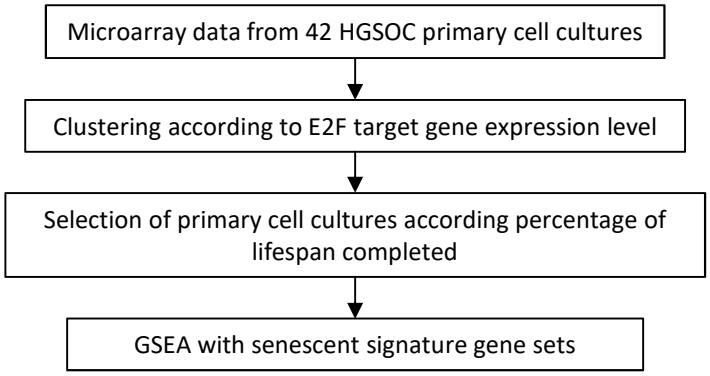
Supplemental Figure 1: Workflow for HGSOC primary cell senescence transcriptome analysis.

a



b

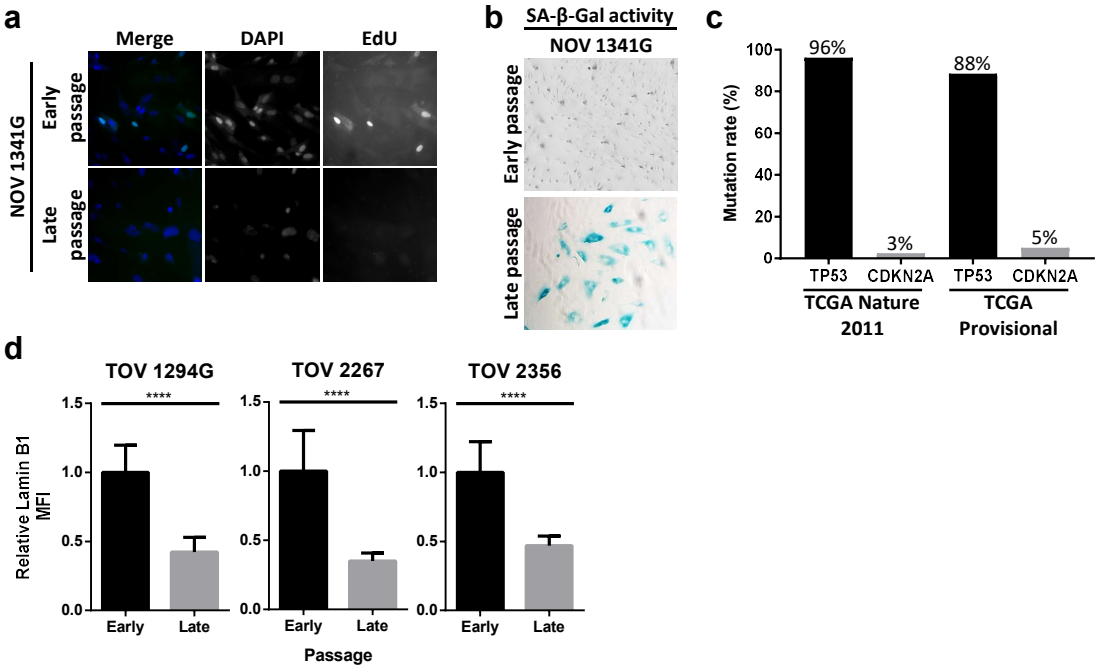
c

Early passage primary cell cultures from Cluster I (<=0.5 of eventual maximal passage number), n=5	Late passage primary cell cultures from Cluster III (>=0.75 of eventual maximal passage number), n=7
OV980 P3 (0.33)	TOV881 P3 (0.75)
TOV1855 EP P2 (0.4)	TOV1007 EP P3 (0.75)
OV960 P4 (0.5)	OV1193 P3 (0.75)
OV889 P3 (0.5)	OV881 P4 (0.8)
OV513 P3 (0.5)	TOV993 P5 (0.83)
	TOV999D P5 (0.83)
	OV665 P6 (0.86)

