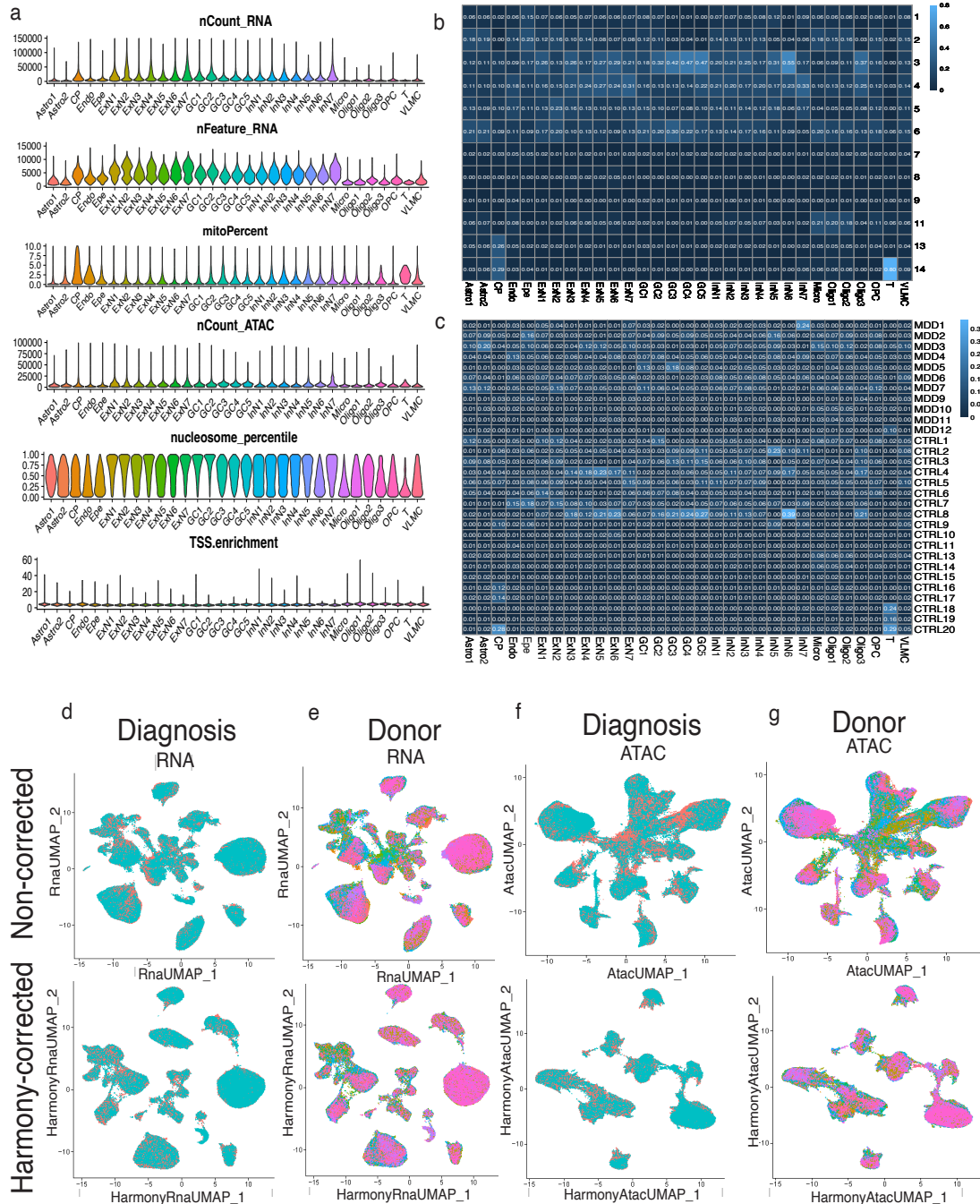
