Supplemental Experimental Procedures

Ovarian cancer patients, cancer tissue samples and cells

Patients diagnosed with ovarian carcinomas were recruited for this study. Human subject used in this study was approved by the local Institutional Review Boards. All patients in our study received standardized platinum-based chemotherapy that was administered every three weeks for six cycles. Platinum sensitive refers to the time-to-relapse following completion of platinum-based chemotherapy for ≥6 months, and platinum resistant refers to the time-to-relapse following completion of platinum-based chemotherapy for <6 months.

We collected 178 formalin-fixed, paraffin-embedded ovarian tumor tissue blocks (Table S3) and 9 fresh ovarian cancer tissues from patients with HGSOC for this study as described previously (Curiel et al., 2004; Kryczek et al., 2006; Peng et al., 2015; Zou et al., 2001). After pathological review, a tissue microarray (TMA) was constructed from the most representative area of paraffin-embedded ovarian tumor tissue. For each tumor, a minimum of two representative tumor areas was selected from a hematoxylin- and eosin-stained section of a donor block. Core cylinders (1 mm) were punched from each of these areas and deposited into a recipient paraffin block. Consecutive 6 μm-thick TMA sections were cut and placed on charged Poly-L-Lysine-coated slides for immunohistochemistry analyses. Further information regarding the TMA was described in our previous work (Cui et al., 2013).

We prepared single cell suspension from fresh ovarian cancer tissues. These single cells were incubated for 2 hours. Then, we used polychromatic flow cytometry analysis to identify $CD45^-EpCAM^-CD24^-CD44^+SMA^+$ fibroblasts from the adherent cells. Ovarian cancer cell lines A2780, NIH: OVCAR3 and primary ovarian cancer cells OC8 were maintained in RPMI 1640 medium containing 10% FBS. A2780 or OC8 cells stably expressing GFP (A2780-GFP or OC8-GFP) were constructed in our laboratory. $CD8^+$ T cells were isolated from peripheral blood mononuclear cells using the EasySep™ Human $CD8^+$ T Cell Isolation Kit (Stemcell), and then stimulated with immobilized anti-CD3 (Clone HIT3α, BD Biosciences) and anti-CD28 (Clone CD28.2, BD Biosciences) for 3 days (Kryczek et al., 2009). Supernatant was collected by centrifugation at 3,000 ×g 10min and followed 0.2 μM filter. Human monoclonal antibodies against CD24, CD45, CD44, CD105, EpCAM (BD Biosciences) and PDGFRα (eBioscience) were used in the work.

TP53 mutations analysis

According to the protocol from International Agency for Research on Cancer (IARC), mutations within exons 2-11 of the human TP53 gene in ovarian tumor cells were analyzed by direct sequencing after PCR amplification.

Tumor and fibroblast co-culture

In the mixed co-culture, ovarian cancer associated fibroblasts (0 - 5×10^4 cells) were seeded in 6-well plate for 24 hours, then A2780-GFP cells (1×10^4 cells) were added and co-cultured for 3 days. Cisplatin (Teva Pharmaceuticals USA) were added into the medium for 40 hours. Annexin V^+ cells were analyzed by FACS in tumor cells with or without GFP gating. In the Transwell co-culture, ovarian cancer associated fibroblasts were seeded in the plates and tumor cells were seeded in the inserts. Cisplatin, Oxiliplatin (Pfizer) or Carboplatin (APP Pharmaceuticals, LLC) were added into medium and Annexin V^+ tumor cells from inserts were analyzed by FACS. In some cases, fibroblasts were pretreated for 8 hours with 30% supernatant from activated $CD8^+$ T cells or with 1- 5 ng/ml IFNγ (R&D systems). To block IFNγ signaling, fibroblasts were pretreated with 2 μg/ml anti-IFNGR1 neutralizing antibody (Clone GIR2082, R&D systems) for 2 hours, or 3 μM JAK inhibitor I (Santa Cruz) for 1 hour.

