LILRB1, IL18, CCL2, CD40, IGLC2, LGALS9, VCAM1, CCL5, IGHAI, 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, NRIH3, CCL18, CITA, HLA-F, GBP1, CCL2, TRIM34, LGALS9, VCAM1, HLA-B, CCL5, HLA-C, PTAFR, OAS3, HLA-DPB1, GBP5, STAT1, HLA-E, TRIM22, TRIM5, TRIM21, OAS2, NLRCS, 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, IFI11, PLAC8, IL12RB1, IGHG1, TNFAIP3, CD8A, HERC5, APOBEC3G, LILRB1, GBP1, TRIM34, IGLC2, EIF2AK2, OAS3, STAT1, HTRA1, IFIH1, IGHM, TRIM5, APOBEC3D, SAMHD1, OAS2, NLRCS, RSAD2, OAS1, TNFRSF14, APOBEC3B, B2M, APOBEC3A, HMGB2, MX1, IGKC, PLSCR1, C19orf66, KLRK1, AIM2, IRF8, IFITM1, TRAF3, CCR2, IGLL5, CD4, CXCL9, IRF1, SPN, CD40, IFIT3, IGHAI, 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, PTPNG, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, SEMA4D, CD4, FYN, XBPI, ICAM1, IRF1, RHOH, SPN, NLRCS, 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, PTPNG, CD2, KLRK1, CCL19, ZAP70, IFNG, CD86, IGHG4, CCR7, CD3E, IL12RB1, HLA-DPA1, TNFSF13B, HLA-DRB1, SIRPG, IGHG1, CCR2, IGLL5, CD4, CD38, XBPI, FYN, GPR183, THBS1, IGF2, SPN, LILRB1, IL18, CCL2, CD40, IGLC2, LGALS9, VCAM1, CCL5, IGHAI, 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, PTPNG, KLRK1, CCL19, CCR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, SEMA4D, CD4, FYN, XBPI, ICAM1, IRF1, RHOH, SPN, NLRCS, IL18, BCL11B, LGALS9, APBB1IP, DOCK8, JAK3, HLA-E, PLA2G2D, FCER1G, PTPRC, HLA-DOA, LAX1, HLA-DMB, HAVCR2

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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, SPI00, JAK2, HLA-DPA1, HLA-DRB1, GBP2, ICAM1, IRF1, NRIH3, CIITA, HLA-F, GBP1, TRIM34, VCAM1, HLA-B, HLA-C, OAS3, PTAFR, HLA-DPB1, STAT1, HLA-E, TRIM22, TRIM5, TRIM21, OAS2, NLRCS5, 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, RAS2, HLA-DPB1, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, PIK3CG, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, COR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, CD4, FYN, XBPL, ICAM1, IRF1, RHOH, SPN, NLRCS3, 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, RAS2, HLA-DPB1, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, PIK3CG, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, COR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, CD4, FYN, XBPL, ICAM1, IRF1, RHOH, SPN, NLRCS3, 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, RAS2, HLA-DPB1, TRAC, LILRB2, RSAD2, TNFRSF14, ITGAL, B2M, CD3D, CD74, PIK3CG, HLA-DRA, PAG1, RASAL3, CD2, PTPN6, KLRK1, CCL19, COR7, HLA-DPA1, CYLD, HLA-DRB1, CCR2, CD4, FYN, XBPL, ICAM1, IRF1, RHOH, SPN, NLRCS3, 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, PLSCL1, 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, IGHAI, CXCL13, GZMB, PLCG2, FCGR3B, AOA, ALOX5, JAK3, TRIM22, TAP1, ALPK1, COR1, LYZ, HAVCR2, ZBP1, IRF7, CYBB, LTF, LYN, HLA-A, PMAIP1, THEMIS2, MB21D1, ISG20, CD86, IGHG4, LCP1, DDX58, CFB, APOL3, PRKCB, SPI00, JAK2, IGHG1, COL1A2, TNFAIP3, CASP1, NRIH3, CD8A, UBE2L6, HTRA1, IFIH1, TRIM5, ORM2, TRIM21, SAMHD1, NLRCS, 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, GF11, SERPINB9, XBP1, KLRCS2, 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, C1QC, HLA-DPB1, IL24, PTAFR, GBP5, ARHGAP32, IGHM, PXDN, ITGB2, CTSS, LILRB2, MLLT11, RSAD2, CD3D, C1QC, CD74, PLSCL1, HLA-DRA, PAG1, CHST11, KLRK1, SOD2, CD300E, CASP4, P2RX5, IFITM1, HLA-DPA1, TRAF3, HLA-DRB1, FYN, CCR2, CD4, SEMA4D, FYN, ICAM1, IRF1, CXCL9, CCL18, PTK2B, BANK1, THBS1, RHOH, RBOCK1, SPN, CD40, LGALS9, CLEC2D, PIK3AP1, HLA-B, IGHAI, 