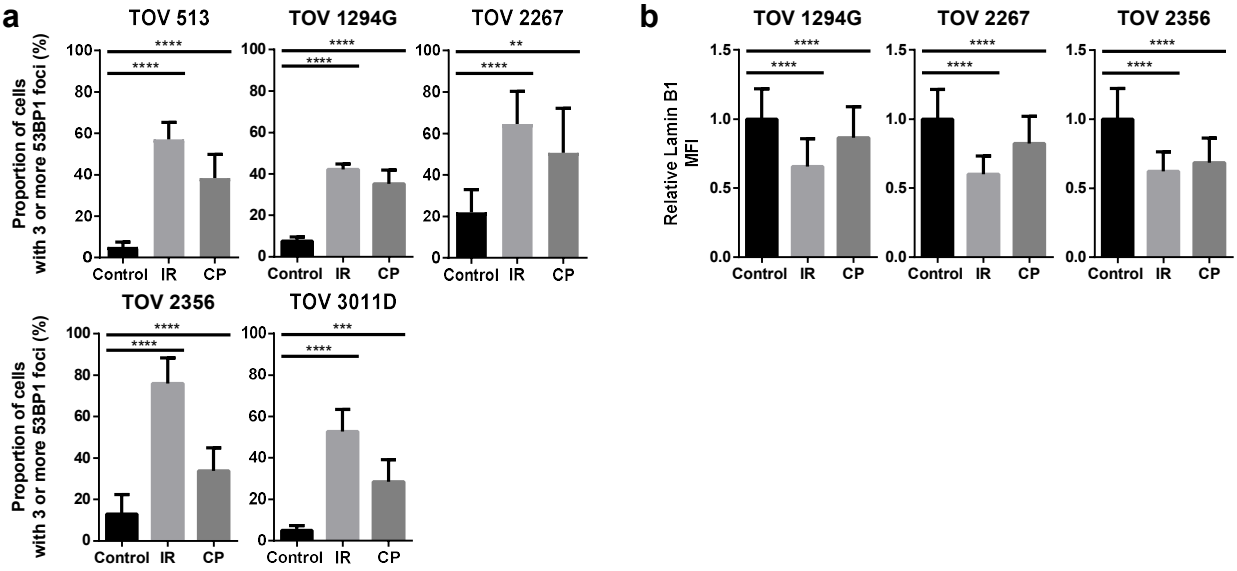
d

9 senescent signature gene sets are significantly enriched (p<0.01) in "Late" primary cell cultures (>=0.75 of eventual maximal passage number)	6 senescent signature gene sets are significantly enriched (p<0.01) in "Early" primary cell cultures (<=0.50 of eventual maximal passage number)
Signature for Replicative Senescence_UP	Signature for Replicative Senescence_DN
Signature of IRIS at day 4 post-irradiation (genes shared among fibroblasts, melanocytes and keratinocytes)_UP	Signature of IRIS at day 4 post-irradiation (genes shared among fibroblasts, melanocytes and keratinocytes)_DN
Genes in the Fibroblast Signature of Senescence Independent of Stimulus_UP	Signature of IRIS at day 20 post-irradiation (genes shared among fibroblasts, melanocytes and keratinocytes)_DN
Signature for Ionizing-Radiation Induced Senescence_UP	Genes in the Fibroblast Signature of Senescence Independent of Stimulus_DN
Signature of IRIS at day 20 post-irradiation (genes shared among fibroblasts, melanocytes and keratinocytes)_UP	Signature of IRIS at day 10 post-irradiation (genes shared among fibroblasts, melanocytes and keratinocytes)_DN
Signature of Melanocytes_DN	Signature of Keratinocytes_DN
Signature of Astrocytes_UP	
Signature of Keratinocytes_UP	
Signature for Oncogene Induced Senescence_DN	

Supplemental Figure 2: HGSOC primary cultures undergo culture stress-induced senescence.



Supplemental Figure 3: HGSOC primary cultures undergo TIS in response to DNA damage and chemotherapy.



Supplemental Figure 4: Clinical characteristics of the patients in the pre- and post-chemotherapy HGSOC cohort used to construct the tissue microarray.