Apoptosis analysis

Tumor cells were pretreated with exogenous GSH (Sigma), GSH precursors N-Acetyl Cysteine (Sigma), L-Cysteine (Sigma) or GSH synthesis inhibitor BSO (Sigma) and then followed with cisplatin treatment; or tumor cells were incubated in fresh RPMI medium, cancer cell medium or fibroblast medium and followed with cisplatin treatment. Tumor cells were stained for Annexin V and 7-AAD (BD Biosciences) as described (Wang et al., 2014), and analyzed by FACS with DIVA software (BD Biosciences).

Cisplatin-induced apoptosis in tumor tissue was detected on paraffin or cryostat sections by TUNEL assay using ApopTag® Peroxidase In Situ Apoptosis Detection Kit (Millipore) according the manufacture's instruction.

Animal studies

GFP labeled ovarian cancer cells and ovarian cancer associated fibroblasts (the ratio 1: 1.5) were subcutaneously inoculated into the flanks of 6-8 week old female nude mice (for A2780 cells) or NSG mice (for OC8 cells). After tumor was established, cisplatin (6 mg/kg) or recombinant human IFNγ (1.5×10^5 U/mice) was administered intraperitoneally every three days for total three treatments or as indicated. Tumor size was measured every three days using calipers and calculated.

To investigate the effect of fibroblasts on cisplatin intra-tumor accumulation, OC8-GFP cells were mixed with ovarian cancer associated fibroblasts and subcutaneously inoculated into the NSG mice. 12 days after tumor inoculation, mice were intravenously transfused activated $CD8^+$ T cells together with anti-human IFNγ antibody. After 4 days mice were intraperitoneally injected with cisplatin. 24 hours later, mice were sacrificed and tumors were immediately excised to prepare single cell suspension by collagenase digestion. Cell suspension was stained with PE-conjugated anti-human CD44 and CD45 (BD biosciences) first and use EasySep™ Human PE Positive Selection Kit (StemCell) to remove $CD44^+$ fibroblast and $CD45^+$ lymphocyte with magnetic nanoparticles. Platinum was quantified in $CD44^-CD45^-GFP^+$ OC8 cells.

To investigate the effect of GSH on cisplatin intra-tumor accumulation, 10^6 A2780 cells were inoculated subcutaneously into nude mice. Eight days after tumor inoculation, glutathione ethyl ester (Cayman Chemical) was injected intraperitoneally (10 ml/kg). Six hours later, cisplatin (6mg/kg) was administered intraperitoneally. Twenty-four later, mice were sacrificed and tumors were immediately excised to quantify platinum accumulation. To monitor tumor volume, the mice received three administrations of cisplatin. All the animal studies were conducted under the approval of the University of Michigan Committee on Use and Care of Animals.

Screening ovarian cancer associated fibroblast derived factors

Tumor cells or primary ovarian cancer associated fibroblast (5×10^5) were cultured in serum free medium for 3 days. The medium was collected and centrifuged at 4000 × g for 10 min to remove cell pellet. The medium was fractioned at 3 KDa MWCO (EMD Millipore) at 4000 × g for 50 min, or incubated with Trypsin (100 μg/ml, 37°C, 2h) or Proteinase K (100 μg/ml, 37°C, 2h) and then filtered using 3KDa MWCO. The protective effect of each fraction on tumor cell apoptosis was determined by Annexin-V and 7-AAD staining.

Thiol, GSH content and GGT activity assay

The Thiol Detection Assay Kit (Cayman Chemical) was used to determine the thiol content in the different medium samples. The GSH-Glo™ Glutathione Assay Kit (Promega) was used to determine the reduced GSH content in the different medium samples. γ-Glutamyltransferase (GGT) Activity Fluorometric Assay Kit (Sigma) was used to determine the GGT activity in fibroblasts. Experiments were performed with biological replicates.

