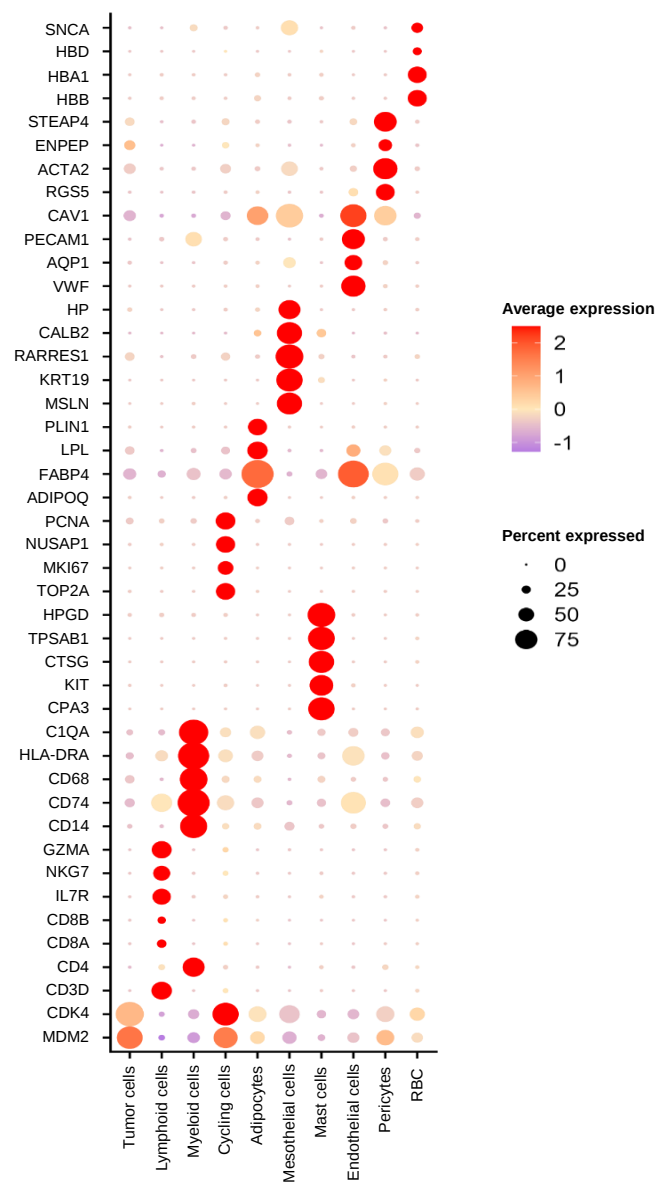
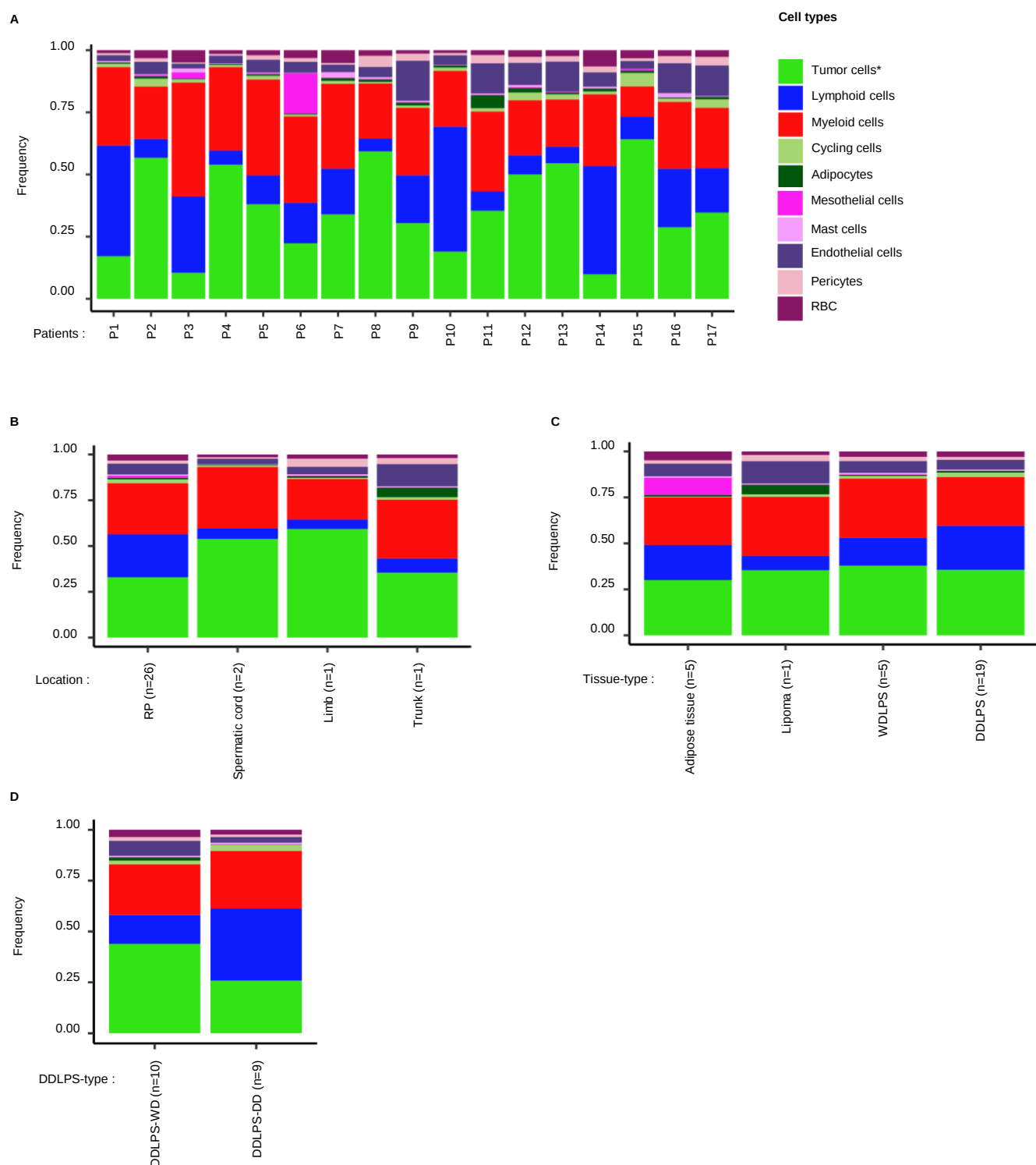




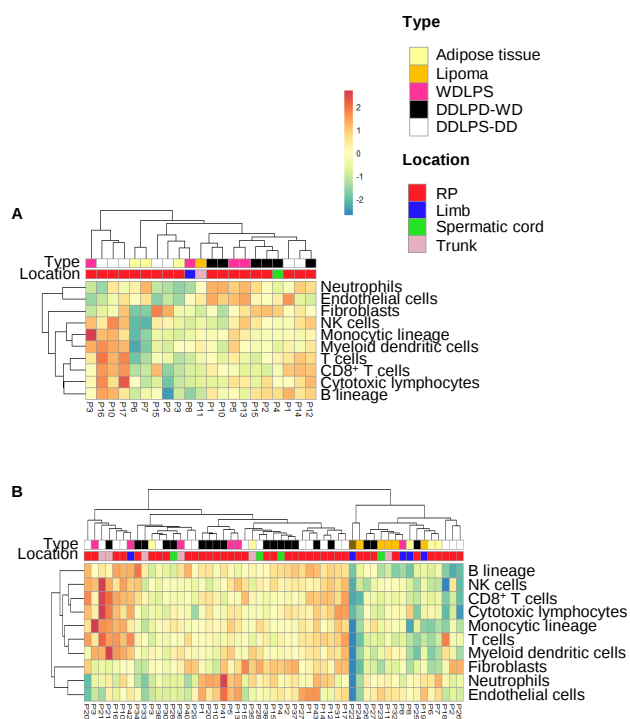
Supplementary Figure 1: Cell populations

Dot plots showing the normalized and scaled expression of the 44 representative marker genes used to annotate and define the 10 main cell populations. Abbreviation: RBC: red blood cells.



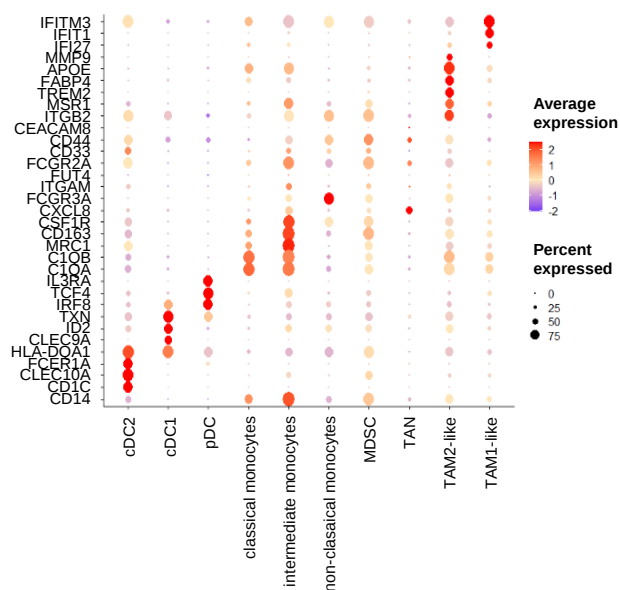
Supplementary Figure 2 : Heterogeneity of tumors and samples

Distribution of the 10 main cell populations according to the patients (A), the tumor locations (B), the histological subtypes (C), and the DDLPS components (D). * cells labelled as “tumor cells” in normal adipose tissue refer to non-stromal cells, i.e. cells from the stromal vascular fraction and are non-malignant cells. Abbreviations: RBC: red blood cells; RP: retroperitoneum. Color scales are similar for panels A, B, C and D. Source data are provided as a Source Data file.