a

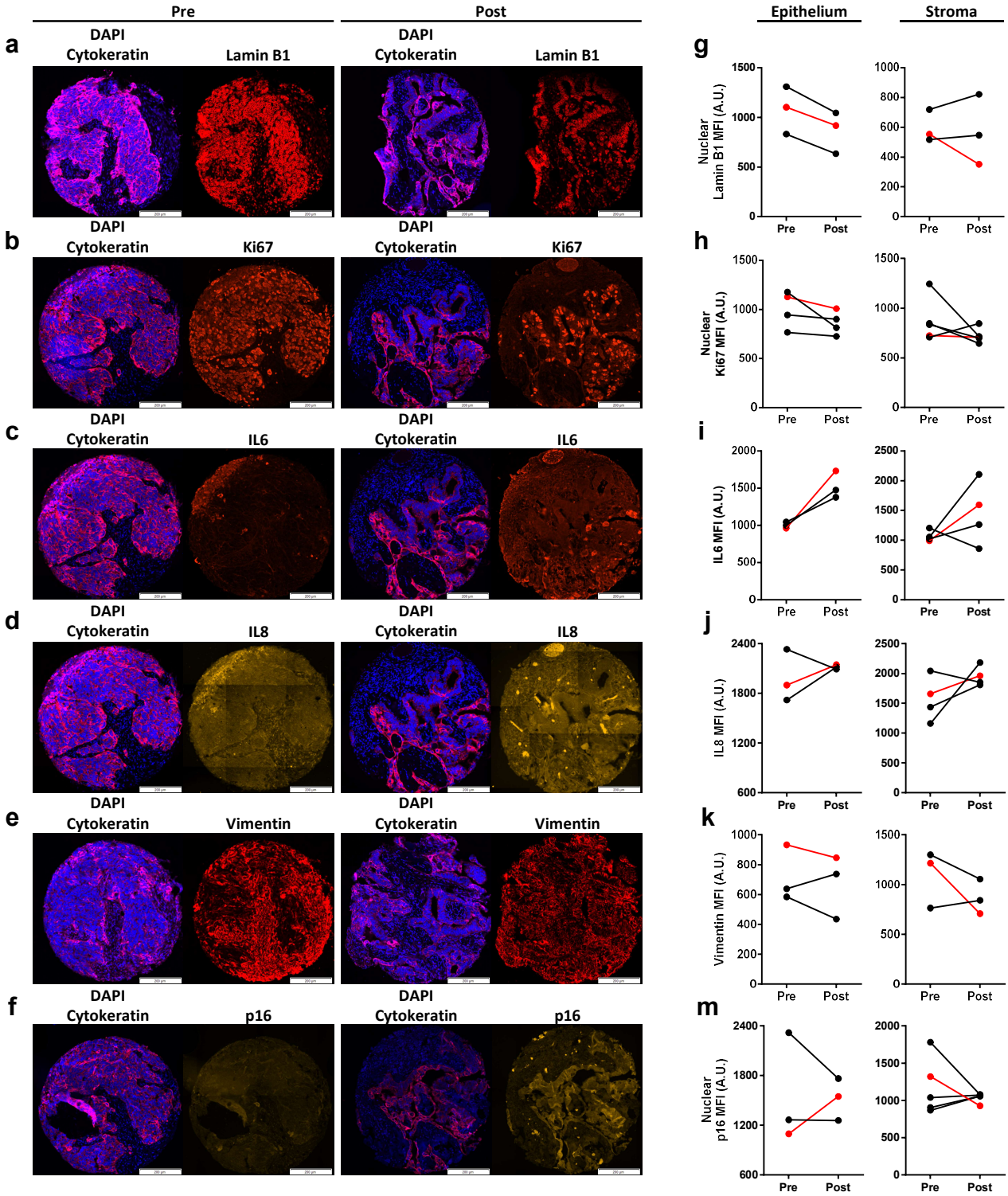
	Total n=148	Pre-chemo n=76	Post-chemo n=72
		Mean (SD)	
Age at Diagnosis (years)	60.21 (9.61)	60.54 (9.70)	59.86 (9.56)
		Median (SD)	
Follow up (months)	32.00 (35.286)	46.50 (40.03)	25.50 (27.12)
		n (%)	
Disease-specific vital status within 5 years follow-up			
Alive	65 (43.9 %)	35 (46.1 %)	30 (41.7 %)
Deceased	83 (56.1 %)	41 (53.9 %)	42 (58.3 %)
FIGO stage at presentation			
1	2 (1.4 %)	2 (2.6 %)	0 (0.0 %)
2	7 (4.7%)	6 (7.9 %)	1 (1.4 %)
3	118 (79.7 %)	60 (78.9 %)	58 (80.6 %)
4	19 (12.8 %)	8 (10.5 %)	11 (15.3 %)
Unknown	2 (1.4 %)	0 (0.0 %)	2 (2.8 %)
Residual Disease After Surgery			
None	33 (22.3 %)	12 (15.8 %)	21 (29.2 %)
1 cm or less	37 (25.0 %)	19 (25.0 %)	28 (25.0 %)
1-2 cm	19 (12.8 %)	11 (14.5 %)	8 (11.1 %)
2 cm and greater	33 (22.3 %)	26 (34.2 %)	7 (9.7 %)
Milliary	7 (4.7 %)	3 (3.9 %)	4 (5.6 %)
Unknown	19 (12.8 %)	5 (6.6 %)	14 (19.4 %)

