

Supplementary Table 1A. Probe-level expression results of PDE4DIP probes in GEO HCC cohorts

Parts S1A-S1D together constitute Supplementary Table S1. Expression values are normalized processed values from the corresponding GEO datasets. Numerical scales are dataset/platform specific and should not be compared directly across platforms.

GSE14520 / GPL571 (Affymetrix)

Dataset	Platform	Manufacturer	Probe ID	Gene symbol	Entrez ID	n adjacent	n tumor	Median adjacent	Median tumor	Tumor - adjacent	Direction	Raw P	BH-adjusted P	MMG8-specific
GSE14520	GPL571	Affymetrix	205872_x_at	PDE4DIP	9659	21	22	4.4920	4.1760	-0.3160	Tumor < Adjacent	1.18E-04	4.31E-04	No
GSE14520	GPL571	Affymetrix	209700_x_at	PDE4DIP	9659	21	22	3.1820	3.1855	0.0035	Tumor > Adjacent	9.23E-01	9.23E-01	No
GSE14520	GPL571	Affymetrix	210305_at	PDE4DIP	9659	21	22	3.4230	3.2120	-0.2110	Tumor < Adjacent	7.87E-05	4.31E-04	No
GSE14520	GPL571	Affymetrix	211751_at	LOC100996724 /// LOC100996761 /// LOC101929792 /// LOC101930416 /// LOC653513 /// PDE4DIP	9659 /// 653513 /// 100996724 /// 100996761 /// 101929792 /// 101930416	21	22	3.1290	3.0290	-0.1000	Tumor < Adjacent	2.62E-02	5.76E-02	No
GSE14520	GPL571	Affymetrix	212390_at	LOC100996724 /// LOC100996761 /// LOC101929792 /// LOC101930416 /// PDE4DIP	9659 /// 100996724 /// 100996761 /// 101929792 /// 101930416	21	22	6.3830	5.3510	-1.0320	Tumor < Adjacent	4.14E-06	4.55E-05	No
GSE14520	GPL571	Affymetrix	212392_s_at	LOC100996724 /// LOC100996761 /// LOC101929792 /// LOC101930416 /// PDE4DIP	9659 /// 100996724 /// 100996761 /// 101929792 /// 101930416	21	22	3.3690	3.2685	-0.1005	Tumor < Adjacent	6.48E-02	1.02E-01	No
GSE14520	GPL571	Affymetrix	213388_at	LOC100996724 /// LOC100996761 /// LOC101929792 /// LOC101930416 /// PDE4DIP	9659 /// 100996724 /// 100996761 /// 101929792 /// 101930416	21	22	5.9360	5.1845	-0.7515	Tumor < Adjacent	4.98E-02	9.13E-02	No
GSE14520	GPL571	Affymetrix	214099_s_at	LOC100996724 /// LOC100996761 /// LOC101929792 /// LOC101930416 /// PDE4DIP	9659 /// 100996724 /// 100996761 /// 101929792 /// 101930416	21	22	4.2360	4.0945	-0.1415	Tumor < Adjacent	1.32E-02	3.63E-02	No
GSE14520	GPL571	Affymetrix	214129_at	LOC100996724 /// LOC100996761 /// LOC101929792 /// LOC101930416 /// PDE4DIP	9659 /// 100996724 /// 100996761 /// 101929792 /// 101930416	21	22	6.7840	6.3705	-0.4135	Tumor < Adjacent	1.57E-01	2.15E-01	No
GSE14520	GPL571	Affymetrix	214130_s_at	LOC100996724 /// LOC100996761 /// LOC101929792 /// LOC101930416 /// PDE4DIP	9659 /// 100996724 /// 100996761 /// 101929792 /// 101930416	21	22	4.7460	4.5955	-0.1505	Tumor < Adjacent	4.34E-01	4.77E-01	No
GSE14520	GPL571	Affymetrix	215575_at	PDE4DIP	9659	21	22	3.2720	3.2580	-0.0140	Tumor < Adjacent	3.88E-01	4.75E-01	No

GSE14520 / GPL3921 (Affymetrix)