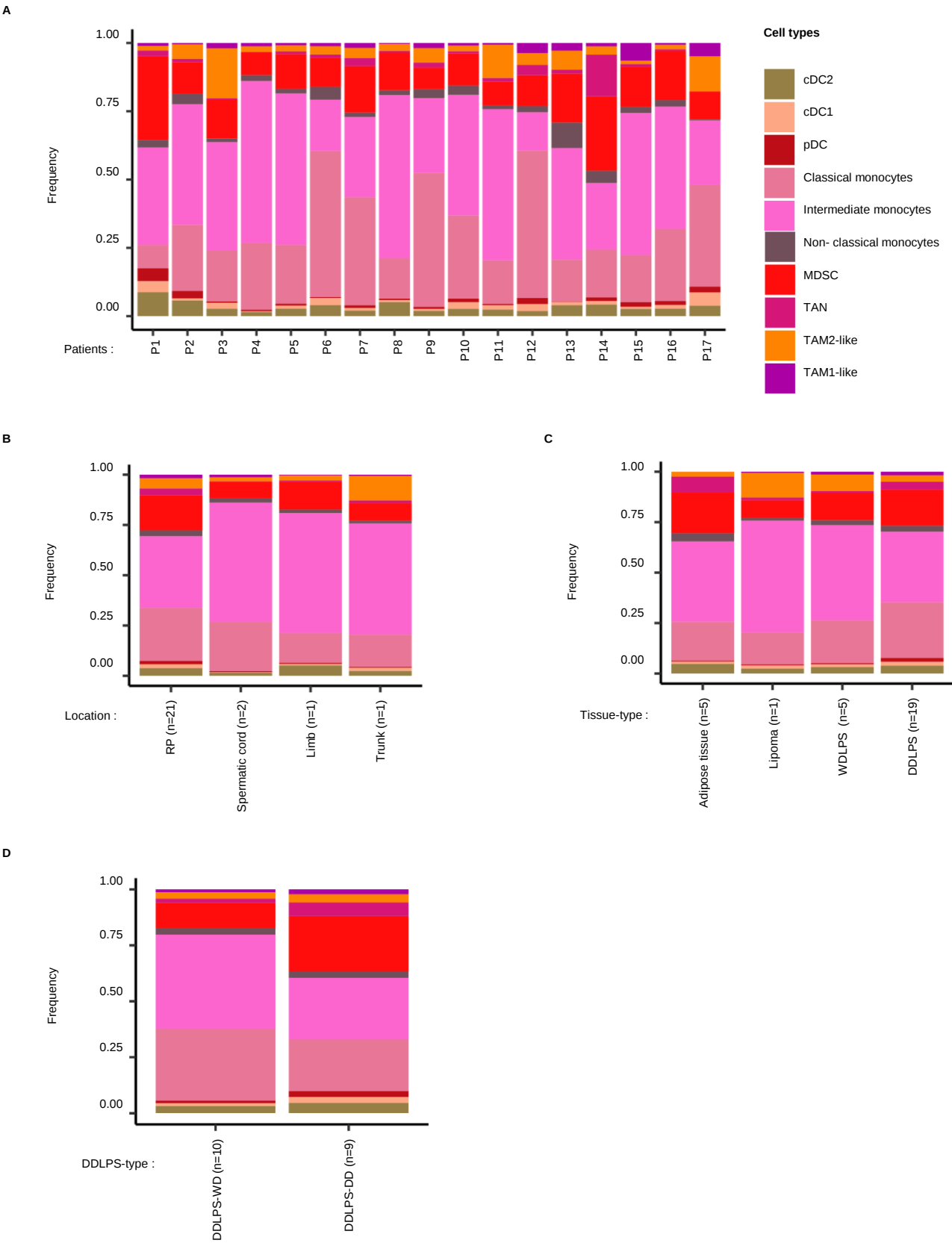
Supplementary Figure 3: Tumor microenvironment

Inference of tumor microenvironment composition using MCP Counter on bulk RNA-seq data obtained from adipocytic tumors. A: Heatmap including the same cohort of samples as the one analyzed by scRNA-seq. B: Heatmap including samples from a larger cohort of 53 adipocytic tumors.



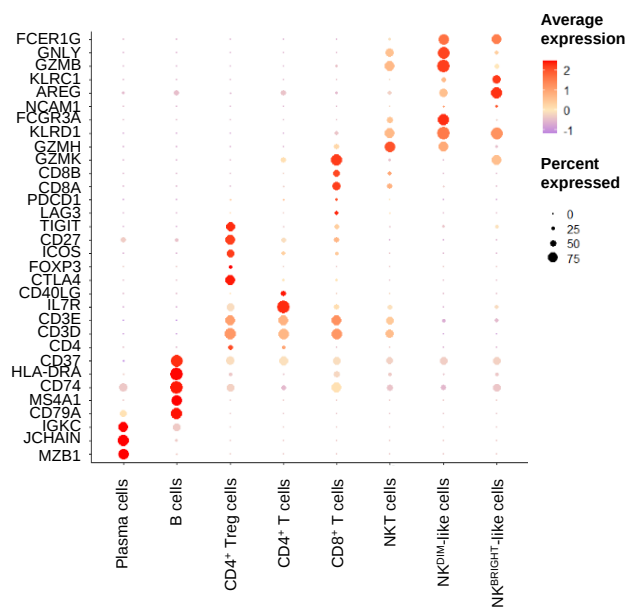
Supplementary Figure 4: Myeloid cell populations

Dot plots showing the normalized and scaled expression of 33 marker genes across the 10 cellular clusters of myeloid cells. Abbreviations: cDC: classical dendritic cells; pDC: plasmacytoid dendritic cells; MDSC: myeloid derived suppressor cells; TAN: tumor associated neutrophils; TAM1-like: M1-like tumor associated macrophages; TAM2-like: M2-like tumor associated macrophages.



Supplementary Figure 5 : Heterogeneity of myeloid cell populations across samples

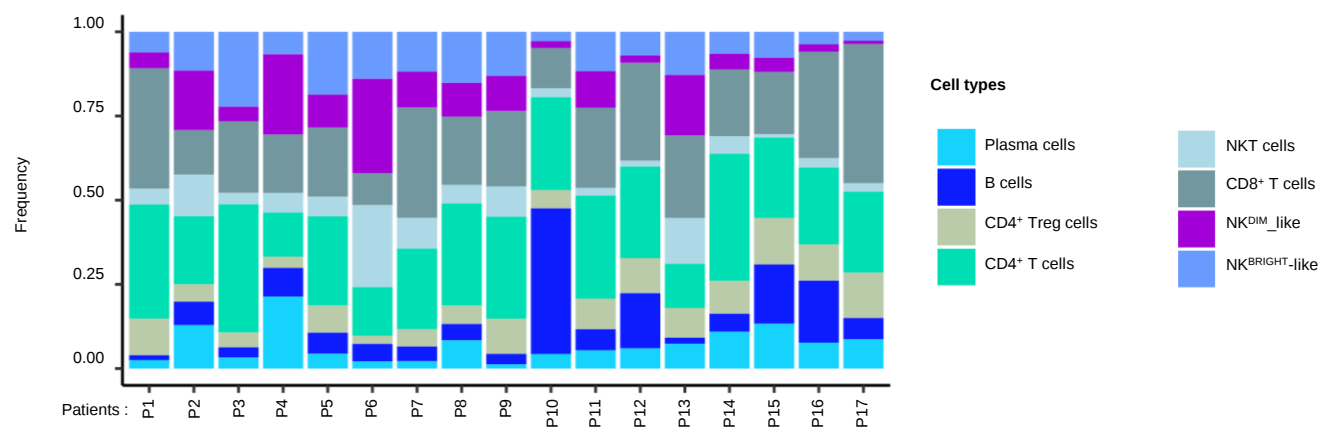
Distribution of the 10 main myeloid cell subpopulations according to the patients (A), the tumor locations (B), the histological subtypes (C), and the DDLPS components (D). Color scales are similar for panels A, B, C and D. Source data are provided as a Source Data file.



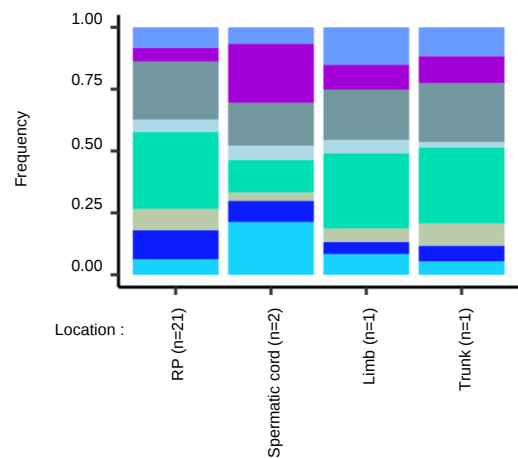
Supplementary Figure 6: Lymphoid cell populations

Dot plots showing the normalized and scaled expression of 32 marker genes across the 8 cellular clusters of lymphoid cells. Abbreviations: NK: natural killer cells