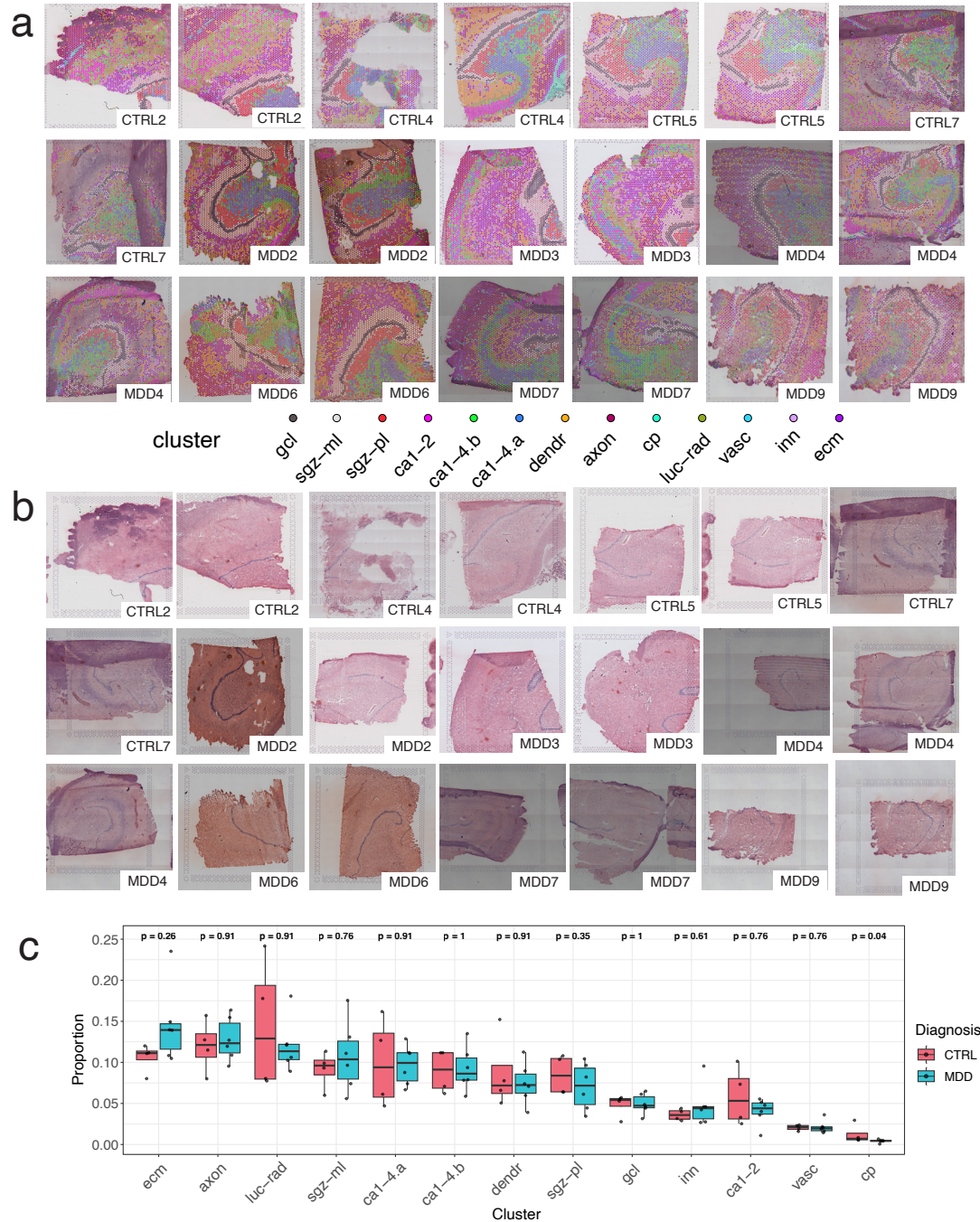