b

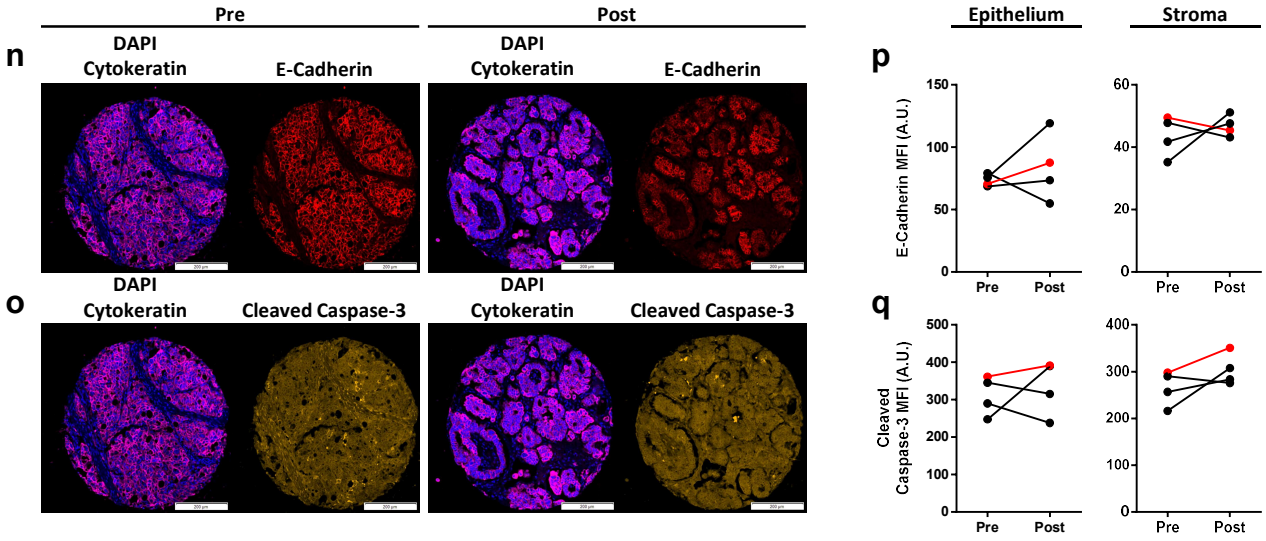
	Overall 5-year survival								
	Total			Pre-chemo			Post-chemo		
Variable	HR[a]	95 % CI[b]	p-value	HR[a]	95 % CI[b]	p-value	HR[a]	95 % CI[b]	p-value
Age at diagnosis	1.006	0.982-1.031	0.613	1.009	0.971-1.048	0.649	1.008	0.977-1.039	0.620
Residual disease after surgery			**0.0475**			0.115			**0.0119**
1 cm or less vs none	1.351	0.637-2.865	0.433	2.495	0.518-12.02	0.254	1.111	0.458-2.694	0.816
1-2 cm vs none	2.311	1.035-5.161	**0.0410**	3.863	0.779-19.16	0.0981	2.837	1.051-7.655	**0.0395**
2 cm and greater vs none	2.558	1.224-5.348	**0.0125**	5.725	1.314-24.95	**0.0202**	2.381	0.730-7.769	0.151
Miliary vs none	3.036	0.965-9.546	0.0575	4.416	0.621-31.39	0.138	12.635	2.405-66.37	**0.00273**

[a]Hazard ratio (HR) estimated from Cox proportional hazard regression model. [b]Confidence interval of the estimated HR.

Supplemental Figure 5: HGSOC tissues display senescence hallmarks following exposure to chemotherapy in patients.