Detection of GSH-related metabolites by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS)

Cancer cell or fibroblast medium was collected and analyzed freshly using LC-triple quadrupole mass spectrometer (Agilent 6490 series) with jet stream electrospray ionization source (Agilent). Chromatography was carried out on a Waters C18 High Strength Silica T3 column (50 mm × 2 mm) on Agilent 1200 Series liquid chromatography. Mobile phase A (5 mM ammonium formate and 0.1% formic acid in HPLC-grade water) supplemented with 1 μg/ml of *N*- (2-mercaptopropionyl)-glycine (MPG) as internal standard was used as extraction solvent. 50 μl medium samples were diluted with 950 μl extraction solvent and vertex briefly. A series of calibration standards (Cystine: 0, 1, 3, 10, 30 μg/ml; others: 0, 0.8, 2.4, 24 μg/ml) were prepared along with samples to quantify metabolites. The following transitions were used to identify and quantify metabolites: Cysteine: m/z 122.0 → m/z 76; Cys-Gly: m/z 179 → m/z 76; γ-Glu-Cys: m/z 251.2 → m/z 84.0; Cystine: m/z 241.0 → m/z 152.0. Data were processed by MassHunter workstation software, version B.06. Experiments were performed with biological replicates.

Western blotting

Tumor cells were cultured with fibroblasts in different conditions. The cells were harvested for Western blotting with human antibodies for γH2AX, caspase 9, caspase 3, p-STAT1, IRF1 and xCT (Cell Signaling Technology), GAPDH (EMD Millipore), SLC3A2 (Novus) and GCLC (Abcam).

Chromatin immunoprecipitation

ChIP assay was described previously (Peng et al., 2015). Sonication was performed with the Misonix 4000 water bath sonication unit at 15% amplitude for 10 minutes on OC8, and at 60% amplitude for 10 minutes on fibroblasts. Chromatin was enriched with RNA polymerase II antibody (clone CTD4H8, EMD Millipore) or STAT1 antibody (Santa Cruz). DNA was analyzed by Real-Time PCR with SYBR Green Master Mix, and normalized to the input. The ChIP primers were listed in Table S7.

Real time PCR

Total RNA was isolated from tumor cells or fibroblasts using RNeasy mini kit (Qiagen) with DNase treatment. cDNA was synthesized using High-Capacity cDNA Reverse Transcription Kit (Thermo Fisher Scientific) with poly-dT and random hexamer primers. The real-time PCR was performed using Fast SYBR® Green Master Mix (Invitrogen). The primer pairs were listed in Table S7.

Luciferase reporter assay

Human xCT promoter sequence and series of deletion variants were PCR-amplified from human fibroblasts genomic DNA with specific primers (Table S7). PCR products were cloned into the pGL4 vector (Promega) upstream of the firefly luciferase reporter gene. Human primary fibroblasts were co-transfected with pGL4 carrying xCT promoter and pRL plasmid that expresses Renilla luciferase using Nucleofector technology with the basic nucleofector kit for primary fibroblasts (Amaxa). For each sample, 2×10^5 cells were nucleofected with 1 μg DNA. IFNγ was added immediately after nucleofection and dual luciferase assay (Promega) was performed after 24h of treatment. All experiments were set up in triplicates.

Detection of cisplatin with inductively coupled plasma-high resolution mass spectrometry (ICP-HRMS)

To detect cisplatin in the whole cells, cell pellets were washed twice with ice-cold PBS and digested overnight in 70% nitric acid at room temperature. A small aliquot of cell pellet was taken for protein concentration determination using BCA Protein Assay kit before digestion. To detect cisplatin DNA accumulation, total DNA was extracted from cells using QIAamp DNA Blood Mini Kit (Qiagen). DNA concentration was assessed by spectrophotometry at 260 and 280 nm. 30 μg DNA was digested in 70% nitric acid. Then, the samples were diluted in 0.1% Triton X-100, 5% nitric acid and 1 ppb Indium (final concentrations). Platinum concentration was measured using ICP-HRMS Element 2 (Thermo Scientific) located at Keck Elemental Geochemistry Laboratory at University of Michigan. Prior measurement indium was added as internal standard. Platinum calibration standard was prepared at concentration of 10 ppb. For some samples prepared from whole cell lysates, concentrations of Platinum and Sulfur were both measured and the ratio of Platinum to Sulfur was calculated.

