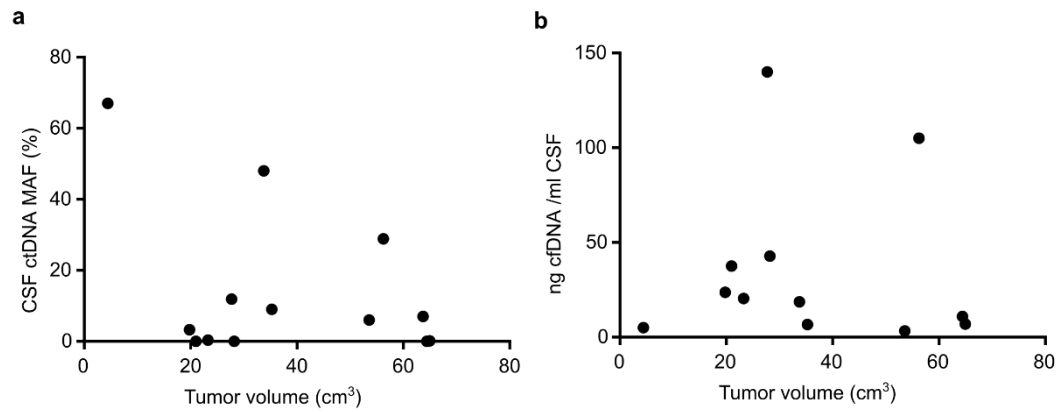


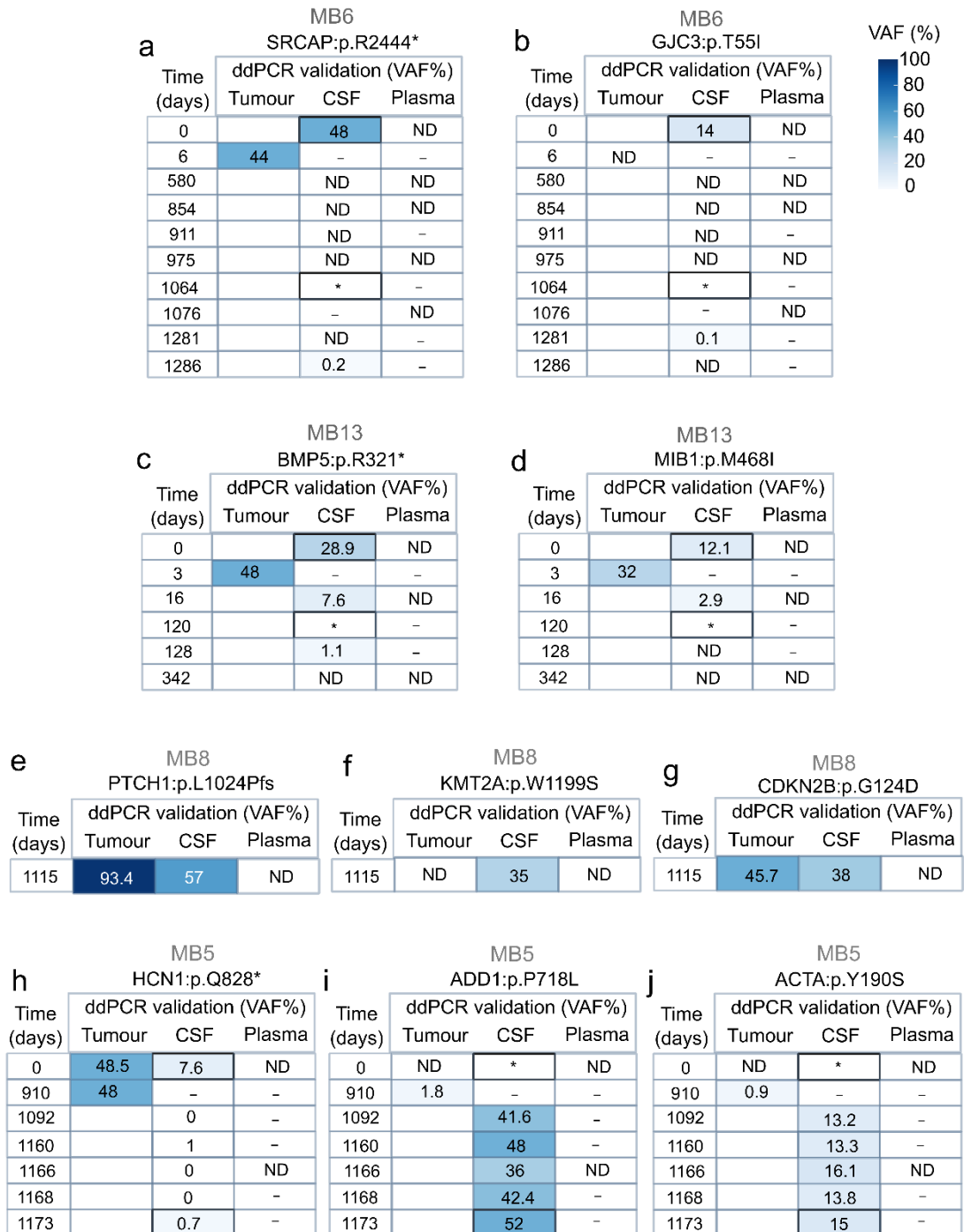
Circulating tumour DNA from the cerebrospinal fluid
allows the characterisation and monitoring of medulloblastoma