Dysregulated adult hippocampal neurogenesis in major depressive disorder

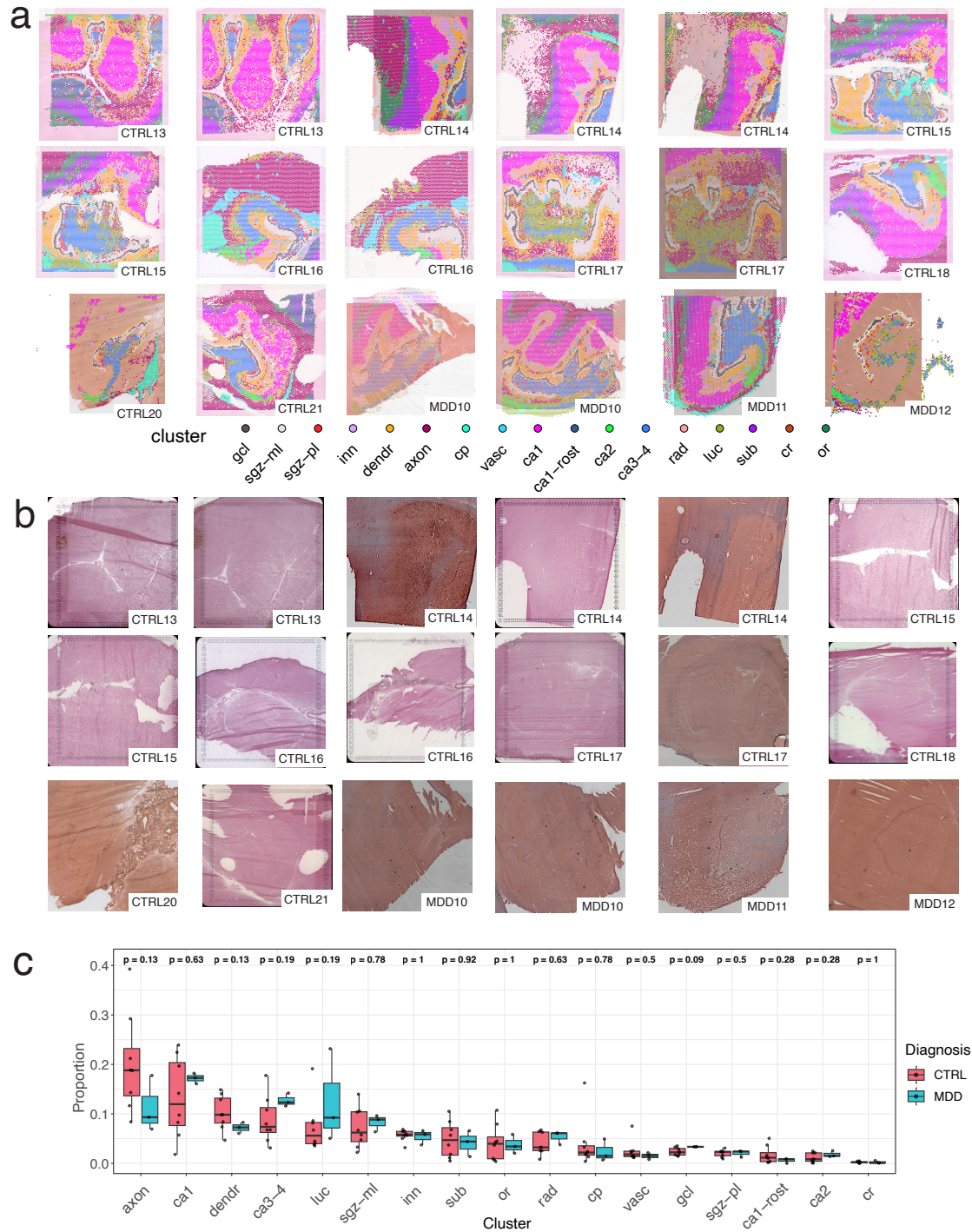
In the format provided by the
authors and unedited



Supplementary Fig. 1 | Single nucleus RNA and ATAC sequencing (snMultiome-seq) data integration, principal component analyses, and quality control. Subjects were 11 MDD and 19 CTRL (with 1-4 technical replicates each; total 44 CTRL and 30 MDD samples), retained after sequencing quality control testing out of the initial 14 MDD and 24 CTRL. **a**. Violin plots depicting quality control (QC) metrics used for filtering in each cluster on post-filtered data. **b-c**. Heat maps depicting proportion of cells contributed by each batch (**b**) and donor (**c**) across cell clusters. Each column sums to 1. Values of 0 indicate that donor or batch does not have any cells in that cluster. Values are rounded to two decimal places. **d,e**. RNA modality Uniform Manifold Approximation and Projection (UMAP) comparing uncorrected Principal Component Analysis (PCA) embeddings and harmony-corrected PCA embeddings colored by Diagnosis (**d**) and donor (**e**). **f,g**. ATAC modality UMAP comparing uncorrected latent semantic indexing (LSI) embeddings and harmony-corrected embeddings colored by diagnosis (**f**) and donor (**g**).



