

Integrative analysis of Multiple Sclerosis using a systems biology approach

Supplementary data

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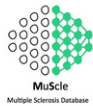
Table S1 Description of gene expression profile studies included in this work.

GEO-ID	EXPREF	PMID	Profile	Groups	Case	Control	Disease case	Disease control	Treatment	Tissue	Subcell	Platform
GSE53716	Exp24850724	24850724	mRNA	12	6	6	CIS	Baseline	IFN- β -1a	Blood		Affymetrix GPL570
GSE26484	Exp22491253	22491253	mRNA	10	6	4	RRMS	Healthy		Blood		Affymetrix GPL570
GSE16461	Exp21216829	21216829	mRNA	8	4	4	RRMS/SPMS	Healthy		Blood	CD4+/CD8+	Affymetrix GPL570
GSE26104	Exp21886806	21886806	mRNA	32	24	8	RRMS	Baseline	IFN- β -1b/1a	Blood		Affymetrix GPL570
GSE24427	Exp20136355	20136355	mRNA	125	100	25	RRMS	RRMS	rIFN- β -1b	Blood		Affymetrix GPL96 & GPL97
GSE23205	Exp20921521	20921521	mRNA	10	6	4	PPMS/Risk haplotype	PPMS/Protective haplotype		Blood		Affymetrix GPL570
GSE21942	Exp22021740	22021740	mRNA	27	12	15	MS	Healthy		Blood		Affymetrix GPL570
GSE23832	Exp21346816	21346816	mRNA	12	8	4	MS	Healthy		Blood		Affymetrix GPL6244
GSE5574	Exp17467740	17467740	mRNA	15	10	5	RRMS	RRMS	IFN- β -1a	Blood		GE Healthcare GPL4191
GSE27688	Exp22252466A	22252466	mRNA	26	16	10	RRMS/SPMS	Healthy	aHSCT	Blood	CD34+/CD34-	Agilent GPL6480
GSE43591	Exp23895517A	23895517	mRNA	19	10	9	RRMS	Healthy		Blood	T-cells	Affymetrix GPL570
GSE21079	Exp20711463	20711463	miRNA	96	59	37	RRMS/SPMS/PPMS	Healthy		Blood		Illumina GPL8178
GSE74579	Exp26831009	26831009	miRNA	72	48	24	RRMS	Healthy		Blood		Affymetrix GPL8786
GSE43590	Exp23895517B	23895517	miRNA	20	11	9	RRMS	Healthy	IFN- β	Blood		Affymetrix GPL14613
GSE46282	Exp23921681B	23921681	miRNA	24	18	6	RRMS/CIS	Baseline	IFN- β -1b	Blood		TaqMan GPL13328
GSE46283	Exp23921681C	23921681	miRNA	6	3	3	RRMS/CIS	Baseline	IFN- β -1b	Blood		Affymetrix GPL14613
GSE27690	Exp22252466B	22252466	miRNA	9	4	5	SPMS	Healthy	aHSCT	Blood	CD34+	Agilent GPL10850
GSE17846	Exp19823682	19823682	miRNA	41	20	21	RRMS	Healthy		Blood		Febit GPL9040

Table S2 Gene expression profile studies - Dataset groups characteristics.