Platinum-DNA (Pt-DNA) adduct detection by Dot-blot

OC8 were cultured with fibroblasts in Transwell co-culture system and treated with cisplatin for 12 hours. Genomic DNA of OC8 was isolated using DNeasy Blood & Tissue Kit (Qiagen). 1 μg DNA was spotted onto a nitrocellular membrane and baked at 80°C for 2 hours in an oven. The blot was subjected to standard Western blot assay using anti-CDDP adducts antibody (1:1000; clone ICR4, EMD Millipore).

Immunohistochemistry (IHC) and immunofluorescence (IF) staining

Tumor tissues were harvested, either fixed in 10% formalin and embedded in paraffin for IHC assay, or embedded in OCT compound embedding medium and frozen for IF staining. IHC staining was performed on a DAKO Autostainer (DAKO, Carpinteria, CA) using DAKO LSAB+ and diaminobenzadine as the chromogen. IF staining was performed on frozen sections or tumor cells chamber slide cultures (Thermo Fisher Scientific). The primary antibody was mouse anti-human α-SMA (clone 1A4, IgG2α, Dako) or rabbit anti-human γH2AX (Cell Signaling Technology). The secondary antibodies were goat anti-mouse IgG2α conjugated with Alexa Fluor 488 or goat anti-rabbit IgG (H+L) conjugated with Alexa Fluor 568.

Radiolabeled Cystine uptake assay

Tumor cells or/and fibroblasts were cultured in different conditions in Cystine-free medium. L-^{14}C-Cystine (0.2 μCi/mL) was added and incubated for 0- 6 hours. Cells were washed three times with cold PBS containing 100 μM cystine and lysed in 200 μl NaOH (100 mM). Lysates were added into 5 ml scintillation fluid and radioactivity was measured by a Beckman liquid scintillation counter. In the meantime, the same number of cells was lysed in 100 μl NaOH (100 mM). The quantity of total protein was determined by the BCA Protein Assay kit and used to normalize the radioactivity. Experiments were performed with biological replicates.

Tissue microarray

Immunohistochemical staining on TMA sections was performed on a DAKO Autostainer using DAKO LSAB+ and diaminobenzadine as the chromogen. The sections were stained with mouse anti-human CD8 mAb (Clone HIT8α, BD Biosciences), or mouse anti-human α-SMA mAb (clone 1A4, 1:100, Dako). Cores from several normal organ tissues were used as tissue controls on each slide.

The cores were quantified and analyzed with an Aperio imaging system (Genetix, San Jose, CA). The specimens were digitalized with an automated platform (Aperio Technologies; Vista, CA) and ScanScope XT and Spectrum Plus using TMA software version 9.1 scanning system. Cores were scored manually on a computer screen with high resolution, and a mean score for duplicate cores from each individual was calculated. Any discrepancies were resolved by subsequent consultation with diagnostic pathologists. The α-SMA intensity in stromal cells, as well as their number and distribution, were semi-quantitatively assessed as following: 0 (negative), 1+ (weak staining, 1-10% positive cells), 2+ (moderate staining, 11-30% positive cells), 3+ (strong staining, 31-50% positive cells), 4+ (very strong staining, 51-100% positive cells). The patients were grouped as "α-SMA^{low}" with α-SMA score 0-2 and "α-SMA^{high}" with α-SMA score 3 and 4. The number of CD8$^+$ cells in stromal area (defined as > one tumor cell diameter away from the tumor) was counted. The stromal areas were varied among patients and TMA cores. We selected five independent stromal areas with the most abundant CD8$^+$ cells in each tissue core for final quantification. The mean of stromal CD8$^+$ T cell counts for each patient was used for statistical analysis. The patients were divided into "CD8^{low}" and "CD8^{high}" based on the median value of CD8$^+$ T cell number.