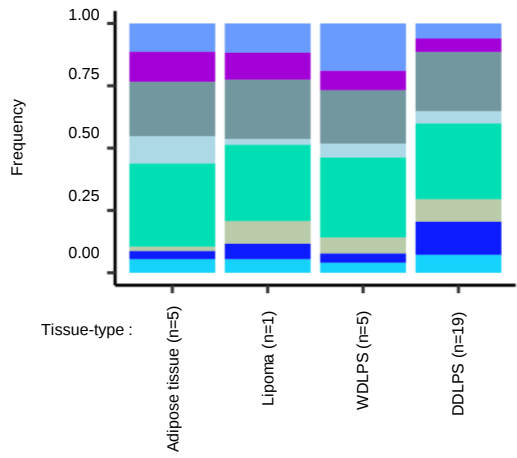
A



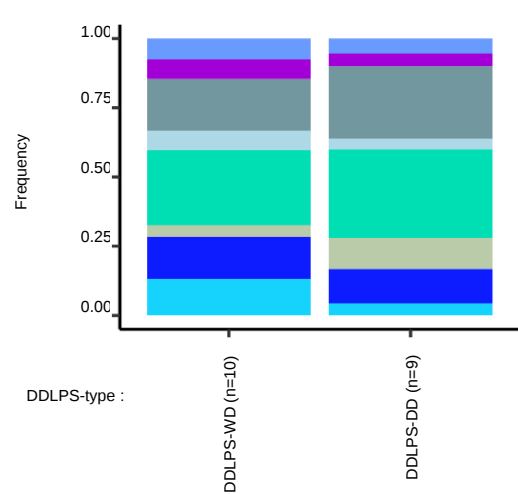
B



C

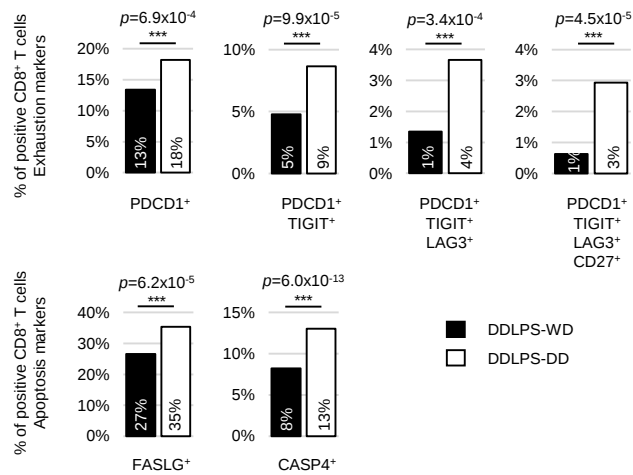


D



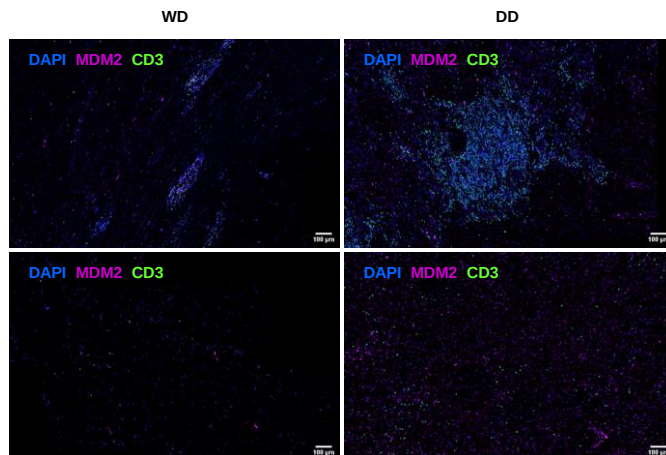
Supplementary Figure 7 : Heterogeneity of lymphoid cell populations across samples

Distribution of the 8 main lymphoid cell subpopulations according to the patients (A), the tumor locations (B), the histological subtypes (C), and the DDLPS components (D). Abbreviation: RP: retroperitoneum. Color scales are similar for panels A, B, C and D. Source data are provided as a Source Data file.



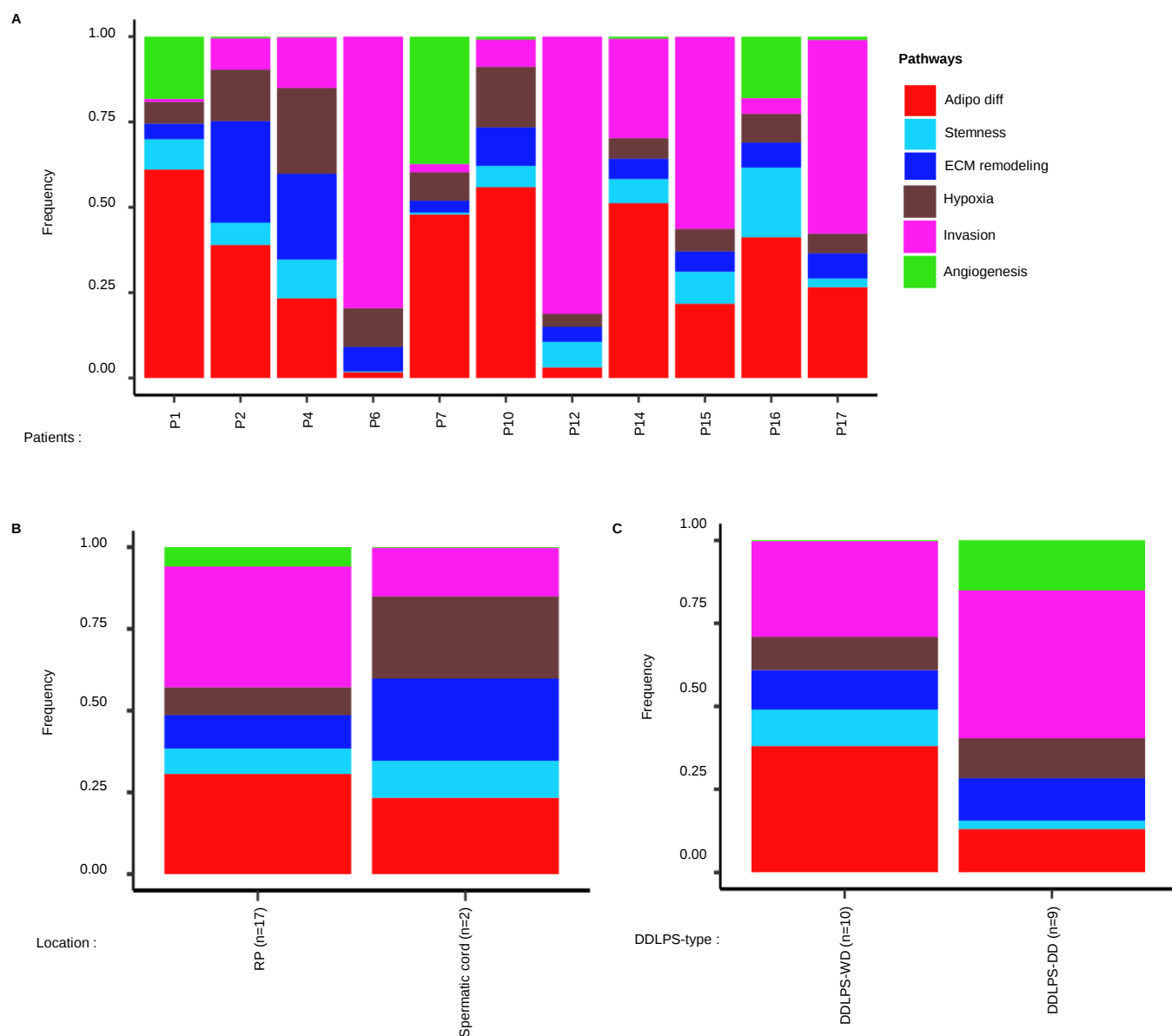
Supplementary Figure 8: CD8⁺ T cell phenotype

Comparison of the expression level of markers of exhaustion (upper panel) and apoptosis (lower panel) in CD8⁺ T cells of WD (N=10) and DD (N=9) components of DDLPS samples. *p*-val are calculated using the Chi² test. ****p*-val ≤ 0.001.



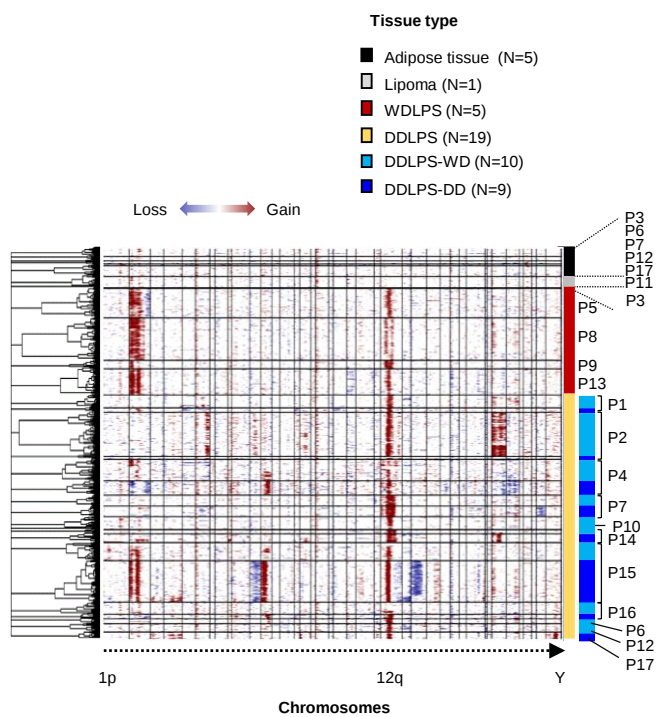
Supplementary Figure 9: Spatial organization of T cells

Heterogeneity of T cell spatial distribution across WD and DD DDLPS components assessed by *in situ* multiplex immunofluorescence with MDM2 (tumor cells, pink) and CD3 (T lymphocytes, green) antibodies. Scale bar: 100 μ m. n=7 tumor samples analyzed.