Dataset	Platform	Manufacturer	Probe ID	Gene symbol	Entrez ID	n adjacent	n tumor	Median adjacent	Median tumor	Tumor - adjacent	Direction	Raw P	BH-adjusted P	MMG8-specific
GSE14520	GPL3921	Affymetrix	205872_x_at	PDE4DIP	9659	220	225	4.6435	4.2200	-0.4235	Tumor < Adjacent	4.52E-19	2.03E-18	No
GSE14520	GPL3921	Affymetrix	209700_x_at	PDE4DIP	9659	220	225	3.4480	3.3620	-0.0860	Tumor < Adjacent	2.03E-06	3.65E-06	No
GSE14520	GPL3921	Affymetrix	210305_at	PDE4DIP	9659	220	225	3.5670	3.3570	-0.2100	Tumor < Adjacent	6.00E-13	1.80E-12	No
GSE14520	GPL3921	Affymetrix	211751_at	PDE4DIP	9659	220	225	3.4105	3.3070	-0.1035	Tumor < Adjacent	2.11E-04	3.17E-04	No
GSE14520	GPL3921	Affymetrix	212390_at	PDE4DIP /// LOC727893	727893 /// 9659	220	225	6.8235	5.6770	-1.1465	Tumor < Adjacent	1.06E-41	9.53E-41	No
GSE14520	GPL3921	Affymetrix	212392_s_at	PDE4DIP /// LOC652526 /// LOC727927	652526 /// 727927 /// 9659	220	225	3.8575	3.7190	-0.1385	Tumor < Adjacent	2.23E-03	2.87E-03	No
GSE14520	GPL3921	Affymetrix	214099_s_at	PDE4DIP /// LOC727927	727927 /// 9659	220	225	4.5315	4.2610	-0.2705	Tumor < Adjacent	1.83E-09	4.12E-09	No
GSE14520	GPL3921	Affymetrix	214130_s_at	PDE4DIP /// LOC727942	727942 /// 9659	220	225	5.2345	5.2720	0.0375	Tumor > Adjacent	3.71E-01	3.71E-01	No
GSE14520	GPL3921	Affymetrix	215575_at	PDE4DIP	9659	220	225	3.2625	3.2500	-0.0125	Tumor < Adjacent	1.34E-01	1.51E-01	No

GSE36376 / GPL10558 (Illumina)

Dataset	Platform	Manufacturer	Probe ID	Gene symbol	Entrez ID	n adjacent	n tumor	Median adjacent	Median tumor	Tumor - adjacent	Direction	Raw P	BH-adjusted P	MMG8-specific
GSE36376	GPL10558	Illumina	ILMN_1659430	PDE4DIP	9659	193	240	6.7257	6.7519	0.0262	Tumor > Adjacent	1.66E-01	2.08E-01	No
GSE36376	GPL10558	Illumina	ILMN_1739674	PDE4DIP	9659	193	240	6.8532	6.9039	0.0507	Tumor > Adjacent	8.88E-03	2.22E-02	No
GSE36376	GPL10558	Illumina	ILMN_1749639	PDE4DIP	9659	193	240	6.3879	6.3851	-0.0028	Tumor < Adjacent	6.25E-01	6.25E-01	No
GSE36376	GPL10558	Illumina	ILMN_2246134	PDE4DIP	9659	193	240	5.8483	5.9339	0.0856	Tumor > Adjacent	1.01E-07	5.04E-07	No
GSE36376	GPL10558	Illumina	ILMN_2291407	PDE4DIP	9659	193	240	5.6246	5.6536	0.0290	Tumor > Adjacent	6.58E-02	1.10E-01	No

Supplementary Table 1B. Probe annotation details

Interpretation applying to all rows: Exact cross-platform exon-level equivalence could not be confidently established from available platform annotations; interpreted as gene-level PDE4DIP evidence rather than MMG8-specific evidence. None of the GEO microarray probes should be interpreted as MMG8 isoform-specific.