DEMOGRAPHREF	EXPREF	Group Size	Treatment	Group classifier	Label	Gender
Dem24850724a	Exp24850724	6	IFN- β -1a	CIS	Before treatment (baseline)	
Dem24850724b	Exp24850724	6	IFN- β -1a	CIS	365 days follow-up	
Dem22491253a	Exp22491253	4		Healthy	Control	
Dem22491253b	Exp22491253	3		RRMS	High Sema4A	
Dem22491253c	Exp22491253	3		RRMS	Low Sema4A	
Dem21216829a	Exp21216829	4		Healthy	CD4+ (Control monozygotic twin)	2/6 (M/F)
Dem21216829b	Exp21216829	4		Healthy	CD8+ (Control monozygotic twin)	2/6 (M/F)
Dem21216829c	Exp21216829	4		RRMS/SPMS	CD4+ (3 RRMS/1 SPMS monozygotic twin)	2/6 (M/F)
Dem21216829d	Exp21216829	4		RRMS/SPMS	CD8+ (3 RRMS/1 SPMS monozygotic twin)	2/6 (M/F)
Dem21886806a	Exp21886806	8	IFN- β -1b/1a	RRMS	Before treatment (baseline)	0/8 (M/F)
Dem21886806b	Exp21886806	4	IFN- β -1b	RRMS	91 days follow-up	0/4 (M/F)
Dem21886806c	Exp21886806	4	IFN- β -1b	RRMS	365 days follow-up	0/4 (M/F)
Dem21886806d	Exp21886806	4	IFN- β -1b	RRMS	730 days follow-up	0/4 (M/F)
Dem21886806e	Exp21886806	4	IFN- β -1a	RRMS	91 days follow-up	0/4 (M/F)
Dem21886806f	Exp21886806	4	IFN- β -1a	RRMS	365 days follow-up	0/4 (M/F)
Dem21886806g	Exp21886806	4	IFN- β -1a	RRMS	730 days follow-up	0/4 (M/F)
Dem20136355a	Exp20136355	25	rIFN- β -1b	RRMS	Before treatment (baseline)	9/16 (M/F)
Dem20136355b	Exp20136355	25	rIFN- β -1b	RRMS	2 days follow-up	9/16 (M/F)
Dem20136355c	Exp20136355	25	rIFN- β -1b	RRMS	30 days follow-up	9/16 (M/F)
Dem20136355d	Exp20136355	25	rIFN- β -1b	RRMS	365 days follow-up	9/16 (M/F)
Dem20136355e	Exp20136355	25	rIFN- β -1b	RRMS	730 days follow-up	9/16 (M/F)
Dem20136355aa	Exp20136355	25	rIFN- β -1b	RRMS	Before treatment (baseline)	9/16 (M/F)
Dem20136355bb	Exp20136355	25	rIFN- β -1b	RRMS	2 days follow-up	9/16 (M/F)
Dem20136355cc	Exp20136355	25	rIFN- β -1b	RRMS	30 days follow-up	9/16 (M/F)
Dem20136355dd	Exp20136355	25	rIFN- β -1b	RRMS	365 days follow-up	9/16 (M/F)
Dem20136355ee	Exp20136355	25	rIFN- β -1b	RRMS	730 days follow-up	9/16 (M/F)
Dem20921521a	Exp20921521	4		PPMS	PRF1 gene/Protective haplotype	4/0 (M/F)
Dem20921521b	Exp20921521	6		PPMS	PRF1 gene/Risk haplotype	6/0 (M/F)
Dem22021740a	Exp22021740	15		Healthy	Control	0/15 (M/F)

Dem22021740b	Exp22021740	12		MS	Case	0/12 (M/F)
Dem21346816a	Exp21346816	4		Healthy	Control	
Dem21346816b	Exp21346816	8		MS	Case	
Dem17467740a	Exp17467740	5	IFN- β -1a	RRMS	Before treatment (baseline)	
Dem17467740b	Exp17467740	5	IFN- β -1a	RRMS	1 days follow-up	
Dem17467740c	Exp17467740	5	IFN- β -1a	RRMS	182 days follow-up	
Dem23921681Ba	Exp23921681B	6	IFN- β -1b	RRMS/CIS	Before treatment (baseline)	0/6 (M/F)
Dem23921681Bb	Exp23921681B	6	IFN- β -1b	RRMS/CIS	First injection follow-up	0/6 (M/F)
Dem23921681Bc	Exp23921681B	6	IFN- β -1b	RRMS/CIS	Second injection follow-up	0/6 (M/F)
Dem23921681Bd	Exp23921681B	6	IFN- β -1b	RRMS/CIS	30 days follow-up	0/6 (M/F)
Dem23921681Ca	Exp23921681C	3	IFN- β -1b	RRMS/CIS	Before treatment (baseline)	0/3 (M/F)
Dem23921681Cb	Exp23921681C	3	IFN- β -1b	RRMS/CIS	30 days follow-up	0/3 (M/F)
Dem22252466Aa	Exp22252466A	5		Healthy	CD34+ HPC Control	2/3 (M/F)
Dem22252466Ab	Exp22252466A	8		RRMS/SPMS	CD34+ HPC	2/6 (M/F)
Dem22252466Ac	Exp22252466A	5		Healthy	CD34- HPC Control	2/3 (M/F)
Dem22252466Ad	Exp22252466A	8		RRMS/SPMS	CD34- HPC	2/6 (M/F)
Dem22252466Ba	Exp22252466B	5		Healthy	CD34+ HPC Control	2/3 (M/F)
Dem22252466Bb	Exp22252466B	4		MS	CD34+ HPC	0/4 (M/F)
Dem23895517Aa	Exp23895517A	9		Healthy	T-cells Control	4/5 (M/F)
Dem23895517Ab	Exp23895517A	10		RRMS	T-cells	6/4 (M/F)
Dem23895517Ba	Exp23895517B	9		Healthy	Control	4/5 (M/F)
Dem23895517Bb	Exp23895517B	11	IFN- β	RRMS	Case	1/10 (M/F)
Dem20711463a	Exp20711463	37		Healthy	Control	
Dem20711463b	Exp20711463	24		RRMS	Case	
Dem20711463c	Exp20711463	17		SPMS	Case	
Dem20711463d	Exp20711463	18		PPMS	Case	
Dem26831009a	Exp26831009	24		Healthy	Control	10/14 (M/F)
Dem26831009b	Exp26831009	24		RRMS	Relapse stage	10/14 (M/F)
Dem26831009c	Exp26831009	24		RRMS	Remission stage	10/14 (M/F)
Dem19823682a	Exp19823682	21		Healthy	Control	
Dem19823682b	Exp19823682	20	IFN- β or Glatiramer acetate	RRMS	Case	



