



Data in Brief

Multi-platform genome-wide analysis of melanoma progression to brain metastasis



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ABSTRACT

Melanoma has a high tendency to metastasize to brain tissue. The understanding about the molecular alterations of early-stage melanoma progression to brain metastasis (MBM) is very limited. Identifying MBM-specific genomic and epigenomic alterations is a key initial step in understanding its aggressive nature and identifying specific novel druggable targets. Here, we describe a multi-platform dataset generated with different stages of melanoma progression to MBM. This data includes genome-wide DNA methylation (Illumina HM450K BeadChip), gene expression (Affymetrix HuEx 1.0 ST array), single nucleotide polymorphisms (SNPs) and copy number variation (CNV; Affymetrix SNP 6.0 array) analyses of melanocyte cells (MNCs), primary melanoma tumors (PRMs), lymph node metastases (LNMs) and MBMs. The analysis of this data has been reported in our recently published study (Marzese et al., 2014).

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Specifications

Organism/cell line/tissue	<i>Homo sapiens</i> /cancer and normal tissues and cell lines.
Sex	Male and female.
Sequencer or array type	–Illumina HumanMethylation450 BeadChip. –[HuEx-1_0-st] Affymetrix Human Exon 1.0 ST Array [transcript (gene) version]. –[GenomeWideSNP_6] Affymetrix Genome-Wide Human SNP 6.0 Array.
Data format	Raw data: CEL files, normalized data: TXT files
Experimental factors	Melanocytes, primary melanomas, regional lymph node metastases and brain metastases.
Experimental features	Genomic DNA and total RNA from melanocytes and melanoma specimens were analyzed by genome-wide DNA methylation, gene expression and SNP arrays.
Consent	All patients gave their written informed consent before study entry.
Sample source location	Melanoma specimens were obtained from John Wayne Cancer Institute at Providence Saint John's Health Center and the Melanoma Institute Australia tissue banks. Melanocytes were obtained from Life Technologies.

Direct link to deposited data

DNA methylation array: <http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE44661>

Gene expression array: <http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE44660>

SNP array: <http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE44019>.

Experimental design, materials and methods

We selected and analyzed three melanoma-related tissue types (PRMs, LNMs and MBMs) and normal melanocytes (MNCs) representing the melanoma progression to MBM. Compared to other solid tumors, the study of melanoma progression involves important challenges. First, the conventionally accepted normal controls for melanoma are short-term cultured MNC cells. Second, due to the small size of PRM and MBM lesions, tissue availability is usually very limited. Our study focused on DNA methylation, which was analyzed for all the samples ($n = 40$; GSE44661). To evaluate the potential transcriptional impact of DNA methylation changes on MBM-development, RNA expression was also assessed in metastatic melanomas and MNCs ($n = 22$; GSE44660). To exclude the influence of SNPs or allele CNV on DNA methylation analysis, genome-wide SNP analysis was performed on metastatic melanomas ($n = 16$; GSE44019).

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Study population and clinical data

This study included three human MNCs isolated from normal skin (Life Technologies, Carlsbad, CA), four paraffin-embedded archival tissue (PEAT) PRMs obtained from AJCC Stage II melanoma patients, seventeen LNMs (PEAT and cultured cells) obtained from AJCC Stage III melanoma patients and sixteen MBMs (PEAT and cultured cells) obtained from AJCC Stage IV melanoma patients. Importantly, LNMs were classified based on disease-free survival (DFS) into good ($n = 10$; DFS > 5 yr) and poor ($n = 7$; DFS < 2 yr) prognosis groups (Table 1). Melanoma patients were included in the study under protocols approved by Providence Saint John's Health Center/JWCI joint institutional review board and Western institutional review board and the Sydney Local Health District, RPAH Zone, Human Ethics Review Committee. Informed consent was obtained from all subjects and the experiments were performed according to the principles set out in the WMA Declaration of Helsinki and the NIH Belmont Report. Tissue specimens were coded according to HIPAA recommendations to ensure the confidentiality of the patients.

DNA methylation profiling

DNA methylation assays were performed using Illumina HumanMethylation450 (HM450K) BeadChip following the manufacturer's protocol (Illumina, San Diego, CA). The chips were scanned with Illumina iScan microarray scanner (Illumina), and the

data was extracted using the R package methylumi on Bioconductor. The methylation levels were reported as a β -value [$\beta = \text{intensity of the Methylated allele} / (\text{intensity of the Unmethylated allele} + \text{intensity of the Methylated allele})$], and calculated using the signal intensity value for each CpG site.