Escudero *et al.*,

SUPPLEMENTARY INFORMATION



Supplementary Figure 1 | Correlation of tumor volume (cm³) with (a) CSF ctDNA VAF (%) and (b) cfDNA (ng/ml). CSF samples were collected before the surgical resection for the 13 patients. CSF ctDNA MAF (%) analysed by ddPCR as previously shown in Fig. 2a for the 13 patients. The concentrations of CSF cfDNA (ng/ml) were calculated from 12 patients. No correlations were identified (Spearman r , two-tailed, $p=0.5634$ and $p= 0.5731$ respectively).



Supplementary Figure 2 | Selected mutations identified from the WES analysis of 4 MB patients (MB5, MB6, MB8 and MB13) were validated using ddPCR in tumour/normal DNA, and follow-up CSF and plasma cfDNA samples. CSF ctDNA VAFs highlighted with a black box correspond to the samples used for WES (CSF1, CSF2). * indicates that all CSF cfDNA was used for WES.

Supplementary Table 1 | Classification

Schwalbe et al., 2017							Hovestadt et al., 2020													
Mutations							Mutations													
WNT	SHH-child	SHH-infant	Grp4-HR	Grp4-LR	Grp3-LR	Grp3-HR	WNT	SHH				Group3			Group4					
								α	β	γ	δ	I	II	III	IV	V	VI	VII	VIII	
TP53	TP53	SUFU				GFI1	CTNNB1	TP53	PTCH1	PTCH1	PTCH1	GFI1 act	GFI1 act				PRDM6 act	KBTBD4	PRDM6 act	
CTNNB1	TP53 GL	PTCH1					DDX3X	PTCH1 (less)	KMT2D	SMO	TERT promoter	GFI1B act	GFI1B act						KDM6A	
	TERT						SMARCA4		SUFU	BCOR			KBTBD4						ZMYM3	
	SUFU												CTDNEP1						KMT2C	
	PTCH1												SMARCA4							
													KMT2D							
Cytogenetics							Cytogenetics													
WNT	SHH-child	SHH-infant	Grp4-HR	Grp4-LR	Grp3-LR	Grp3-HR	WNT	SHH				Group3			Group4					
								α	β	γ	δ	I	II	III	IV	V	VI	VII	VIII	
6-	9p+	9q-	i17q	17p+	7+	5+	6-	9p+	2+	9q-	9q-	OTX2 amp	8+	7+	14+	7+	7+	7+	i17q	
	17p-			7+	14+	8+		9q-	SUFU del	PTEN del	14q-		1q+	10q-	7+	16q-	8-	8-		
	9q-			18+	18+	13+		10q-	PTEN del				MYC amp	MYC amp	8-	MYC amp	11-	i17q (less)		
	MYCN amp			i17q	4-	i17q		17p-					i17q (less)	i17q	10-	MYCN amp	MYCN amp (less)			
	GLI2 amp			8-	8-	16q-		MYCN amp							11-	i17q	i17q			
				11-	10-	MYC amp		GLI2 amp							16-					
				16q-	11-															
				11-	10-															
				16q-	11-															
				MYCN amp	13-															
					15-															
					16-															
					21-															