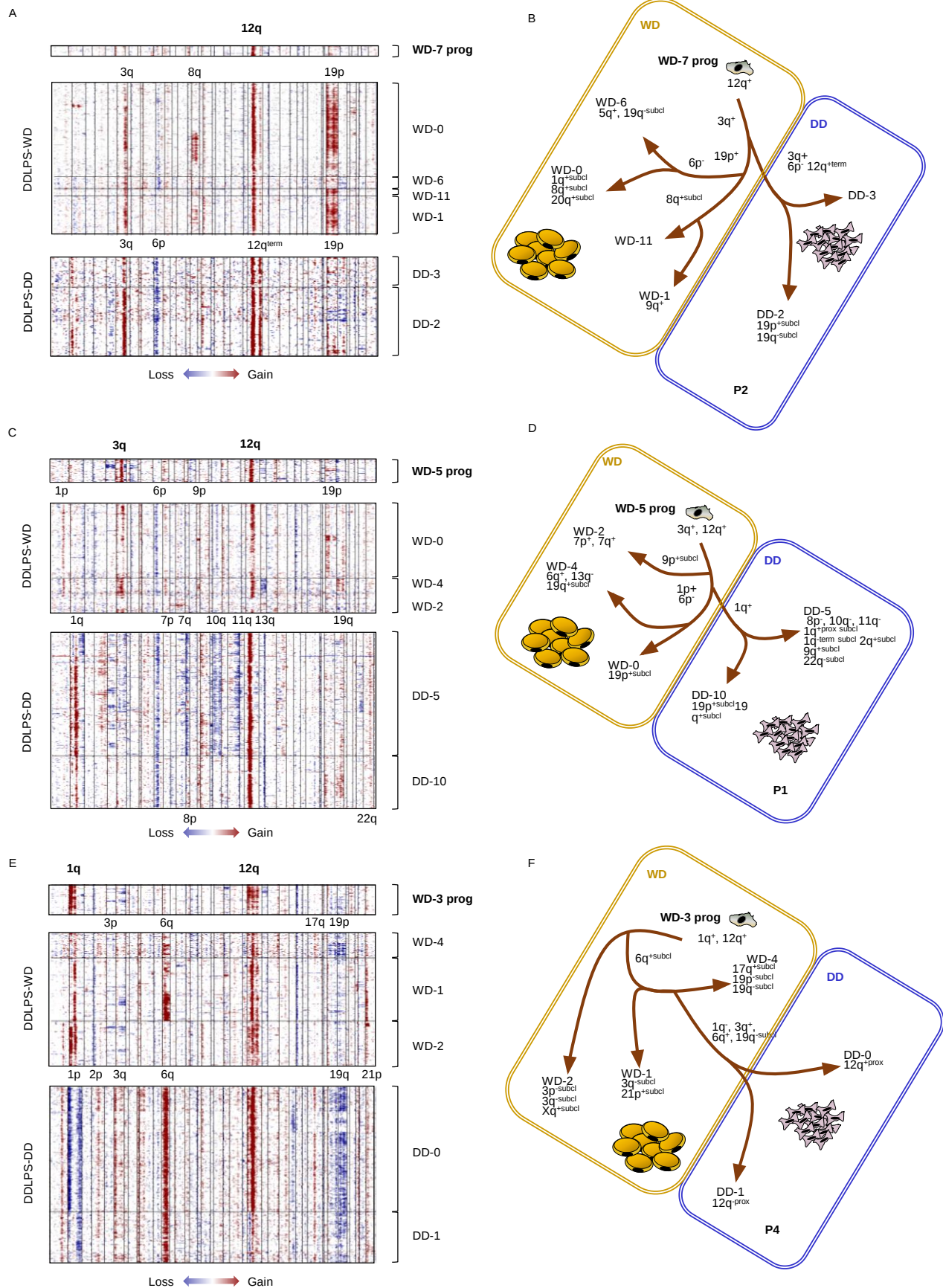
Supplementary Figure 10 : Heterogeneity of tumor cell populations

Distribution of the 6 main tumoral cell subpopulations according to DDLPS patients (A), DDLPS tumor locations (B) and DDLPS components (C). Abbreviations: adipo diff: adipocytic differentiation; ECM: extracellular matrix; RP: retroperitoneum. Color scales are similar for panels A, B, and C. Source data are provided as a Source Data file.



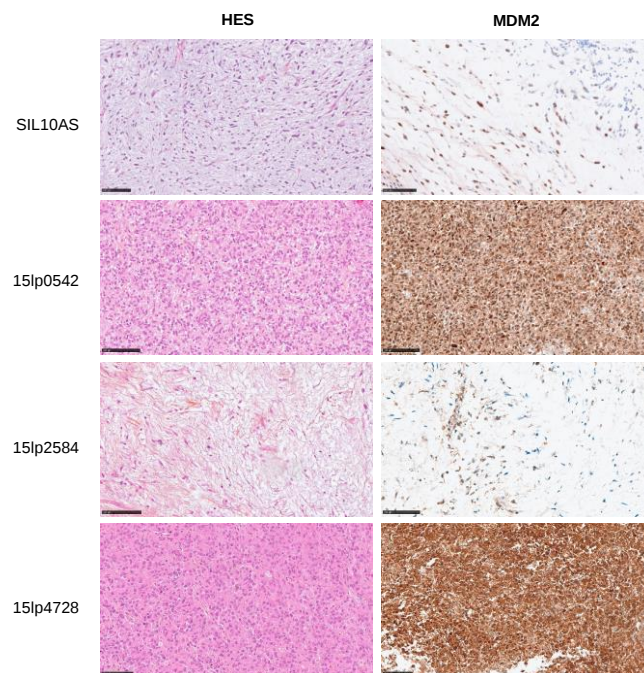
Supplementary Figure 11: InferCNV analysis in all samples

Hierarchical heatmap showing large-scale Copy Number Variations in DDLPS, WDLPS, Lipoma and Adipose tissues using inferCNV analysis on scRNA-seq samples with annotated endothelial cells as normal reference.



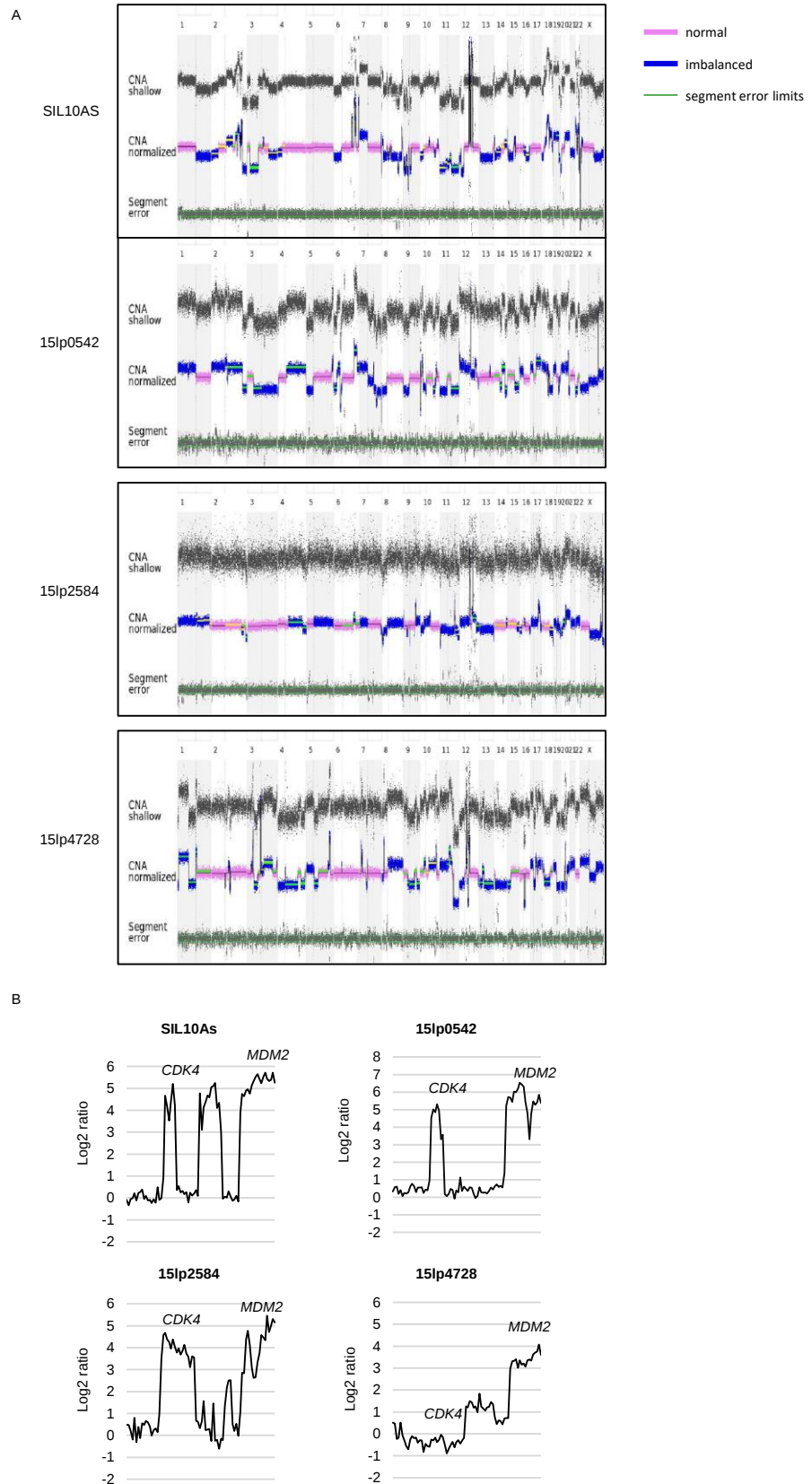
Supplementary Figure 12 : Reconstitution of DDLPS genomic evolution

Inference of copy number variations (CNV) using InferCNV in all tumor cell clusters of P2 (A), P1 (C) and P4 (E). Reconstitution of genomic clonal and subclonal evolution based on CNV found in each cell cluster for patients P2 (B), P1 (D) and P4 (F).