Supplementary Fig. 2 | Tissue sections with Visium v1 unsupervised spatial clusters and cluster proportion in MDD and CTRL. Visium v1 spatial cluster analysis was performed in 6 MDD and 9 CTRL subjects, with 2-3 biological replicates each; total 13 MDD and 8 CTRL samples. **a.** Unsupervised clustering of spatial spots overlaid on tissue sections; study ID numbers are shown; spots with lower than 500 genes/spot were removed. **b.** Hematoxylin and Eosin staining of the same tissue sections, hematoxylin stains nuclei and eosin stains cytoplasm and extracellular matrix structures; ID numbers are shown on each section. **c.** The proportion of each anatomical region sampled per donor is not significantly different between MDD and CTRL in any region except for choroid plexus (cp) which is less represented in MDD (each dot represents a donor). Pairwise comparisons were performed using two-sided Wilcoxon rank-sum tests. Resulting p -values were adjusted for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) procedure, and an FDR-adjusted p -value < 0.05 was considered statistically significant.



Supplementary Fig. 3 | Tissue sections with Visium v2 unsupervised spatial clusters and cluster proportion in MDD and CTRL. Visium v2 spatial cluster analysis was performed in 6 MDD and 9 CTRL subjects, with 1-3 biological replicates each; total 4 MDD and 13 CTRL samples. **a.** Unsupervised clustering of spatial spots overlayed on tissue sections; study ID numbers are shown; spots with lower than 500 genes/spot were removed. **b.** Hematoxylin and Eosin staining of the same tissue sections, hematoxylin stains nuclei and eosin stains cytoplasm and extracellular matrix structures; ID numbers are shown on each section. **c.** The proportion of each anatomical region sampled per donor is not different between MDD and CTRL in any region (each dot represents a donor). Pairwise comparisons were performed using two-sided Wilcoxon rank-sum tests, adjusting for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) procedure, and an FDR-adjusted p -value < 0.05 represented statistical significance.

Supplementary Table 1 | Multiome Sample Quality Control (QC)

Nuclei isolation procedure	Study ID	snMultiome Sequencing ID	Cell Ranger Cell N Report	Post QC Cell Count	Percent Cells Retained	Sample excluded from analyses	snMultiome RNA Mean Raw Reads Per Cell	snMultiome ATAC Mean Raw Reads Per Cell
Manual	CTRL1	CM044	12,247	8,974	73		43,198	15,821
Manual	CTRL1	CM115	19,752	13,938	71		36,139	22,051
Manual	CTRL1	CM116	13,918	10,088	72		88,466	36,202
Manual	CTRL2	CM021	3,502	2,222	63		108,350	71,214
Manual	CTRL2	CM053	20,000	10,746	54		30,008	22,274
Manual	CTRL3	CM038	10,982	8,610	78		51,016	18,745
Manual	CTRL3	CM109	13,686	8,123	59		40,807	22,746
Manual	CTRL3	CM110	20,000	11,055	55		21,187	14,157
Manual	CTRL4	CM023	7,350	5,304	72		90,878	38,188
Manual	CTRL4	CM071	10,904	7,766	71		46,785	20,325
Manual	CTRL4	CM072	20,000	11,296	56		14,968	21,594
Manual	CTRL5	CM024	10,446	6,903	66		58,183	30,647
Manual	CTRL5	CM069	20,000	11,796	59		20,884	13,123
Manual	CTRL5	CM070	16,716	11,068	66		22,320	18,798
Manual	CTRL6	CM026	7,554	4,750	63		64,492	17,967
Manual	CTRL6	CM059	20,000	9,777	49		20,975	17,789
Manual	CTRL6	CM060	20,000	10,203	51		37,878	15,080
Manual	CTRL7	CM043	20,000	11,180	56		30,430	11,484
Manual	CTRL7	CM091	20,000	9,474	47		24,492	8,934
Manual	CTRL7	CM092	2,795	968	35		175,002	90,780
Singulator	CTRL7	MM001	3,757	2,850	76		307,384	93,041
Manual	CTRL8	CM055	20,000	12,807	64		30,546	21,638
Manual	CTRL8	CM056	20,000	12,822	64		29,444	19,245
Manual	CTRL9	CM085	4,077	3,006	74		102,605	77,367
Manual	CTRL9	CM086	3,221	2,432	76		93,544	91,661
Manual	CTRL10	MM015	5,612	0	0	Excluded	213,993	61,898
Manual	CTRL10	MM016	7,544	5,167	68		76,366	58,102
Manual	CTRL11	MM023	5,038	3,188	63		152,613	72,347
Manual	CTRL11	MM024	3,540	2,272	64		180,301	121,070
Singulator	CTRL13	MM080	11,520	8,136	71		59,244	21,788
Singulator	CTRL13	MM081	10,257	7,280	71		65,166	17,354
Singulator	CTRL14	MM082	11,254	5,919	53		53,993	22,333
Singulator	CTRL14	MM083	9,869	5,259	53		73,151	25,299