Statistical analysis

Data were shown as mean ± SEM or mean ± SD. Two sample t-tests or Wilcoxon rank-sum tests were used to compare two independent groups; Paired t tests or Wilcoxon signed rank tests were used for paired group comparisons. ANOVA models were used to compare continuous outcomes across multiple experimental conditions, and Bonferroni correction was used to adjust p values for multiple comparisons. Interaction term in the ANOVA model was tested to evaluate whether the effect of an experiment factor depends on another experimental factor. Logistic regression models were used to associate CD8$^+$ and tumor stromal fibroblasts to chemotherapeutic. Median overall survival was estimated by the Kaplan-Meier method. Cox proportional hazards regression was conducted to model survival as a function of CD8$^+$or tumor stromal fibroblasts, after adjusting for age, grade, histology, optimal debunking, stage, and study cohort. The adequacy of the Cox regression model was assessed with graphical and numerical methods. All analyses were done using SAS 9.4 software. $P < 0.05$ was considered significant.

Supplemental Tables

Table S1. Characteristics of ovarian cancer patients, Related to Experimental Procedures

Age	Pathology
47	Primary invasive high grade papillary serous carcinoma
62	Primary high grade papillary serous carcinoma
57	Primary high grade papillary serous carcinoma
77	Primary invasive high grade papillary serous carcinoma
75	Primary invasive high grade serous carcinoma
69	Primary high grade serous carcinoma
71	Primary recurrent high grade papillary serous carcinoma
63	Primary mixed high grade carcinoma with serous and endometriod differentiation
55	Metastatic high grade serous carcinoma

Note: Fibroblasts were isolated and sorted from fresh ovarian cancer tissues in these patients.

Table S2. TP53 gene mutations in OC8 and OVCAR3 ovarian cancer cells, Related to Figure 1

Cells	Position	WT codon	MUT codon	Wt AA	MUT AA	p.Mutant	c.Mutant	Frequency	Comment
OC8	220	TAT	TGT	Tyr	Cys	p.Tyr220Cys	c.659A>G	414	hot spot mutant
OVCAR3	248	CGG	CAG	Arg	Gln	p.Arg248Gln	c.743G>A	1016	hot spot mutant

Table was generated by MUT-TP53 2.0.
Frequency: frequency of the mutant in the Universal Mutation Database (UMD-TP53 mutation database).
Comment: about p53 mutant frequency in the database.

Table S3. Characteristics of ovarian cancer patients, Related to Figure 7

		Survival analysis*			Chemoresistant %	Chemosensitive %
		P	**HR**	**95% CI**		
Age		0.0255	1.016	1.002 – 1.030	59.5 (19, 87)	59 (22, 85)
Stage	I, II	0.0013	3.106	1.559 – 6.190	3 (11.5)	23 (88.5)
	III, IV				59 (38.8)	93 (61.2)
Stromal α-SMA	Low	0.0002	2.016	1.394 – 2.916	15 (19.7)	61 (80.3)
	High				47 (47.0)	53 (53.0)
Stromal CD8	Low	< 0.0001	0.422	0.286 – 0.622	44 (42.7)	59 (57.3)
	High				18 (24.7)	55 (75.3)
Overall Survival: median (95%CI)					17 (13, 23)	62 (52, 76)

*Each of the above variables was analyzed using Cox proportional hazards regression model after controlling for study cohorts, which was treated a strata in the Cox model.

Table S4. The association between stroma and chemoresistance, Related to Figure 7

	P	Point Estimate	95% Wald Confidence Limits
α-SMA	0.0002	0.263	(0.129, 0.536)

Table S5. The impact of α-SMA on ovarian cancer patient overall survival, Related to Figure 7

	Chemoresistance not included				Chemoresistance included			
	P	Hazard Ratio	95% Hazard Ratio Confidence Limits		P	Hazard Ratio	95% Hazard Ratio Confidence Limits	
α-SMA	**0.0006**	**1.912**	**1.321**	**2.767**	**0.1139**	**1.383**	**0.925**	**2.067**
Chemoresistance					**< 0.0001**	**0.223**	**0.144**	**0.347**
Stage	0.0087	2.565	1.269	5.184	0.0697	1.942	0.948	3.979
Age	0.2540	1.009	0.994	1.024	0.3411	1.007	0.992	1.023