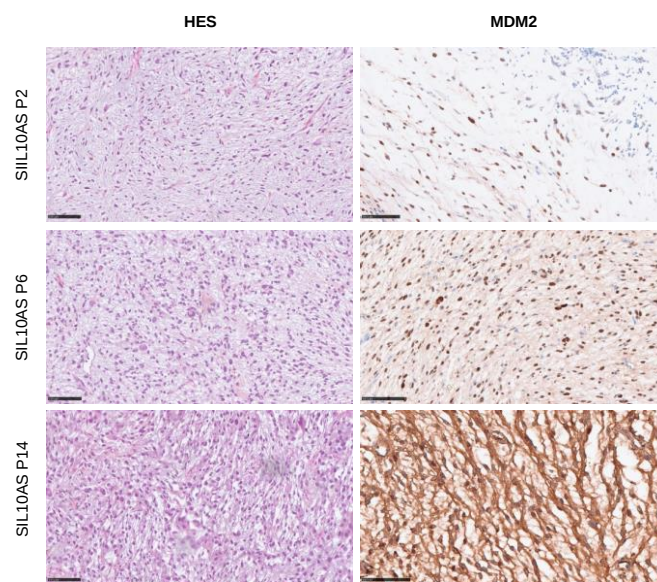
Supplementary Figure 13: Pathological characterization of PDX models

Hematoxylin and eosin-safran (HES) staining of the four PDX models (left panel) and immunohistochemical staining with MDM2 antibody (right panel). Scale bar: 100 μ m.



Supplementary Figure 14: Genomic characterization of PDX models

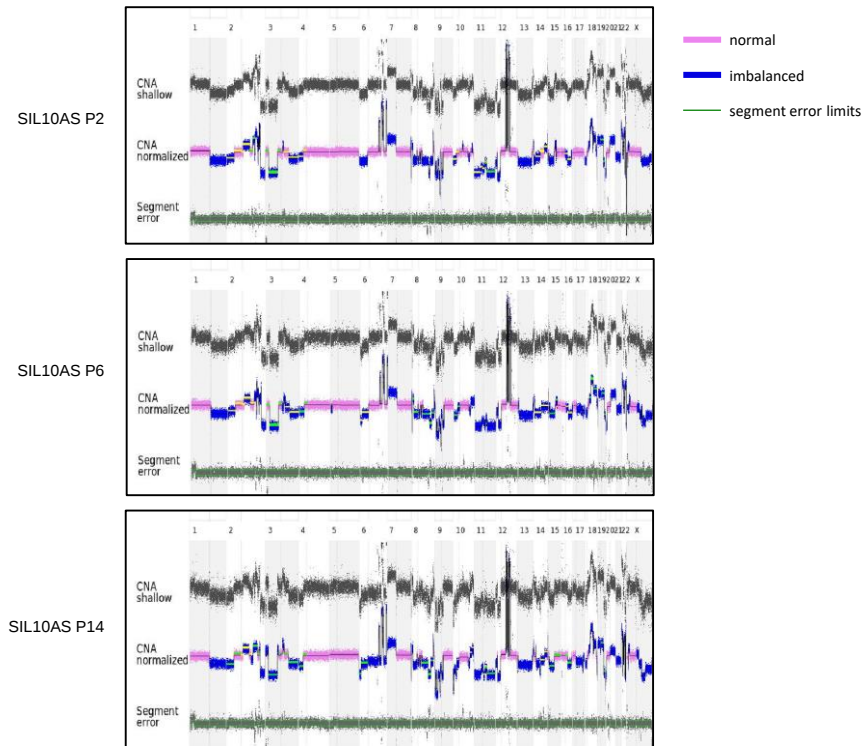
Pan genomic profiles assessed by shallow whole genome sequencing of the four PDX models (A) and focus on the 12q amplicon containing *MDM2* and *CDK4* (B).



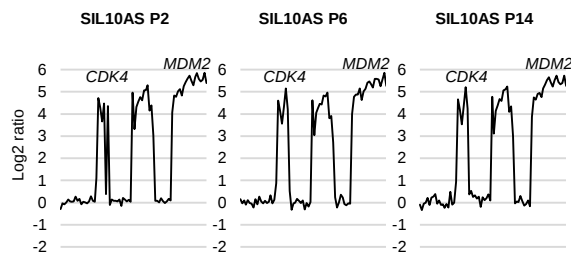
Supplementary Figure 15: Pathological characterization of PDX SIL10AS over passages

Hematoxylin and eosin-safran (HES) staining and MDM2 immunohistochemical staining of PDX SIL10AS over passages 2 (P2), 6 (P6), and 14 (P14). Scale bar= 100 μ m.

A

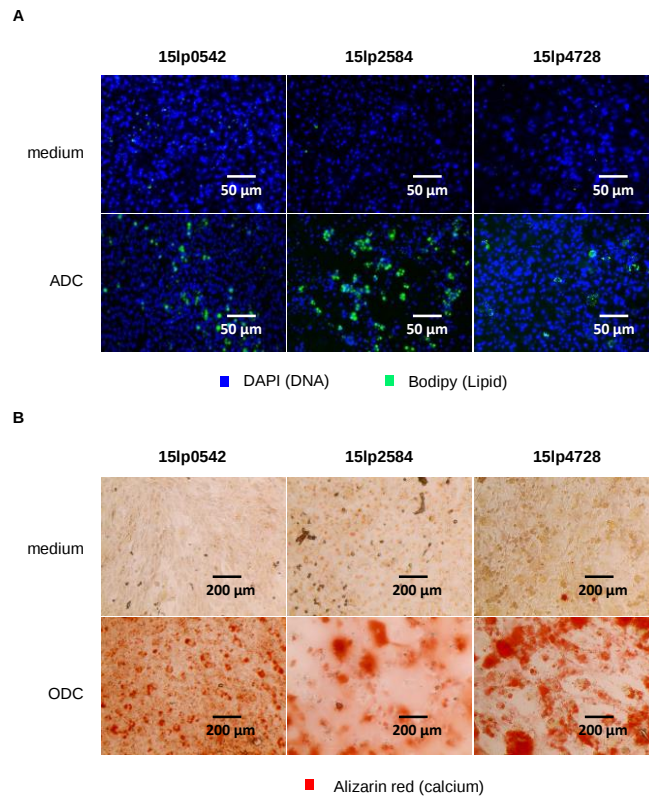


B



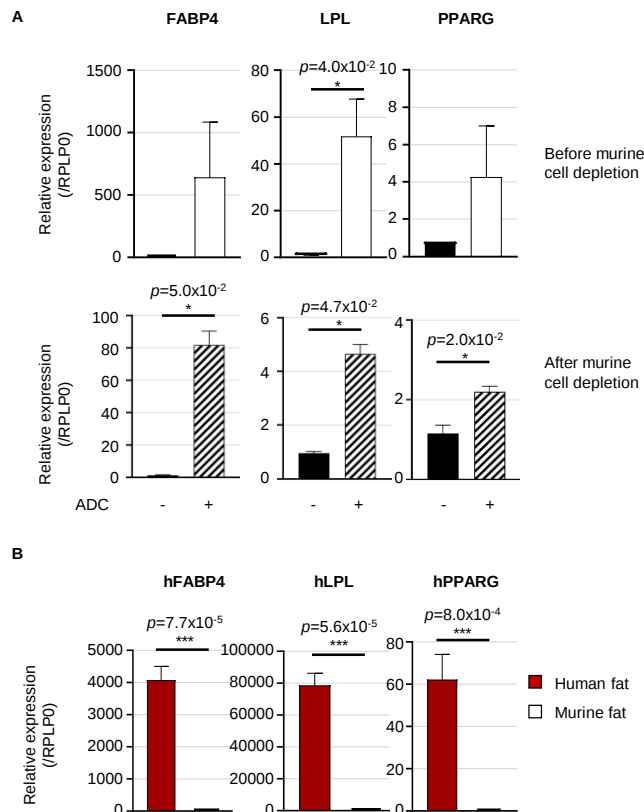
Supplementary Figure 16: Genomic characterization of PDX SIL10AS over passages

Pan genomic profiles (A) and focus on the 12q amplicon containing *MDM2* and *CDK4* (B) assessed by shallow whole genome sequencing of PDX SIL10AS over passages 2 (P2), 6 (P6), and 14 (P14).