Singulator	CTRL15	MM096	8,297	2,674	32		75,476	43,280
Singulator	CTRL15	MM097	7,226	2,412	33		60,986	36,396
Singulator	CTRL16	MM100	7,702	3,248	42		59,222	24,691
Singulator	CTRL16	MM101	6,095	2,715	45		116,975	47,558
Singulator	CTRL17	MM102	8,697	4,180	48		73,919	29,720
Singulator	CTRL17	MM103	6,524	3,289	50		90,025	25,267
Singulator	CTRL18	MM151	2,678	2,217	83		130,249	197,083
Singulator	CTRL18	MM152	2,351	1,762	75		206,916	161,918
Singulator	CTRL19	MM149	1,942	978	50		200,394	234,071
Singulator	CTRL19	MM150	1,763	881	50		181,712	278,627
Singulator	CTRL20	MM147	5,017	3,571	71		125,600	107,251
Singulator	CTRL20	MM148	3,986	2,865	72		171,729	124,399
Manual	MDD1	CM027	3,629	2,930	81		165,571	78,257
Manual	MDD1	CM075	9,669	7,837	81		36,545	59,296
Manual	MDD2	CM025	8,183	6,278	77		78,275	38,052
Manual	MDD2	CM057	20,000	11,724	59		31,346	19,126
Manual	MDD2	CM058	20,000	11,717	59		21,978	22,672
Manual	MDD3	CM042	19,502	13,565	70		32,042	11,440
Manual	MDD3	CM113	20,000	14,088	70		31,084	16,045
Manual	MDD3	CM114	18,132	12,950	71		31,933	17,335
Manual	MDD4	CM028	5,154	4,039	78		198,314	59,910
Manual	MDD4	CM073	20,000	11,865	59		22,817	18,445
Manual	MDD4	CM074	20,000	12,340	62		11,545	15,728
Manual	MDD5	CM040	8,382	5,906	70		63,188	22,457
Manual	MDD5	CM111	16,946	7,046	42		29,884	21,468
Manual	MDD5	CM112	14,036	6,858	49		37,956	19,180
Manual	MDD6	CM039	14,818	10,254	69		65,159	22,182
Manual	MDD6	CM087	1,001	725	72		499,851	222,389
Manual	MDD6	CM088	20,000	10,437	52		65,984	7,247
Singulator	MDD6	MM002	3,303	1,235	37		230,765	52,644
Manual	MDD7	CM041	15,518	10,746	69		39,186	13,575
Manual	MDD7	CM089	20,000	13,070	65		53,002	16,918
Manual	MDD7	CM090	20,000	12,884	64		23,567	12,223
Singulator	MDD8	MM003	5,447	0	0	Excluded	154,750	51,126
Singulator	MDD8	MM004	5,988	0	0	Excluded	152,801	57,612
Singulator	MDD8	MM005	5,612	0	0	Excluded	213,993	61,898
Singulator	MDD9	MM006	10,553	2,537	24		93,193	34,443
Singulator	MDD9	MM007	6,318	1,525	24		93,563	74,016
Singulator	MDD9	MM008	6,206	2,728	44		123,524	53,676