Table S6. The association between CD8 and chemoresistance in patients with high α-SMA, Related to Figure 7

	F Value	P
All patients	6.19	0.0138
High stroma	14.71	0.0002
Low stroma	0.81	0.37

Table S7. Sequences of oligonucleotide primers for real-time PCR, ChIP and luciferase reporter assays, Related to Experimental Procedures

Sequences of primers for quantitative real-time PCR	
Genes	**Primer sequence (5'-3')**
CTR1	ATGGAACCATCCTTATGGAGACA
	GGAAGTAGCTTATGACCACCTGG
CTR2	ATACAGCGGTGCTTCTGTTTG
	GGTTGGCAGGTTCACCAGTA
ATP7A	CAGGAATTGCAAGTCATACCC
	CTGCGTAGCTCCAGAGGTTT
ATP7B	TACCCATTGCAGCAGGTGTC
	ACTTGAGCTGCAGGGATGAG
MRP1	GTCGGGGCATATTCCTGGC
	CTGAAGACTGAACTCCCTTCCT
MRP4	AGCTGAGAATGACGCACAGAA
	ATATGGGCTGGATTACTTTGGC
TMEM20	CAGGTGCCTGGGGCATGCAA
	GCCCACATGGCAGCTGTGGT
OCT1	CGAGAACCTTGGGAGAAAAGC
	TCTTCATCCCTCCAACACGAC
MATE1	GTGGTCAGGGATCATCATCTGT
	CTCCGAGGCACGTTGTTTAC
LAMP	AATGATACTTGTCTGCTGGCTAC
	ACTTAATGGTGCTGCTATTGAGTC
NCP1	AAGGGGACGACTTCTTTGTGT
	AAGGGCAGTGGCGTTATTG
GGT1	CTGAGCTGATCGAGCACCC
	CTCTACGATGCGGTGGTACG
GGT5	GTCAGCCTAGTCCTGCTGG
	GGATGGCTCGTCCAATATCCG
GGT7	CCTTGTGTTTGGGTATCGTGG
	TTCGTCGGATGTCATGTACCA
xCT	TGCTGGGCTGATTTTATCTTCG
	GAAAGGGCAACCATGAAGAGG
SLC3A2	CTGGTGCCGTGGTCATAATC
	GCTCAGGTAATCGAGACGCC
CXCL10	CTCCAGTCTCAGCACCATGA
	GCTCCCCTCTGGTTTTAAGG
IRF1	GAGACCCTGGCTAGAGATGC
	CATGGCACAGCGAAAGTTGG
GAPDH	TGGTATCGTGGAAGGACTC
	AGTAGAGGCAGGGATGATG

pre-xCT-P1	TTGCCATCCATTCACTCCTCA
	GCATGTCTCTGACCATCTGGA
pre-xCT-P2	GAGGAGTTCCACCCAGACTC
	ATGCTGGGTGTCTTGAAAATGT
pre-CXCL10	ACACGTGGACAAAATTGGCTT
	GTGCTAACCTTCTCTGCTGT
pre-GAPDH	TGACATCAAGAAGGTGGTGA
	CCTGCACTTTTTAAGAGCCA