Supplementary Figure 17: Differentiation properties of PDX models

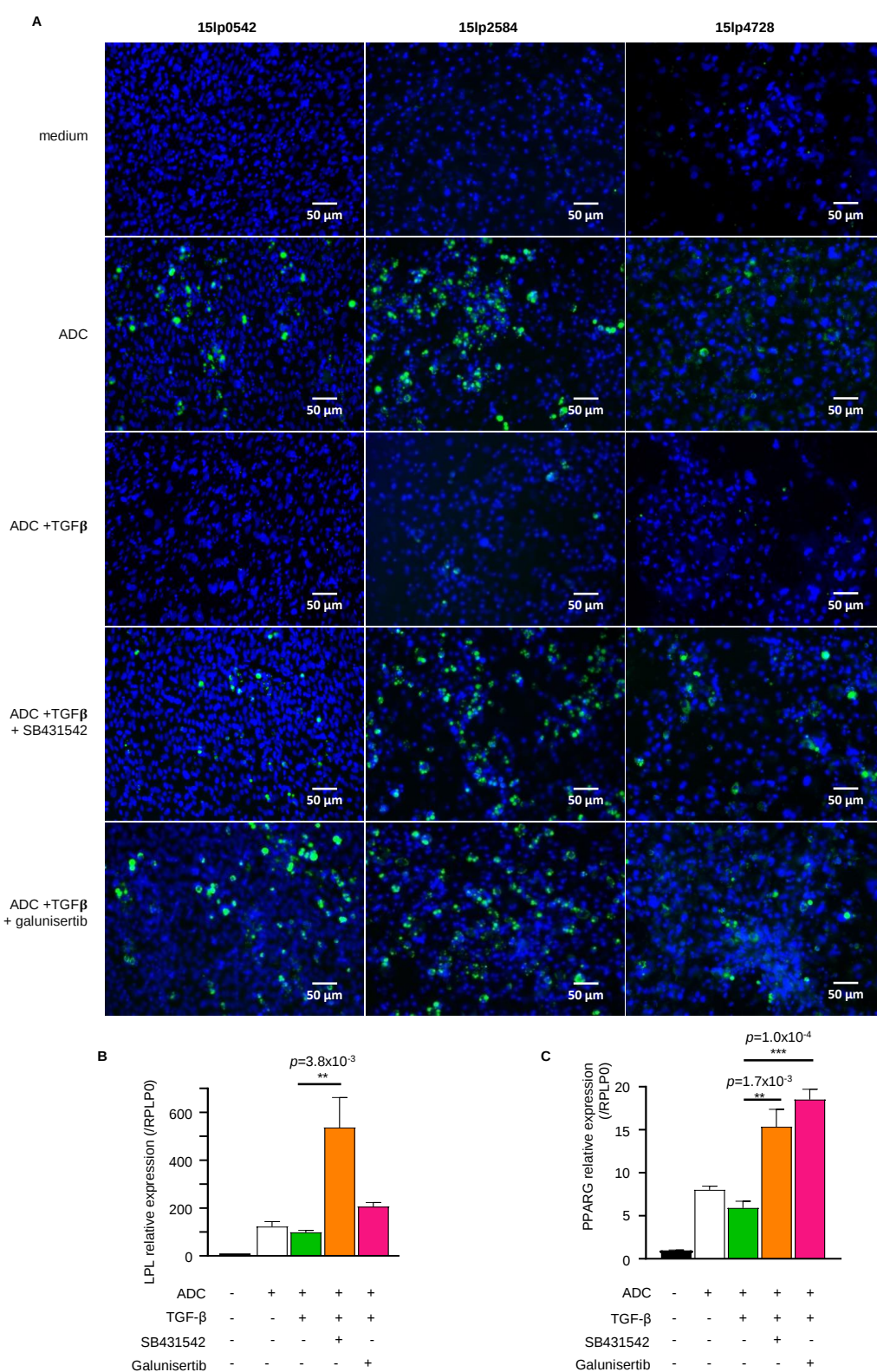
Bodipy staining (green) after culture with ADC (A), and Alizarin red staining (red) after culture with ODC (B) showing the mutipotent properties of PDX 15lp0542, 15lp2584 and 15lp4728 tumor cells (Gx10). n=3 independent experiments. Abbreviations: ADC: adipocytic differentiation cocktail; ODC: osteogenic differentiation cocktail.

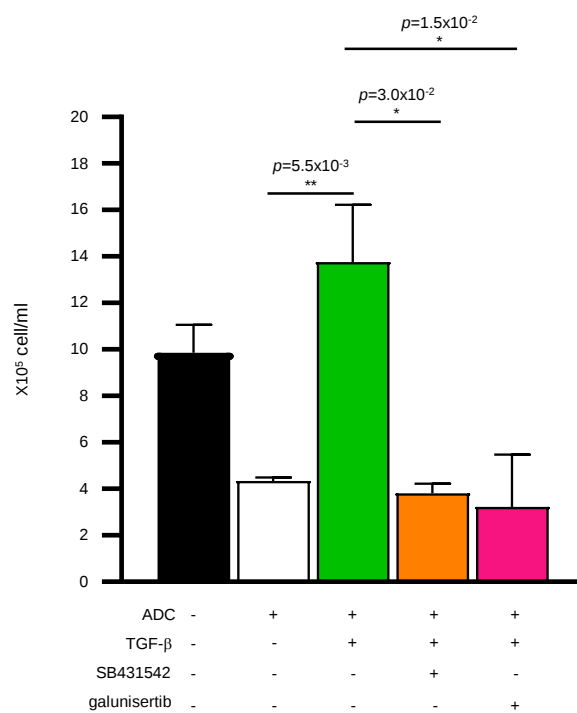


Supplementary Figure 18: RT-qPCR for human and murine adipocytic differentiation genes

A: Evaluation of the expression of human marker genes for adipocytic differentiation (*FABP4*, *LPL* and *PPARG*) by RT-qPCR in PDX SIL10AS cells after exposure to ADC, before (upper panel) or after (lower hatched panel) murine cell depletion. N=3 independent experiments (mean $\pm$ SD). B: Expression of human marker genes (*FABP4*, *LPL* and *PPARG*) for adipocytic differentiation by RT-qPCR in human and murine fat samples showing that the probes used in (A) are specific to detect human differentiation genes and do not detect murine adipocytic differentiation genes. *p*-val are calculated using the One-way ANOVA test (A) or unpaired *t*-test (B).

p*-val $\leq$ 0.05, **p*-val $\leq$ 0.001. Source data are provided as a Source Data file.

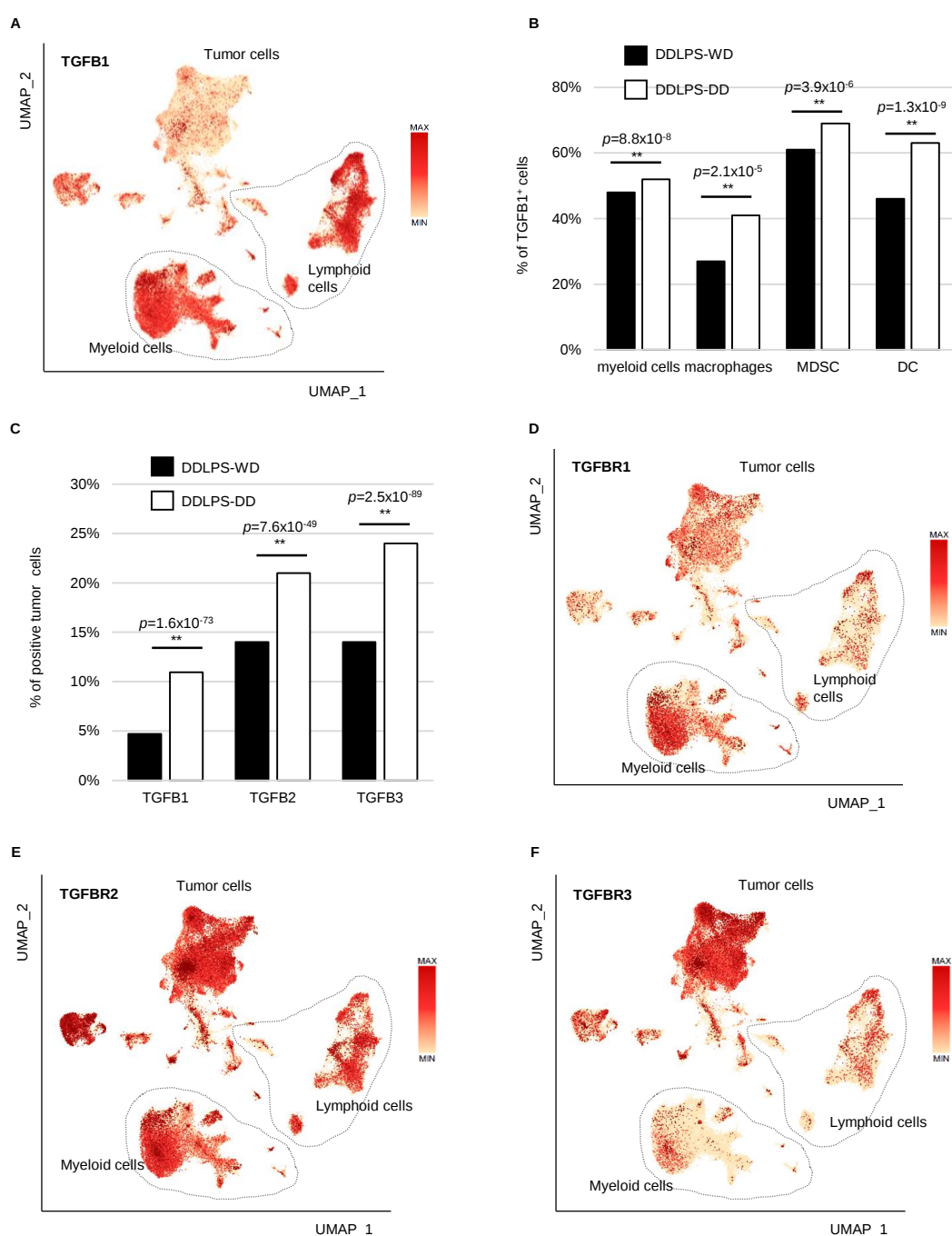




Supplementary Figure 20 : TGF- β regulation of cell proliferation in PDX SIL10AS cells

Quantification of cell concentration in PDX SIL10AS cultures after 3 days of treatment with ADC, TGF- β , and TGF- β R inhibitors (N=3 independent experiments, mean $\pm$ SD). p -val are calculated using the One-way ANOVA test. * p -val ≤ 0.05 , ** p -val ≤ 0.01 , *** p -val ≤ 0.001 . Abbreviation: ADC: adipocytic differentiation cocktail.

Source data are provided as a Source Data file.



Supplementary Figure 21: TGFB and TGFB1 expression in DDLPS samples

A: UMAP representing the expression of *TGFB1* by scRNAseq in DDLPS samples (N=19). B : Proportion of cells expressing *TGFB1* in myeloid cells, macrophages, MDSC and DC within DDLPS-WD (N=10) and DDLPS-DD (N=9) samples. C: Proportion of tumor cells in DDLPS-WD and DDLPS-DD samples expressing *TGFB1*, *TGFB2*, and *TGFB3*. D, E, F : UMAP representing the expression of *TGFB1* (D), *TGFB2* (E), and *TGFB3* (F) by scRNAseq in DDLPS samples (N=19). *p*-val are calculated using the Chi² test. ***p*-val ≤ 0.001. Source data are provided as a Source Data file.