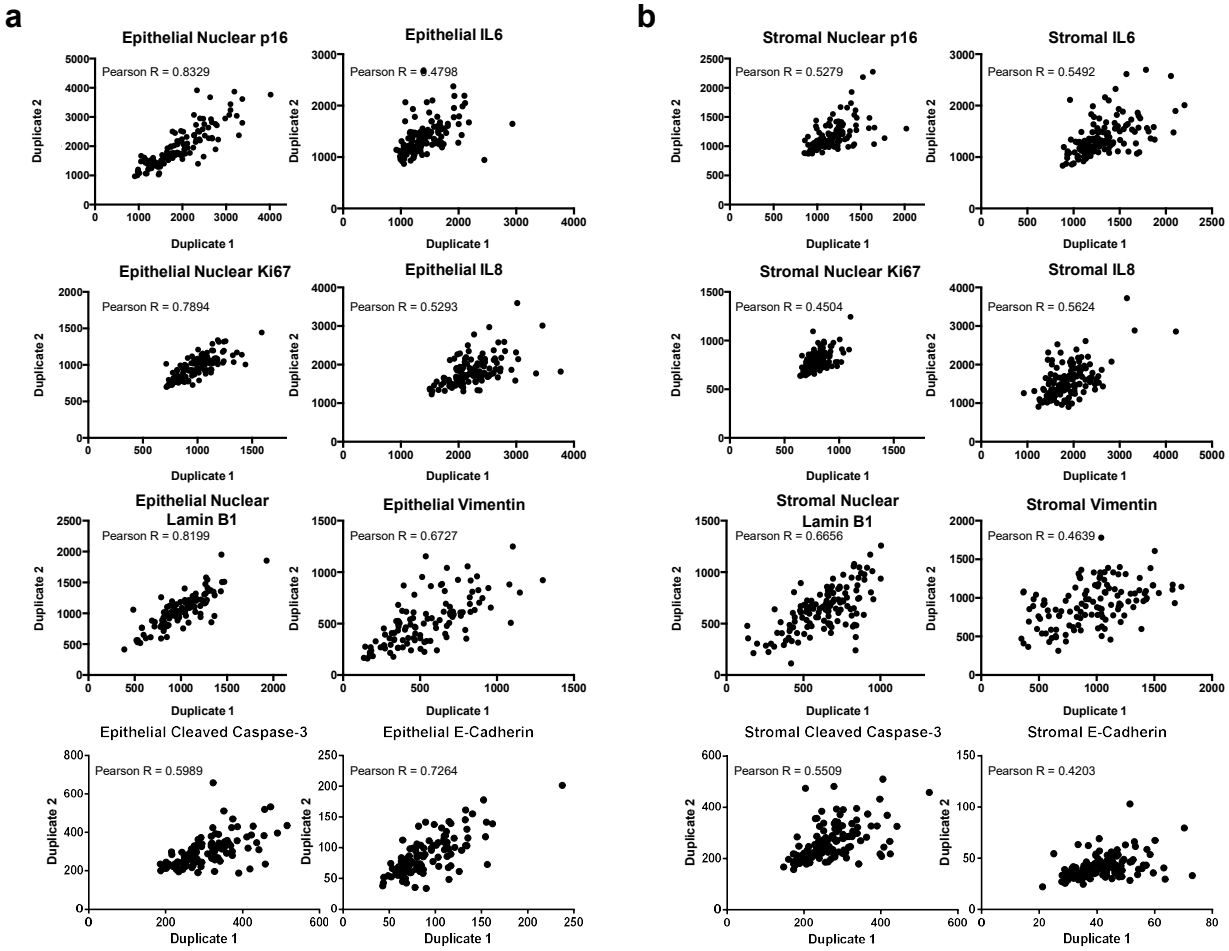


Supplemental Figure 5 (cont'd): HGSOC tissues display senescence hallmarks following exposure to chemotherapy in patients.



Supplemental Figure 6: Senescence-associated marker levels in post-chemotherapy HGSOC tissues correlate with 5-year survival.

a

	Epithelium		Stroma	
Marker	**Variation after chemotherapy**	**Kaplan-Meier Log Rank p-value**	**Variation after chemotherapy**	**Kaplan-Meier Log Rank p-value**
p16	-	0.0165 (H>L)	-	0.442
Ki67	↓	0.129 (L>H)	↓	0.0736 (H>L)
Lamin B1	↓	0.0445 (L>H)	↓	0.823
IL-6	↑	0.305	-	0.243
IL-8	-	0.0520 (H>L)	↑	0.0617 (H>L)
Vimentin	↑	0.141 (H>L)	-	8.33×10^{-4} (L>H)
E-Cadherin	↑	0.951	-	0.0775 (H>L)
Cleaved Caspase-3	-	0.562	↑	0.102 (H>L)

Supplemental Figure 7 : MFI correlations between duplicate cores.