GSE14520 / GPL571 (Affymetrix)

[illegible]

Probe ID	Gene symbol	Entrez ID	RefSeq transcript ID	Representative public ID	Probe sequence / note	Genomic coordinate / note	Annotation status
214130_s_at	LOC100996724 /// LOC100996761 /// LOC101929792 /// LOC101930416 PDE4DIP	9659 /// 100996724 /// 100996761 /// 101929792 /// 101930416	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_001195260 /// NM_001195261 /// NM_001198832 /// NM_001198834 /// NM_014644 /// NM_022359 /// XM_003846757 /// XM_003846758 /// XM_005272981 /// XM_005275858 /// XM_005276096 /// XM_005276138 /// XM_005277442 /// XM_005277443 /// XM_005277446 /// XM_005277502 /// XM_006710077 /// XM_006710078 /// XM_006710079 /// XM_006710080 /// XM_006710081 /// XM_006711101 /// XM_006711642 /// XM_006711643 /// XM_006711644 /// XM_006711645 /// XM_006711646 /// XM_006711647 /// XM_006711648 /// XM_006711649 /// XM_006711650 /// XM_006711651 /// XM_006711652 /// XM_006711653 /// XM_006711654 /// XM_006711655 /// XM_006711656 /// XM_006711706 /// XM_006726347 /// XM_006726359	AI821791	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP-containing multi-annotation probe set
215575_at	PDE4DIP	9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_001195260 /// NM_001195261 /// NM_001198832 /// NM_001198834 /// NM_014644 /// NM_022359 /// XM_005272981 /// XM_005277442 /// XM_005277443 /// XM_005277446 /// XM_006711642 /// XM_006711643 /// XM_006711644 /// XM_006711645 /// XM_006711646 /// XM_006711647 /// XM_006711648 /// XM_006711649 /// XM_006711650 /// XM_006711651 /// XM_006711652 /// XM_006711653 /// XM_006711654 /// XM_006711655 /// XM_006711656	AU157078	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP probe set identified by matching gene symbol and Entrez ID

GSE14520 / GPL3921 (Affymetrix)

Probe ID	Gene symbol	Entrez ID	RefSeq transcript ID	Representative public ID	Probe sequence / note	Genomic coordinate / note	Annotation status
205872_x_at	PDE4DIP	9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_943179	NM_022359	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP probe set identified by matching gene symbol and Entrez ID
209700_x_at	PDE4DIP	9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_943179	AB042555	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP probe set identified by matching gene symbol and Entrez ID
210305_at	PDE4DIP	9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_943179	AB042557	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP probe set identified by matching gene symbol and Entrez ID
211751_at	PDE4DIP	9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_943179	BC005949	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP probe set identified by matching gene symbol and Entrez ID
212390_at	PDE4DIP /// LOC727893	727893 /// 9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_001126231 /// XM_001126245 /// XM_943179	AB007923	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP-containing multi-annotation probe set
212392_s_at	PDE4DIP /// LOC652526 /// LOC727927	652526 /// 727927 /// 9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_001126165 /// XM_942005 /// XM_943179	AI950145	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP-containing multi-annotation probe set
214099_s_at	PDE4DIP /// LOC727927	727927 /// 9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_001126165 /// XM_943179	AK001619	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP-containing multi-annotation probe set
214130_s_at	PDE4DIP /// LOC727942	727942 /// 9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_001126195 /// XM_943179	AI821791	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP-containing multi-annotation probe set
215575_at	PDE4DIP	9659	NM_001002810 /// NM_001002811 /// NM_001002812 /// NM_014644 /// NM_022359 /// XM_943179	AU157078	Affymetrix probe set; exact oligonucleotide sequences were not retrieved from standard GEO platform annotation.	Exact oligonucleotide-level genomic coordinate not available from standard GEO/Affymetrix platform annotation.	PDE4DIP probe set identified by matching gene symbol and Entrez ID

Supplementary Table S1B. Probe annotation details (continued)

GSE36376 / GPL10558 (Illumina)