	Percent.mt before filtering	Percent.mt after filtering	nCount_RNA before filtering	nCount_RNA after filtering	nFeature_RNA before filtering	nFeature_RNA after filtering
count (nb of cells)	154740.000000	102753.000000	154740.000000	102753.000000	154740.000000	102753.000000
mean	10.137880	7.204645	6960.388484	6251.233716	1841.888174	1807.626055
std	10.058141	4.173237	9646.781610	6438.358861	1407.542820	1200.425148
min	0.000000	0.000000	498.000000	511.000000	198.000000	207.000000
25%	4.513086	4.306632	1538.000000	1790.000000	704.000000	806.000000
50%	7.088791	6.546811	3981.000000	4348.000000	1450.000000	1557.000000
75%	11.626598	9.425844	8832.000000	8501.000000	2620.250000	2551.000000
max	95.341167	19.994530	259520.000000	104876.000000	10547.000000	8747.000000

Supplementary Table 1: QC statistics

Quality control statistics of the single-cell RNAseq dataset before and after filtering, including percentage of mitochondrial genes (percent.mt), number of unique molecular identifiers (NCount_RNA), and number of genes (NFeatures_RNA).

A

Main types	Cell count
DDLPS	67,343
WDLPS	24,144
Lipoma	2,863
Adipose tissue	8,403
Total	102,753

DDLPS subtype	Cell count
DDLPS-WD	36,326
DDLPS-DD	31,017
Total	67,343

B

Patient ID	Main type	Subtype	Cell count
P1	DDLPS	DDLPS-DD	6,280
P1	DDLPS	DDLPS-WD	2,044
P2	DDLPS	DDLPS-DD	801
P2	DDLPS	DDLPS-WD	6,183
P4	DDLPS	DDLPS-DD	2,409
P4	DDLPS	DDLPS-WD	3,299
P6	DDLPS	DDLPS-WD	1,970
P7	DDLPS	DDLPS-DD	2,900
P7	DDLPS	DDLPS-WD	1,715
P10	DDLPS	DDLPS-DD	2,484
P10	DDLPS	DDLPS-WD	3,345
P12	DDLPS	DDLPS-WD	8,301
P14	DDLPS	DDLPS-DD	6,674
P14	DDLPS	DDLPS-WD	4,146
P15	DDLPS	DDLPS-DD	5,124
P15	DDLPS	DDLPS-WD	2,719
P16	DDLPS	DDLPS-DD	2,195
P16	DDLPS	DDLPS-WD	2,604
P17	DDLPS	DDLPS-DD	2,150
P3	WDLPS		5,087
P5	WDLPS		6,489
P8	WDLPS		5,983
P9	WDLPS		2,501
P13	WDLPS		4,084
P11	Lipoma		2,863
P12	Adipose tissue		480
P17	Adipose tissue		2,172
P3	Adipose tissue		2,486
P6	Adipose tissue		1,589
P7	Adipose tissue		1,676
Total			102,753

Supplementary Table 2: Cell counts

Number of cells successfully analyzed by scRNA-seq according to the main histological subtypes (A) and to individual samples (B).

Cell type	Lipoma N=1		WDLPS N=5		DDLPS N=19		DDLPS-WD N=10		DDLPS-DD N=9	
	N	%	N	%	N	%	N	%	N	%
Tumor cells	1 014	35,4%	9,129	37,8%	24,000	35,6%	15,982	44,0%	8,018	25,9%
Lymphoid cells	222	7,8%	3,646	15,1%	16,110	23,9%	5,131	14,1%	10,979	35,4%
Myeloid cells	920	32,1%	7,802	32,3%	17,835	26,5%	9,041	24,9%	8,794	28,4%
Mast cells	16	0,6%	188	0,8%	414	0,6%	185	0,5%	229	0,7%
Cycling cells	39	1,4%	335	1,4%	1,590	2,4%	655	1,8%	935	3,0%
Adipocytes	149	5,2%	162	0,7%	600	0,9%	579	1,6%	21	0,1%
Mesothelial cells	4	0,1%	55	0,2%	145	0,2%	78	0,2%	67	0,2%
Endothelial cells	348	12,2%	1,558	6,5%	3,575	5,3%	2,691	7,4%	884	2,9%
Pericytes	95	3,3%	564	2,3%	1,054	1,6%	687	1,9%	367	1,2%
RBC	56	2,0%	705	2,9%	2,020	3,0%	1,297	3,6%	723	2,3%
Total	2,863	100%	24,144	100%	67,343	100%	36,326	100%	31,017	100%

Supplementary Table 3: Main cellular populations

Absolute count (N) and distribution (%) of each cellular population according to the histological subtype.
RBC: red blood cells.

Sample	Number of SC								
	Tumor cells	Myeloid cells	Mast cells	Cycling cells	Adipocytes	Mesothelial cells	Endothelial cells	Pericytes	RBC
P1.DD	369	2,135	36	70	0	0	75	34	91
P1.WD	1,054	489	8	43	41	5	123	35	8
P4.DD	1,278	704	5	17	2	2	87	7	38
P4.WD	1,798	1,210	5	33	19	1	91	35	48
P10.DD	24	269	8	59	0	3	11	6	1
P10.WD	1,082	1,037	2	21	50	2	212	47	66
P15.DD	3,478	543	5	413	2	48	30	23	222
P15.WD	1,551	413	1	12	69	2	221	62	34
P16.DD	372	749	75	61	0	0	68	26	97
P16.WD	1,008	541	5	4	18	4	513	110	18
P7.DD	915	1,497	82	61	0	3	21	8	10
P7.WD	908	262	14	10	47	3	156	26	44
P2.DD	264	143	3	14	15	2	163	23	7
P2.WD	3,695	1,330	20	209	51	28	191	79	219
P14.DD	724	2,179	14	98	1	6	286	166	167
P14.WD	342	943	54	27	127	4	344	84	545

Group 1	Group 2	<i>p</i> -val_adj	<i>p</i> -val_adj signif	Direction	Cell type
P1.DD	P1.WD	0,0E+00	****	DD > WD	TME
P1.DD	P1.WD	1,8E-260	****	DD > WD	Lymphoid cells
P1.DD	P1.WD	8,4E-18	****	DD > WD	Myeloid cells
P4.DD	P4.WD	1,4E-01	<i>ns</i>	DD > WD	TME
P4.DD	P4.WD	2,1E-51	****	DD > WD	Lymphoid cells
P4.DD	P4.WD	1,9E-09	****	WD > DD	Myeloid cells
P10.DD	P10.WD	7,2E-201	****	DD > WD	TME
P10.DD	P10.WD	0,0E+00	****	DD > WD	Lymphoid cells
P10.DD	P10.WD	7,7E-75	****	WD > DD	Myeloid cells
P15.DD	P15.WD	8,7E-22	****	WD > DD	TME
P15.DD	P15.WD	8,0E-19	****	WD > DD	Lymphoid cells
P15.DD	P15.WD	1,7E-09	****	WD > DD	Myeloid cells
P16.DD	P16.WD	3,9E-62	****	DD > WD	TME
P16.DD	P16.WD	5,7E-56	****	DD > WD	Lymphoid cells
P16.DD	P16.WD	1,4E-25	****	DD > WD	Myeloid cells
P7.DD	P7.WD	4,2E-47	****	DD > WD	TME
P7.DD	P7.WD	4,9E-05	****	WD > DD	Lymphoid cells
P7.DD	P7.WD	1,5E-133	****	DD > WD	Myeloid cells
P2.DD	P2.WD	2,5E-47	****	DD > WD	TME
P2.DD	P2.WD	6,0E-52	****	DD > WD	Lymphoid cells
P2.DD	P2.WD	8,5E-03	**	WD > DD	Myeloid cells
P14.DD	P14.WD	5,2E-06	****	WD > DD	TME
P14.DD	P14.WD	1,5E-07	****	DD > WD	Lymphoid cells
P14.DD	P14.WD	1,0E-28	****	DD > WD	Myeloid cells

Supplementary Table 4: Cellular heterogeneity in DDLPS samples

Absolute count of each cellular population and comparison of the distribution of all tumor microenvironment (TME), myeloid cells and lymphoid cells between paired WD and DD samples from DDLPS patients. Statistical test: pairwise comparison between proportion (one-sided) with Bonferroni correction for multiple testings. *p*-val_adj: *p*-value with Bonferroni correction for multiple comparisons. **: *p*-val_adj ≤ 0.01; ****: *p*-val_adj ≤ 0.001.

Cluster	SC	
	N	%
cDC2	967	3,6%
cDC1	468	1,8%
pDC	383	1,4%
classical monocytes	6,726	25,3%
intermediate monocytes	10,422	39,2%
non-classical monocytes	718	2,7%
MDSC	4,326	16,3%
TAN	786	3,0%
TAM2-like	1,319	5,0%
TAM1-like	442	1,7%
Total	26,557	100%

Supplementary Table 5: Myeloid cell populations

Number (N) and proportion (%) of each myeloid cluster in the whole dataset.

Cell type	Lipoma		WDLPS		DDLPS		DDLPS-WD		DDLPS-DD	
	N	%	N	%	N	%	N	%	N	%
DC	41	4%	398	5%	1,379	8%	509	6%	870	10%
Monocytes	668	73%	5,530	71%	11,668	65%	6,967	77%	4,701	53%
MDSC	81	9%	1,057	13%	3,188	18%	1,016	11%	2,172	25%
TAN	12	1%	65	1%	709	4%	174	2%	535	6%
TAM	118	13%	752	10%	891	5%	375	4%	516	6%
Total	920	100%	7,802	100%	17,835	100%	9,041	100%	8,794	100%

Chi² <i>p</i> -val			
Lipoma vs WDLPS	DDLPS vs Lipoma	DDLPS vs WDLPS	DDLPS-DD vs DDLPS-WD
<i>ns</i>	2,5E-04	2,3E-14	1,6E-26
<i>ns</i>	7,5E-06	1,2E-17	9,7E-241
5,3E-05	1,5E-12	9,8E-18	1,1E-121
<i>ns</i>	4,0E-05	1,1E-41	7,6E-46
2,3E-03	1,0E-24	2,5E-44	1,4E-07

Supplementary Table 6: Heterogeneity of myeloid cell populations across histological subtypes

Absolute count (N) and proportion (%) of DC, monocytes, MDSC, TAN and TAM according to histological subtypes (Chi² test).

