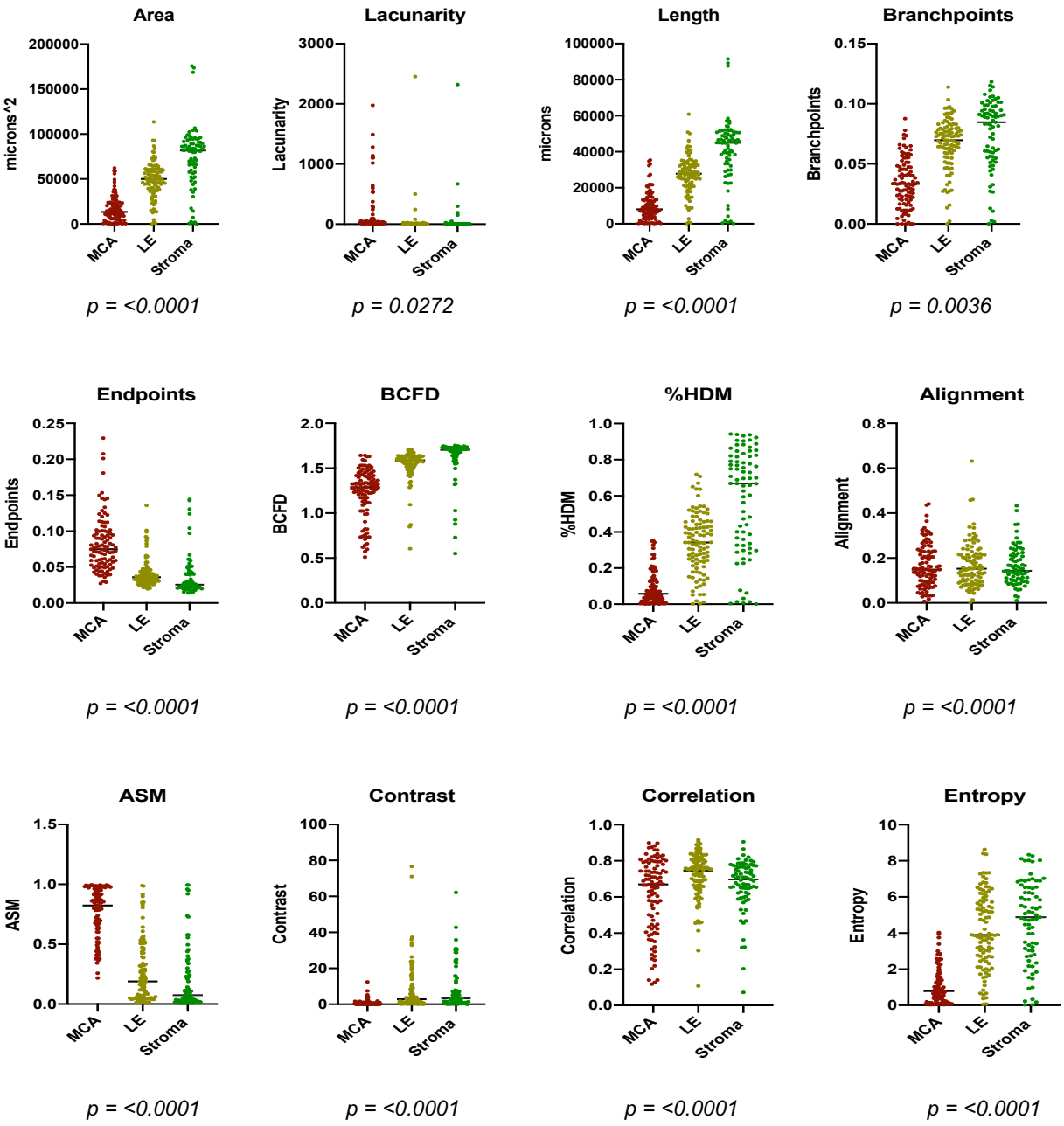

Supplementary Figure 1: Analysis of how the structure and texture of collagen, identified by Masson's Trichrome, varies across the malignant cell area, leading edge and stroma of advanced clear cell ovarian cancer

In 36 samples of advanced clear cell ovarian cancer, collagen was identified using Masson's Trichrome and subsequently underwent structural (TWOMBLI) and textural (Haralick Features; QuPath) analysis. The metrics were then compared across the malignant cell area (MCA), leading edge (LE) and stroma of samples to identify changes in the collagen extracellular matrix across the tumour microenvironment. BCFD; box counting fractal dimension, %HDM; percentage high density matrix, ASM; angular second moment.