PATIENT_ID	Schwalbe et al., 2017							Hovestadt et al., 2020													
	WNT	SHH-chiId	SHH-infant	Grp4-HR	Grp4-LR	Grp3-LR	Grp3-HR	WNT	SHH				Group3				Group4				
									α	β	γ	δ	I	II	III	IV	V	VI	VII	VIII	
MB1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
MB2	-	-	-	-	7+	7+	-	-	-	-	-	-	7+	7+	7+	7+	7+	7+	7+	-	-
MB3	-	-	-	-	-	-	MYC amp	-	-	-	-	-	MYC amp	MYC amp	-	MYC amp	-	-	-	-	-
MB4	-	-	-	-	7+;16q-	7+	-	-	-	-	-	-	7+	7+	7+;16q-	7+	7+	7+	7+	-	-
MB5	-	TP53 GL; MYCN amp; GLI2 amp; 17p-	-	-	MYCNamp; 16q;7+	7+	-	-	TP53 GL; MYCN amp; GLI2 amp; 17p;10q-	SUFUdel; 2+	-	-	-	-	7+;10q-	7+	MYCNamp; 16q-	(MYCNamp); 7+	7+	-	-
MB6	-	17p-	-	-	-	-	-	-	17p-	-	-	-	-	-	-	-	-	-	-	-	-
MB7	-	17p-	-	-	7+;11-	7+;11-	-	-	17p-	-	-	-	-	-	7+;11-	7+	7+;11-	-	-	-	-
MB8	-	PTCH1; TP53; MYCNamp; 17p;9q-	-	-	8-	8-	-	-	PTCH1; TP53; MYCNamp; 17p;9q-	PTCH1	9q-	-	-	-	8-	-	8-	8-	8-	-	-
MB9	CTNNB1; 6-	17p-	-	-	-	-	-	CTNNB1; 6-	17p-	-	-	-	-	-	-	-	-	-	-	-	-
MB10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
MB11	-	17p-	-	-	-	-	-	-	17p-	-	-	-	-	-	-	-	-	-	-	-	-
MB12	-	PTCH1; MYCN amp; GLI2 amp	-	-	-	-	-	-	PTCH1; MYCN amp; GLI2 amp; 10q-	PTCH1; KMT2D; PTEN del	PTCH1; BCOR; PTEN del	-	-	10q-	-	-	-	-	-	-	-
MB13	-	TP53 GL; GLI2 amp	-	-	11-	10-;11-	-	-	TP53 GL; GLI2 amp	-	-	14q-	-	-	-	10-;11-	-	11-	-	-	-
MB5CSF	-	TP53 GL; MYCN amp; GLI2 amp; 17p- (33%)	-	-	MYCNamp	7+	-	-	TP53 GL; MYCN amp; GLI2 amp; 17p- (33%)	-	-	-	-	-	-	MYCNamp	(MYCNamp)	-	-	-	-
MB6CSF	-	17p-	-	-	-	-	-	-	17p-	-	-	-	-	-	-	-	-	-	-	-	-
MB8CSF	-	PTCH1; TP53; MYCNamp; 17p;9q-	-	-	8-	8-	-	-	PTCH1; TP53; MYCNamp; 17p;9q-	PTCH1	9q-	-	OTX2amp	-	8-	-	8-	8-	8-	-	-
MB13CSF	-	TP53 GL; GLI2 amp	-	-	11-	10-;11-	-	-	TP53 GL; GLI2 amp	-	-	14q-	-	-	-	10-;11-	-	11-	-	-	-

Supplementary Table 2. Patient monitoring and ctDNA dynamics for 9 MB patients

PATIENT_ID	MUTATION	TIME (Days)	TUMOUR_VAF (%)	PLASMA_VAF (%)	CSF_VAF (%)
MB1	RIOK2:p.S456L	0	-	ND	7
		6	47	-	-
		487	-	-	ND
MB2	PUS7:p.D535A	0	15,9	ND	3,3
		1431	-	ND	ND
MB3	TRRAP:p.E3107K	0	63	ND	11,9
		1414	-	ND	ND
MB4	XRCC5:p.K35N	0	50	ND	0,38
		527	-	-	ND
		1347	-	ND	ND
MB7	YY1AP1:p.R665*	0	29	ND	0,18
		744	-	ND	ND
MB9	CTNNB1:p.S37C	0	47,2	2,2	ND
		525	-	ND	ND
MB10	HSPG2:p.R3992H	0	45	ND	ND
		476	-	-	ND
MB11	NFIA:p.R322H	0	15,5	ND	9
		394	ND	ND	ND
MB12	BCOR:p.E518*	0 (biopsy)	97,9	-	-
		240	-	ND	ND
		652	-	-	ND