Singulator	MDD10	MM084	20,000	5,151	26		37,522	11,415
Singulator	MDD10	MM085	10,489	5,219	50		34,602	27,888
Singulator	MDD11	MM086	8,805	4,770	54		62,727	42,446
Singulator	MDD11	MM087	8,711	4,515	52		85,999	39,629
Singulator	MDD12	MM145	4,416	2,918	66		88,889	98,028
Singulator	MDD12	MM146	1,367	1,009	74		267,584	273,924
Manual	Average		14,070	8,572	62		62,351	30,800
	SD		6,460	3,640	11		64,282	25,125
	MIN		2,795	968	35		14,968	8,934
	MAX		20,000	13,938	78		307,384	93,041
Singulator	Average		9,761	5,536	55		105,487	60,447
	SD		6,265	4,397	22		85,617	62,730
	MIN		1,001	0	0		11,545	7,247
	MAX		20,000	14,088	83		499,851	278,627
Whole Sample	Average		11,916	7,054	58		83,919	45,624
	SD		6,362	4,018	16		74,949	43,927
	MIN		1,898	484	17		13,256	8,091
	MAX		20,000	14,013	81		403,617	185,834
Note:								
snMultiome Transcriptome	snMultiome Pipeline Version	Chemistry						
GRCh38-2020-A	cellranger-arc-2.0.0	Single Cell Multiome ATAC + Gene expression v1						

Supplementary Table 2 | Visium Sample Quality Control (QC)

Study ID	Visium Sequencing ID	SpaceRanger N Spots Report	Visium Spots per Sample post QC	Percent Spots Retained	Sample Excluded from Analyses	Visium RNA mean reads per spot
Visium v1						
CTRL2	CM019	3201	2784	86		41,160
CTRL2	CM020	3692	3664	99		50,376
CTRL4	CM013	2576	2550	98		47,678
CTRL4	CM014	3793	3784	99		70,345
CTRL5	CM017	2878	2811	97		59,905
CTRL5	CM018	2695	2677	99		58,810
CTRL7	MM072	4824	3412	70		46,439
CTRL7	MM073	4174	2112	50		39,933
MDD2	CM117	4500	4430	98		82,578
MDD2	CM118	3473	2985	85		69,921
MDD3	CM015	3846	3832	99		44,670
MDD3	CM016	4112	4104	99		96,710
MDD6	CM119	3333	3297	98		93,321
MDD6	CM120	3779	3725	98		89,406
MDD9	MM063	2294	1927	84		77,057
MDD9	MM064	2350	2291	97		99,468
MDD4	MM067	1993	1977	99		110,741
MDD4	MM070	4505	3632	80		50,052
MDD4	MM071	4043	3267	80		67,778
MDD7	MM068	2897	2713	93		65,544
MDD7	MM069	3803	3159	83		34,865
v1 Average		3465	3102	90		66,512
v1 SD		797	708	13		22,153
v1 MIN		1993	1927	50		34,865
v1 MAX		4824	4430	99		110,741
Note:	Visium Pipeline Version	Visium Chemistry	Visium Transcriptome			
	spaceranger-1.3.0	Spatial 3' v1	GRCh38-2020-A			
Visium v2						
CTRL13	MM134	14091	12200	86		44,837
CTRL13	MM135	13981	12039	86		51,147
CTRL14	MM130	9784	8729	89		65,233
CTRL14	MM139	12398	10083	81		56,442
CTRL14	MM143	12468	7687	61		121,329
CTRL15	MM128	13158	13150	99		59,533
CTRL15	MM140	12656	12617	99		138,712
CTRL16	MM133	11246	11232	99		66,932
CTRL16	MM138	7593	7433	97		199,623
CTRL17	MM136	14336	13021	90		50,004
CTRL17	MM142	14336	13389	93		124,224
CTRL18	RM010	11559	11023	95		68,145
CTRL20	RM002	12493	2652	21		24,285
CTRL21	RM004	12472	11202	89		40,415
CTRL24	RM009	13763	0	0	Excluded	38,434
MDD10	MM129	9977	7571	75		59,295
MDD10	MM132	12490	11609	92		106,544

MDD11	MM131	9468	9145	96		89,318
MDD12	RM001	12266	2784	22		35,254
MDD13	RM007	12463	0	0	Excluded	43,363
MDD14	RM008	12516	0	0	Excluded	46,750
MDD1	RM006	12256	0	0	Excluded	109,291
MDD5	RM005	13789	0	0	Excluded	102,450
v2 Average		12242	7720	64		78,361
v2 SD		1696	5044	40		43,127
v2 MIN		7593	0	0		24,285
v2 MAX		14336	13389	99		199,623
Note:	Visium Pipeline Version	Visium Chemistry	Visium Transcriptome			
	spaceranger-3.1.2	Spatial Probe based v2	GRCh38-2020-A			