Marker	FIGO III/IV (n)	ARID1A Wildtype (n)	ARID1A mutant (n)
CD3	28	15	12
CD8	28	15	12
CD4	20	11	9
FOXP3	20	11	9
CD45RO	20	12	8
CD68	36	21	14
CD163	19	11	8
CD20	20	12	8
CD138	20	12	8
MCT	20	10	9
CD1a	12	6	5
LAMP3	12	6	6
CD66b	12	5	6
aSMA	34	19	14
PD1	12	5	6
PDL1	12	6	6
PDL2	12	6	6
VCAN	12	6	6
Massons Trichrome	36	21	14
ARID1A	36	21	14

Supplementary Table 1: Sample size for immunohistological profiling of advanced clear cell ovarian cancer

Due to a limited number of FFPE slides available per patient, we allocated samples into cohorts to allow immunohistological profiling of each immune marker. This table shows the total sample number of FIGO stage III/IV clear cell ovarian cancer and subsequently how many of these were ARID1A wildtype or mutant; one sample had mixed ARID1A expression and was excluded from wildtype versus mutant analysis.

Target	Company	Catalog Number	Concentration	Species	Primary Incubation	Antigen Retrival			Peroxidase Blocking			DAB Time (minutes)	Control
						pH	*Tempreture*	*Duration*	*H202*	*Dilutant*	*Duration*		
Mast Cell Tryptase	Abcam	ab134932	1:5000	Rabbit	Overnight	6	95	20	0.3%	PBS	15	2.5	Tonsil
CD1a	Abcam	ab108309	1:250	Rabbit	Overnight	6	95	20	0.3%	PBS	15	2.5	Skin
CD66b	Abcam	ab197678	1:200	Rabbit	Overnight	6	95	20	0.3%	PBS	15	2.5	Spleen
FOXP3	ThermoFisher	eBIO7979	1:500	Mouse	Overnight	9	95	25	0.3%	PBS	15	1	Tonsil
CD163	ThermoFisher	MA5-11458	1:1000	Mouse	1 hour RT	9	95	30	2%	Methanol	30	1	Tonsil
CD68	ThermoFisher	14-0688-82	1:12,000	Mouse	1 hour RT	9	95	30	2%	Methanol	30	3	Tonsil
CD45RO	ThermoFisher	MA1-19452	1:8000	Mouse	1 hour RT	9	95	30	2%	Methanol	30	3	Tonsil
CD20	ThermoFisher	14-0202-82	1:800	Mouse	1 hour RT	9	95	30	2%	Methanol	30	3	Tonsil
CD8	Agilent	GA62361-2	1:1500	Mouse	1 hour RT	9	95	30	2%	Methanol	30	3	Tonsil
CD3	Agilent	MA725429-2	1:800	Rabbit	1 hour RT	9	95	30	2%	Methanol	30	2	Tonsil
CD4	Agilent	IS64930-2	1:400	Mouse	Overnight	9	95	20	2%	Methanol	15	6	Tonsil
LAMP3	Abcam	ab111090	1:1000	Rabbit	Overnight	6	95	20	0.3%	PBS	15	4	Lung
CD16	Abcam	ab203883	1:200	Rabbit	Overnight	6	95	20	2%	Methanol	15	4	Spleen
CD138	Abcam	ab128936	1:200	Rabbit	Overnight	9	95	20	2%	Methanol	15	1	Tonsil
PD-1	BioLegend	367402	1:200	Mouse	1 hour RT	9	95	30	2%	Methanol	30	3	Tonsil
PD-L1	Cell Signal	13684T	1:400	Rabbit	1 hour RT	9	95	30	2%	Methanol	30	3	Placenta
PD-L2	ThermoFisher	PA5-20344	2.5:1000	Rabbit	1 hour RT	9	95	30	2%	Methanol	30	3	Placenta
PD-L2	Sigma Aldrich	HPA013411	1:500	Rabbit	1 hour RT	9	95	30	2%	Methanol	30	3	Placenta
Versican	Sigma Aldrich	HPA004726	1:500	Rabbit	Overnight	6	60	60	2%	Methanol	15	20	Placenta
αSMA	Abcam	ab5694	1:200	Rabbit	1 hour RT	no antigen retrival			2%	Methanol	30	5	Kidney
ARID1A	Abcam	ab182561	1:1000	Rabbit	1 hour RT	9	95	25	0.3%	PBS	15	1	Tonsil

Supplementary Table 2 Variable conditions for each immunohistochemistry markers

This table lists the immunohistochemical target, the antibody and concentration used as well as the host species it is derived from which guides in secondary antibody selection. The primary incubation times vary between one hour at room temperature or overnight at 4°C. Antigen retrieval varies in terms of pH, temperature and duration. The peroxidase block also varies in the concentration of hydrogen peroxide and the dilutant used. The final column on the right lists the control tissues used.