Sequences of primers for CHIP-qPCR

Genes	Primer sequence (5'-3')
xCT(TSS)	CAGGAGGAGCTTGTTGCTCA
	CTCTGGGAAGGTCTGTTCCG
xCT(+900)	ACTTCTGCTGAACACTCCGT
	GCCGGGCAGTTGTACACTTA
xCT(+6k)	CACCCAGACTCGTACAAAAGC
	CAGGAGCTTTGTCTTATGCTGAA
xCT(GAS1)	GTGGCCTTTGCCATCCATTC
	GTGGGCATGTCTCTGACCAT
xCT(GAS2)	TCAGCTTCCTCATGGGCTTG
	TGAGCAACAAGCTCCTCCTG
xCT(GAS3)	ACCCTGAAGCTACCTTTATACGC
	GACTCCCTTCTTTCCCTGCC
IRF1(TSS)	GCTGCGGAGCTTCATTTCT
	AGGAGAGTGCTGATCCCATC
GAPDH(TSS)	TACTAGCGGTTTTACGGGCG
	TCGAACAGGAGGAGCAGAGAGCGA
CXCL10(TSS)	TGTAGCCTCCAAGTTACGGA
	TCATGTTTTGGAAAGTGAAACCT

Sequences of primers for cloning luciferase reporter constructs

Construct	Primer sequence (5'-3')
xCT(-1630/+1000)	CGGGGTACCTGTGAGTGAAAGGAGATGTAGGAG
	CTAGCTAGCTAAGACTTCTGCTGAACACTCCG
xCT(+310/+1000)	CGGGGTACCTGTTGTGTCCACCATCTCCAAAG
	CTAGCTAGCTAAGACTTCTGCTGAACACTCCG
xCT(-620/+310)	CGGGGTACCTGGTGATTTAAAATACTGGTTTATTATGAGTAGTAAG
	CTAGCTAGCGATGGTGGACACAACAGGCTTTC
xCT(-1630/-620)	CGGGGTACCTGTGAGTGAAAGGAGATGTAGGAG
	CTAGCTAGCACCAGTATTTTAAATCACCATCCGAG

Supplemental References:

Cui, T.X., Kryczek, I., Zhao, L., Zhao, E., Kuick, R., Roh, M.H., Vatan, L., Szeliga, W., Mao, Y., Thomas, D.G., *et al.* (2013). Myeloid-derived suppressor cells enhance stemness of cancer cells by inducing microRNA101 and suppressing the corepressor CtBP2. Immunity *39*, 611-621.

Curiel, T.J., Coukos, G., Zou, L., Alvarez, X., Cheng, P., Mottram, P., Evdemon-Hogan, M., Conejo-Garcia, J.R., Zhang, L., Burow, M., *et al.* (2004). Specific recruitment of regulatory T cells in ovarian carcinoma fosters immune privilege and predicts reduced survival. Nat Med *10*, 942-949.

Kryczek, I., Banerjee, M., Cheng, P., Vatan, L., Szeliga, W., Wei, S., Huang, E., Finlayson, E., Simeone, D., Welling, T.H., *et al.* (2009). Phenotype, distribution, generation, and functional and clinical relevance of Th17 cells in the human tumor environments. Blood *114*, 1141-1149.

Kryczek, I., Zou, L., Rodriguez, P., Zhu, G., Wei, S., Mottram, P., Brumlik, M., Cheng, P., Curiel, T., Myers, L., *et al.* (2006). B7-H4 expression identifies a novel suppressive macrophage population in human ovarian carcinoma. J Exp Med *203*, 871-881.

Peng, D., Kryczek, I., Nagarsheth, N., Zhao, L., Wei, S., Wang, W., Sun, Y., Zhao, E., Vatan, L., Szeliga, W., *et al.* (2015). Epigenetic silencing of TH1-type chemokines shapes tumour immunity and immunotherapy. Nature *527*, 249-253.

Wang, W., Zhou, J., Shi, J., Zhang, Y., Liu, S., Liu, Y., and Zheng, D. (2014). Human T-cell leukemia virus type 1 Tax-deregulated autophagy pathway and c-FLIP expression contribute to resistance against death receptor-mediated apoptosis. J Virol *88*, 2786-2798.

Zou, W., Machelon, V., Coulomb-L'Hermin, A., Borvak, J., Nome, F., Isaeva, T., Wei, S., Krzysiek, R., Durand-Gasselin, I., Gordon, A., *et al.* (2001). Stromal-derived factor-1 in human tumors recruits and alters the function of plasmacytoid precursor dendritic cells. Nat Med *7*, 1339-1346.