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, SPI00, CD3E, JAK2, GPC3, IGHG1, COL1A2, TNFAIP3, GPR183, CASP1, NRIH3, 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, NLRCS, ARHGAP15, TNFRSF14, ITGAL, CTGF, B2M, HMGB2, IGKC, SELL, PIK3CG, RASAL3, PTPN6, CCL19, PSME1, AIM2, GPRCSA, CCR7, CYLD, ZEB2, CD109, FCGR3A, IGLL5, CD38, GF11, SERPINB9, XBP1, LAIR1, SLAMF7, AKT1S1, IL18, NLRCS3, FGD2, FCRL5, CD79A, PSMB9, WIPF1, HCLSI, 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, IFNG, CD86, MS4A1, CD3E, CSF1, IL12RB1, HLA-DPA1, CCL8, TNFSF13B, HLA-DRB1, CCR2, CD4, CD38, FYN, GPR183, TNFAIP3, IRF1, IGFB, SPN, 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, IGFB, SPN, LILRB1, IL18, CCL2, CD40, IGLC2, LGALS9, VCAM1, CCL5, IGHAI1, 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, PIK3API, HLA-B, CXCL10, IGHAI1, CXCL13, PLOC2, 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, IGFB, LILRB1, CCL2, TRIM34, RAC2, COL1A1, CXCL11, POSTN, TYMP, STAT1, HTRA1, IFIH1, TRIM5, SAMHD1, NLRCS, TNFRSF14, APOBEC3B, B2M, APOBEC3A, HMGCB2, IGKC, PIK3CG, IFI44, CCL19, IRF8, AIM2, CCR7, CD109, IGLL5, SERPINB9, XBP1, GF11, IL18, PSMB9, WIPF1, IFIT3, MEF2C, IFIT2, STAP1, BIRC3, NR4A1, HLA-E, FCER1G, GNLV, 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, IGFB, 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, NLRCS, LILRB2, RSAD2, TNFRSF14, B2M, CD74, HMGCB2, CD2, KLRK1, CCL19, AIM2, IRF8, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, CCR2, CD4, XBP1, IRF1, BANK1, THBS1, SPN, IL18, NLRCS, CD40, LGALS9, DTX4, HLA-B, PLOC2, 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, NLRCS, LILRB2, RSAD2, TNFRSF14, B2M, CD74, HMGCB2, PIK3CG, CD2, KLRK1, CCL19, AIM2, IRF8, CCR7, HLA-DPA1, TRAF3, CYLD, HLA-DRB1, TRAF3, CYLD, HLA-DRB1, CCR2, CD4, XBP1, IRF1, BANK1, THBS1, SPN, IL18, NLRCS, CD40, LGALS9, DTX4, HLA-B, PLOC2, 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, IGFB, 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, IGFB, 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, TFEF, CXCL10, SFRP2, IL16, APO12, IL12RB1, SLA2, BLNK, LCP2, IL10RA, P2RY13, CDCA2EP4, HERC5, NCF4, HLA-F, RASSF4, KLHL6, CD96, IGLC2, EIF2AK2, VCAM1, IDO1, CCL5, KRT14, OAS3, PTAOF66, KLK1, NCALD, SOD2, MS4A1, HCP5, CTSS, LILRB2, OAS1, RSAD2, C1QC, MX1, ERAP2, MMP13, C19orf66, KLK1, 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, GHG4, DDX58, CFB, PRKCB, SPI100, JAK2, GPC3, SPI10, ANTXR1, SIRPG, GPR183, CASP1, CD8A, NRIH3, APOBEC3G, IGFB2, LILRB1, XAF1, TRIM34, DKK3, COL1A1, RAC2, ARHGAP25, PDCD5, POSTN, GRAP, IFI1, SECTM1, ADAMDEC1, ORM2, TRIM21, SAMHD1, NUAK2, NLR5, 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, APO1, GABRP, CASP4, CD300E, IFITM1, TRAF3, GJB2, FYB, ICAM1, CXCL9, THBS1, RHOB, CD40, BCL11B, LGALS9, PIK3AP1, APBB1IP, CXCL16, IGH1, GZMB, FCGR3B, AOA4, TAP1, ALPK1, HAVCR2, ZBP1, CYBB, LTF, PMAIP1, THEMIS2, DAP1, 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, GF11, KLRC2, KRT17, SLAMF7, AKT1S1, NLR3, FGD2, FORL5, PSMB9, DTX4, IFIT3, HCLS1, MEF2C, IFIT2, STAP1, BIRC3, RNF213, PTPRC, GNLV, 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, IGFB2, 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.