Immune Marker	**Advanced CCOC** *(n)*	**Early CCOC** *(n)*	**MCA** *(p)*	**LE** *(p)*	**Stroma** *(p)*
CD3	*28*	*9*	0.6862	0.6429	0.8438
Mast Cell Tryptase	*20*	*9*	0.8983	0.6373	0.2503
CD20	*20*	*9*	0.1295	0.0783	0.23
CD68	*36*	*9*	0.6471	0.243	0.1654
aSMA	*34*	*9*	0.647	0.081	**0.024**

Supplementary Table 3: Significance values for the comparison of immune cell markers between early (FIGO stage I and II) and advanced stage (FIGO III and IV) clear cell ovarian cancer (CCOC)

Immune markers were identified using immunohistochemistry and quantified by either positive cells per high powered field (CD3, CD20, Mast Cell Tryptase) or percentage positive area (CD68 and αSMA). The distribution of the markers across the malignant cell area (MCA), leading edge (LE) and stroma were subsequently compared between a cohort of early and advanced stage CCOC. The only significant result, shown here in red, was that of stromal αSMA, which was significantly higher in the stroma of advanced stage disease.

Pathway	NES	FDR q-val
GOBP_COLLAGEN_METABOLIC_PROCESS	-2.2148983	0.00303189
GOBP_COLLAGEN_BIOSYNTHETIC_PROCESS	-2.1887088	0.00438903
GOBP_POSITIVE_REGULATION_OF_COLLAGEN_METABOLIC_PROCESS	-2.03516	0.01093186
GOCC_COLLAGEN_CONTAINING_EXTRACELLULAR_MATRIX	-2.0267718	0.00814786
GOBP_REGULATION_OF_COLLAGEN_METABOLIC_PROCESS	-1.928109	0.01429047
GOBP_COLLAGEN_FIBRIL_ORGANIZATION	-1.865479	0.0196563
REACTOME_ASSEMBLY_OF_COLLAGEN_FIBRILS_AND_OTHER_MULTIMERIC_STRUCTURES	-1.8605988	0.04044084
GOCC_COLLAGEN_TRIMER	-1.8583226	0.0329106
REACTOME_COLLAGEN_FORMATION	-1.8391806	0.04604144
GOBP_COLLAGEN_CATABOLIC_PROCESS	-1.8389298	0.02112176
REACTOME_COLLAGEN_DEGRADATION	-1.8341143	0.04659602

Supplementary Table 4: Pathway enrichment for collagen pathways between ARID1A wildtype and mutant clear cell ovarian cancer

When the differentially expressed genes were ranked by T statistic, pathway enrichment using the Broad Institute Gene Set Enrichment Analysis (GSEA) platform, demonstrated 11 pathways involved in collagen biology that were significantly different at an FDR q value of 0.05

	Univariate analysis		Multivariate analysis	
Metric - *Region*	**P-Value**	**HR (95% CI for HR)**	**P-Value**	**HR (95% CI for HR)**
CD8 - *Malignant Cell Area*	0.022	3.5 (1.2-10)	0.0162	4.53 (1.32283-15.513)
CD45RO - *Malignant Cell Area*	0.055	3.3 (0.97-11)	0.0718	3.25856 (0.90062-11.790)
CD4 - *Leading Edge*	0.0066	5.4 (1.6-18)	0.00874	9.0332 (1.74325-46.808)
aSMA - *Leading Edge*	0.038	2.5 (1.1-6.2)	0.0546	2.4953 (0.9823-6.339)
Correlation - *Leading Edge*	0.024	0.41 (0.19-0.89)	0.00108	0.2016 (0.07713-0.5268)
CD4 - *Stroma*	0.014	7.4 (1.5-36)	0.0052	13.2447 (2.16308-81.098)
Alignment - *Stroma*	0.01	0.28 (0.11-0.74)	0.0177	0.2425 (0.07517-0.782)
ASM - *Stroma*	0.012	3.4 (1.3-8.7)	0.0426	3.2994 (1.04057-10.462)

Supplementary Table 5: The tumour microenvironment metrics which were significantly associated with overall survival following univariate and multivariate analysis

Cox proportional hazards analysis and Kaplan-Meier analysis were preformed, taking into account FIGO stage, ARID1A status, Aletti score and whether adjuvant chemotherapy was received or not. Five metrics remained significant following multivariate analysis; CD8 cells within the malignant cell area, CD4 cells at the leading edge (LE) and stroma, collagen correlation at the LE, collagen alignment and angular second moment in the stroma.