Probe ID	Gene symbol	Entrez ID	RefSeq transcript ID	Representative public ID	Probe sequence / note	Genomic coordinate / note	Annotation status
ILMN_1659430	PDE4DIP	9659	NM_014644.3	NM_014644.3	TCCATCATTCGA GTCATTCTGCTG TGTTGCTTCTA AACCATCATCAA CC	chr1:143585330-143585379	PDE4DIP probe identified by matching gene symbol and Entrez Gene ID 9659
ILMN_1739674	PDE4DIP	9659	XM_943170.1	XM_943170.1	ACATATCAATCC CTAAATTGAATG GTGGAGGTTGCA AAGTGATTTGC AC	Not available in GPL10558 annotation	PDE4DIP probe identified by matching gene symbol and Entrez Gene ID 9659
ILMN_1749639	PDE4DIP	9659	NM_014644.3	NM_014644.3	GCTGAGATCAGC CTCGTGGCCTGG GAAATATGATT CCTGATTCAGGA TC	chr1:143588602-143588628:143590392-143590414	PDE4DIP probe identified by matching gene symbol and Entrez Gene ID 9659
ILMN_2246134	PDE4DIP	9659	NM_001002811.1	NM_001002811.1	TGCAGGAGCTGT GGGATGATCTCT GTGAAGATTATT TGCCGCTCCGGG TC	chr1:144930586-144930635	PDE4DIP probe identified by matching gene symbol and Entrez Gene ID 9659
ILMN_2291407	PDE4DIP	9659	NM_022359.3	NM_022359.3	GCGGCGGCCACA CCCTGGATGAGA GATTATTTTGCA GAGGATGATGGG GA	chr1:143732497-143732524:143786987-143787008	PDE4DIP probe identified by matching gene symbol and Entrez Gene ID 9659

Supplementary Table 1C. Platform-level summary

Dataset	Platform	Probe rows	Tumor less than adjacent	Tumor greater than adjacent	Main direction	Interpretation
GSE14520	GPL3921 (Affymetrix HT Human Genome U133A)	9	8	1	Predominantly Tumor < Adjacent	Gene-level PDE4DIP evidence; not MMG8 isoform-specific.
GSE14520	GPL571 (Affymetrix Human Genome U133A 2.0)	11	10	1	Predominantly Tumor < Adjacent	Gene-level PDE4DIP evidence; not MMG8 isoform-specific.
GSE36376	GPL10558 (Illumina HumanHT-12 V4.0)	5	1	4	Predominantly Tumor > Adjacent	Gene-level PDE4DIP evidence; not MMG8 isoform-specific.

Overall conclusion. The two GEO cohorts were generated using different microarray platforms. Exact cross-platform exon-level equivalence of PDE4DIP probes could not be established from available annotations; therefore, GEO results should be interpreted as gene-level PDE4DIP expression, not MMG8-specific expression.

Supplementary Table 1D. Analysis notes and interpretation boundaries

Item	Description
Scope	This supplementary table reports probe-level PDE4DIP annotation and tumor-versus-adjacent/non-tumor expression comparisons for GSE14520 and GSE36376.
Expression values	Expression values represent normalized processed values from the corresponding GEO series matrices and platform-specific processed datasets. The numerical scales are dataset/platform specific and should not be compared directly across platforms.
Probe selection	PDE4DIP probe rows were identified from platform annotations using gene symbol, Entrez Gene ID 9659, and available RefSeq transcript information.
Expression statistics	Tumor and adjacent/non-tumor samples were compared using the Wilcoxon rank-sum test. Benjamini-Hochberg-adjusted P values were calculated separately within each dataset/platform using the probe rows included in the corresponding platform-specific analysis. For GSE14520/GPL3921, adjustment was performed across the nine PDE4DIP-associated probe sets shown in this table.
Affymetrix probe-set note	For GSE14520, Affymetrix probe sets may contain multiple 25-mer oligonucleotides; exact oligonucleotide-level genomic coordinates were not retrieved from the standard GEO platform annotations used here.
Exon-level interpretation	Because the cohorts used different microarray platforms and the available standard annotations did not establish identical exon targeting, cross-platform PDE4DIP exon equivalence could not be confidently determined.
Isoform-specific interpretation	None of the GEO microarray probes should be interpreted as MMG8 isoform-specific. The GEO analyses provide gene-level PDE4DIP evidence only.
Multi-annotation probes	Rows with multi-gene annotations were retained only when PDE4DIP/Entrez Gene ID 9659 was included; these rows should be interpreted cautiously.
GEO series sources	GSE14520: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE14520 ; GSE36376: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE36376
GEO platform sources	GPL571: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL571 ; GPL3921: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL3921 ; GPL10558: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL10558