Cell type	DDLPS-WD		DDLPS-DD		Chi ² <i>p</i> -val
	N	%	N	%	DDLPS-WD vs DDLPS-DD
MDSC	1,016	11%	2,172	25%	1,1E-121
TAM2-like	248	3%	318	4%	8,8E-04
TAN	174	2%	535	6%	7,6E-46
Total	1,438	16%	3,025	35%	9,9E-179

Supplementary Table 7: Heterogeneity of immunosuppressive myeloid cells within DDLPS

Proportion of the immunosuppressive cell populations MDSC, TAM2-like macrophages, and TAN within DDLPS WD and DD components (Chi² test).

Cluster	SC	
	N	%
Plasmocytes	1,312	7%
B cells	2,298	12%
CD4 ⁺ Treg cells	1,697	9%
CD4 ⁺ T cells	6,136	31%
CD8 ⁺ T cells	4,666	23%
NKT cells	1,001	5%
NK ^{DIM} cells	1,174	6%
NK ^{BRIGHT} cells	1,694	9%
Total	19,978	100%

Supplementary Table 8: Lymphoid cell populations

Number (N) and proportion (%) of each lymphoid cluster in the whole dataset.

Cell type	Lipoma		WDLPS		DDLPS		DDLPS-WD		DDLPS-DD	
	N	%	N	%	N	%	N	%	N	%
Plasma cells	12	5%	145	4%	1,155	7%	676	13%	479	4%
B cells	14	6%	138	4%	2,146	13%	781	15%	1,365	12%
CD4 ⁺ T cells	88	40%	1,404	39%	6,341	39%	1,607	31%	4,734	43%
CD8 ⁺ T cells	53	24%	781	21%	3,832	25%	962	19%	2,870	27%
NKT cells	5	2%	203	6%	793	5%	357	7%	436	4%
NK cells	50	23%	975	26%	1,843	11%	748	15%	1,095	10%
Total	222	100%	3,646	100%	16,110	100%	5,131	100%	10,979	100%

Chi ² p-val			
Lipoma vs WDLPS	DDLPS vs Lipoma	DDLPS vs WDLPS	DDLPS-DD vs DDLPS-WD
<i>ns</i>	<i>ns</i>	2,2E-12	1,0E-90
<i>ns</i>	2,2E-03	1,9E-59	1,2E-06
<i>ns</i>	<i>ns</i>	<i>ns</i>	2,8E-46
<i>ns</i>	<i>ns</i>	2,3E-03	1,0E-24
3,3E-02	<i>ns</i>	<i>ns</i>	3,3E-16
<i>ns</i>	3,0E-07	8,3E-126	1,2E-17

Supplementary Table 9: Heterogeneity of lymphoid cell populations across histological subtypes

Number (N) and proportion (%) of plasma cells, B cells, CD4⁺ T cells, CD8⁺ T cells, NKT cells and NK cells according to the different histological subtypes (Chi² test).

Cell type	DDLPS-WD		DDLPS-DD		Chi ² <i>p</i> -val
	N	%	N	%	DDLPS-WD vs DDLPS-DD
NK cells	748	15%	1,095	10%	3,0E-144
NKT cells	357	7%	436	4%	2,7E-77
CD4 ⁺ Treg cells	214	4%	1,231	11%	2,0E-08
CD8 ⁺ T cells	96	19%	2,870	26%	6,7E-199
Total	1,415	45%	5,632	51%	6,9E-176

Supplementary Table 10: Heterogeneity of lymphoid cell subpopulations within DDLPS

Number (N) and proportions (%) of NK cells, NKT cells, CD4⁺ Treg cells and CD8⁺ T cells within DDLPS WD and DD components (Chi² test).

Marker for	Gene	DDLPS-WD		DDLPS-DD		Chi ² <i>p</i> -val
		N	%	N	%	DDLPS-WD vs DDLPS-DD
exhaustion	PDCD1 ⁺	129	13%	522	18%	6,9E-04
exhaustion	PDCD1 ⁺ TIGIT ⁺	46	5%	248	9%	9,9E-05
exhaustion	PDCD1 ⁺ TIGIT ⁺ LAG3 ⁺	13	1%	105	4%	3,4E-04
exhaustion	PDCD1 ⁺ TIGIT ⁺ LAG3 ⁺ CD27 ⁺	6	1%	84	3%	4,5E-05
apoptosis	FASLG ⁺	79	27%	374	35%	6,2E-05
apoptosis	CASP4 ⁺	256	8%	1,015	13%	6,0E-07

Supplementary Table 11: CD8⁺ T cell phenotype in DDLPS

Comparison of the absolute count (N) and proportion (%) of CD8⁺ T cells expressing markers of exhaustion and markers of apoptosis within DDLPS WD and DD components (Chi² test).

Cell category	Cell type	Function	DDLPS-WD	DDLPS-DD
Lymphoid cells	B cells	Protection	15%	12%
	NK cells	Protection	15%	10%
	NKT cells	Protection	7%	4%
	CD4 ⁺ Treg cells	Immunosuppression	4%	11%
	Exhausted CD8 ⁺ T cells	Immunosuppression	19%	26%
Myeloid cells	MDSC	Immunosuppression	11%	25%
	TAM2-like	Immunosuppression	3%	4%
	TAN	Immunosuppression	2%	6%

Supplementary Table 12: Tumor microenvironment in DDLPS components

Comparison of the proportions of lymphoid and myeloid cell populations within DDLPS samples.

Cell type	Adipose tissue		Lipoma		WDLPS		DDLPS		DDLPS-WD		DDLPS-DD	
	N	%	N	%	N	%	N	%	N	%	N	%
Adipo diff	1,288	51%	459	46%	4,013	45%	7,123	30%	6,078	38%	1,045	12%
Stemness	743	29%	192	19%	1,390	15%	1,963	8%	1,760	11%	203	3%
ECM remodeling	258	10%	125	12%	1,502	16%	2,928	12%	1,901	12%	1,027	13%
Hypoxia	186	7%	145	14%	1,044	11%	2,557	11%	1,594	10%	963	12%
Angiogenesis	14	1%	18	2%	90	1%	1,246	5%	41	0%	1,205	15%
Invasion	31	1%	75	7%	1,090	12%	8,183	34%	4,608	29%	3,575	45%
Total	2,520	100%	1,014	100%	9,129	100%	24,000	100%	15,982	100%	8,018	100%

DDLPS vs Adipose tissue	DDLPS vs Lipoma	DDLPS vs WDLPS	DDLPS-DD vs DDLPS-WD
3,40E-107	3,8E-26	1,9E-133	0,0E+00
1,10E-247	6,0E-33	1,7E-80	3,3E-113
4,0E-03	<i>ns</i>	2,9E-04	4,1E-02
2,90E-07	2,5E0-04	4,1E-02	1,4E-06
2,30E-25	1,1E-06	1.1E-.67	0,0E+00
1,5E-252	3,6E-70	0,0E+00	2,8E-130

Supplementary Table 13: Tumor cell subpopulations in the whole dataset

Number (N) and proportions (%) of cells in each tumor cell cluster according to histological subtypes in the whole dataset (Chi² test).

Schalie et al, P1	Merrick et al, G1	Emont et al, hASPC2
<i>ANXA3</i>	<i>ANXA3</i>	<i>ALDH1A3</i>
<i>ITGB1</i>	<i>BMP7</i>	<i>CD55</i>
<i>CD34</i>	<i>CD34</i>	<i>CEBPD</i>
<i>CD55</i>	<i>CD55</i>	<i>CREB5</i>
<i>CREB5</i>	<i>DACT2</i>	<i>FBN1</i>
<i>IL13RA1</i>	<i>DPP4</i>	<i>KCNAB1</i>
<i>SCA1</i>	<i>GAP43</i>	<i>KCNB2</i>
<i>SMAD3</i>	<i>GPR1</i>	<i>MFAP5</i>
	<i>PI16</i>	<i>PDE11A</i>
	<i>PTGS2</i>	<i>PDGFRA</i>
	<i>SEMA3C</i>	<i>PI16</i>
	<i>STMN4</i>	<i>PRG4</i>
	<i>THY1</i>	<i>SEMA3C</i>
	<i>WNT10B</i>	<i>SFRP4</i>
	<i>WNT2</i>	

Supplementary Table 14: Stem cell signatures

List of genes used to defined adipose stem cell signatures in Schwalie *et al* (P1), Merrick *et al* (G1) and Emont *et al* (hASPC2).

PDX ID	Date of establishment	Center of establishment	Patient tumor type	Patient tumor location	Treatment before engraftment	Patient tumor histology	Patient tumor grade
SIL10AS	2018	Institut Curie	primary	retroperitoneal	none	DDLPS	3
15lp0542	2015	Institut du Cancer de Montpellier	primary	retroperitoneal	none	DDLPS	3
15lp2584	2015	Institut du Cancer de Montpellier	primary	retroperitoneal	none	DDLPS	3
15lp4728	2015	Institut du Cancer de Montpellier	primary	trunk	none	DDLPS	3

Supplementary Table 15: PDX models

Characteristics of the tumors used to establish the four Patient-Derived Xenograft (PDX) models used in *ex vivo* experiments.

	Human GPX3			Murine Gpx3		
	medium	ADC		medium	ADC	
SIL10AS P11	147	932	↗	1264	103	↘
SIL10AS P12	37	61	↗	1345	150	↘
SIL10AS P15	426	580	↗	4767	1719	↘

Supplementary Table 16: RTqPCR for human and murine *GPX3*

Human and murine GPX3 mRNA level in 3 independent experiments on PDX SIL10AS cultured *ex vivo* in presence or absence of adipocytic differentiation cocktail (ADC). Results are expressed as normalized N-fold differences in *GPX3* target (human or murin) gene expression relative to the «Total-*TBP*» expression. Total-*TBP* primer was selected to amplify both the mouse and the human *TBP* genes.