Genome variation profiling

Genotyping of DNA from melanoma specimens was performed using Affymetrix Genome-Wide Human SNP Array 6.0 by following the manufacturer's recommendations (Affymetrix, Santa Clara, CA). The genotype calls of each specimen were determined by the Birdseed 2.0 genotype calling algorithm included in the Affymetrix Genotyping Console 4.0. Quality control (QC) of arrays was conducted using the Contrast Quality Control (CQC) algorithm, with a minimal call rate of >95%. Copy number (CN) analysis was performed using regional GC correction and default software settings. CN segments were reported with an HMM algorithm using the default CN map in Genotyping Console 4.0 (Toronto DGV map).

Gene expression profiling

Total RNA was analyzed by GeneChip Human Exon ST Array 1.0 (HuEx 1.0) following the manufacturer's protocol (Affymetrix). Data were analyzed in Expression Console 1.1 software (Affymetrix) using

Table 1
Specimens included in the study.

Name	Source	PEAT/cells	LNM prognostic	HM450K	SNP 6.0	HuEx 1.0
Melanocyte 1	MNC	Cells	N/A	✓	x	✓
Melanocyte 2	MNC	Cells	N/A	✓	x	✓
Melanocyte 3	MNC	Cells	N/A	✓	x	✓
Primary melanoma 1	PRM	PEAT	N/A	✓	x	x
Primary melanoma 2	PRM	PEAT	N/A	✓	x	x
Primary melanoma 3	PRM	PEAT	N/A	✓	x	x
Primary melanoma 4	PRM	PEAT	N/A	✓	x	x
Lymph node metastasis 1	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 2	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 3	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 4	LNM	Cells	Poor	✓	x	✓
Lymph node metastasis 5	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 6	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 7	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 8	LNM	Cells	Poor	✓	x	✓
Lymph node metastasis 9	LNM	Cells	Poor	✓	x	✓
Lymph node metastasis 10	LNM	Cells	Good	✓	x	x
Lymph node metastasis 11	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 12	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 13	LNM	Cells	Good	✓	✓	✓
Lymph node metastasis 14	LNM	PEAT	Poor	✓	x	x
Lymph node metastasis 15	LNM	PEAT	Poor	✓	x	x
Lymph node metastasis 16	LNM	PEAT	Poor	✓	x	x
Lymph node metastasis 17	LNM	PEAT	Poor	✓	x	x
Brain metastasis 1	MBM	Cells	N/A	✓	x	x
Brain metastasis 2	MBM	Cells	N/A	✓	✓	✓
Brain metastasis 3	MBM	Cells	N/A	✓	✓	✓
Brain metastasis 4	MBM	Cells	N/A	✓	✓	✓
Brain metastasis 5	MBM	Cells	N/A	✓	✓	✓
Brain metastasis 6	MBM	Cells	N/A	✓	✓	✓
Brain metastasis 7	MBM	Cells	N/A	✓	✓	✓
Brain metastasis 8	MBM	Cells	N/A	✓	✓	✓
Brain metastasis 9	MBM	PEAT	N/A	✓	x	x
Brain metastasis 10	MBM	PEAT	N/A	✓	x	x
Brain metastasis 11	MBM	PEAT	N/A	✓	x	x
Brain metastasis 12	MBM	PEAT	N/A	✓	x	x
Brain metastasis 13	MBM	PEAT	N/A	✓	x	x
Brain metastasis 14	MBM	PEAT	N/A	✓	x	x
Brain metastasis 15	MBM	PEAT	N/A	✓	x	x
Brain metastasis 16	MBM	PEAT	N/A	✓	x	x

the core transcript set and employing the robust multi-array average algorithm (RMA) for background correction and normalization of data.

Basic analysis

As we described [1], DNA methylation data was filtered to exclude probes associated with SNPs, regions with commonly occurring CNV and sex chromosomes. Additionally, after background correction, probes with no significant difference from the background noise ($P > 0.01$) were called “failed” and excluded from downstream analyses. Samples presenting $\geq 0.5\%$ of failed probes were excluded from the study. Candidate CpG sites with differential methylation among study groups were validated as functional by seeking statistical differences in RNA expression. Top candidates were then selected for direct assay verification as we described [1].

Discussion

In this *Data in Brief* article, we described in detail the contents of the dataset associated with the study published by Marzese and colleagues in the *Human Molecular Genetics* journal in 2014 [1]. This multiplatform analysis offers the opportunity of identifying genetic and epigenetic alterations that can be used as potential theranostic biomarkers for melanoma progression to MBM.

Reference

- [1] D.M. Marzese, R.A. Scolyer, J.L. Huynh, S.K. Huang, H. Hirose, K.K. Chong, E. Kiyohara, J. Wang, N.P. Kavas, N.C. Donovan, et al., Epigenome-wide DNA methylation landscape of melanoma progression to brain metastasis reveals aberrations on homeobox D cluster associated with prognosis. *Hum. Mol. Genet.* 23 (2014) 226–238.