Welcome to the Multiple Sclerosis (MuScle) database

MuScle is a multiple sclerosis data base integrated by data curated and mined from large scale studies (genomic & miRNA).

This cluster of datasets, as well as its statistical analyses and crossmapping with other databases through CluSO (gene/protein cluster) was created to perform a systems biology approach. Promising outcomes of the implementation of an integrative approach, through gene ontologies and pathway analyses along with their interaction allow us to reach a potential data-driven hypothesis.

By the data mining of multiple sclerosis studies carry out in MuScle, plus the addition of multi-omic levels of information, its analyses can give rise to a more complete and meaningful biological connexion among the different processes and mechanisms involved in the disease, as well as the unravelling of the key elements involved in its manifestation and progression.

Database access via:

Query:
Search for: Molecules Tissue or Source Disease
 Case sensitive

or Browse (client-side search)

- [Study](#)
- [Sample](#)
- [Tissue](#)
- [Disease](#)
- Molecules, [grouped \(search\)](#)

Select first letter of gene name to jump to the right entry list

[A](#) [B](#) [C](#) [D](#) [E](#) [F](#) [G](#) [H](#) [I](#) [J](#) [K](#) [L](#) [M](#) [N](#) [O](#) [P](#) [Q](#) [R](#) [S](#) [T](#) [U](#) [V](#) [W](#) [X](#) [Y](#) [Z](#) | [1](#) | [2](#) | [3](#) | [4](#) | [5](#) | [6](#) | [7](#) | [8](#) | [9](#) | [other](#)

Current stats:

Total number of molecule entries (redundant): 105543	Total number of studies listed in the database: 19	Total number of samples in Demographics file: 64
Number of unique (non-redundant) molecules: 34260	Number of unique studies listed in the database: 19	Number of unique samples in Demographics file: 64

MuScle - Study list

Show 10 entries

Search:

Study ID	Tissue / Source	Disease	# of molecules	PMID/DOI
Exp23921681B	Blood	Multiple sclerosis	17	23921681
Exp22252466B	Blood	Multiple sclerosis	46	22252466
Exp23921681C	Blood	Multiple sclerosis	173	23921681
Exp20711463	Blood	Multiple sclerosis	254	20711463
Exp26831009	Blood	Multiple sclerosis	262	26831009
Exp19823682	Blood	Multiple sclerosis	271	19823682
Exp23895517B	Blood	Multiple sclerosis	322	23895517
Exp21346816	Blood	Multiple sclerosis	523	21346816
Exp24850724	Blood	Multiple sclerosis	1880	24850724
Exp23921681A	Blood	Multiple sclerosis	2284	23921681

Showing 1 to 10 of 19 entries

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MuScle - Study ID [Exp23921681B](#)

PubMed ID	23921681
Authors	Hecker M, Thamarasam M, Koczan D, Schroder J et al.
Title	MicroRNA expression changes during interferon-beta treatment in the peripheral blood of multiple sclerosis patients.
Journal	Int J Mol Sci
Abstract	The purpose of this study was to investigate the expression dynamics of mRNAs and microRNAs in response to subcutaneous IFN-beta-1b treatment (Betaferon, 250 microg every other day) in patients with clinically isolated syndrome (CIS) suggestive of multiple sclerosis (MS) or relapsing-remitting type of the disease (RRMS). By using Affymetrix microarrays, we obtained microRNA expression profiles of peripheral blood mononuclear cells from 3 patients within the first month of IFN-beta treatment.

Sample characteristics

Species	Tissue / Source	Compartment	Disease	N	Sample
Homo sapiens	Blood	Mononuclear cells	Multiple sclerosis	24	Dem23921681Ba , Dem23921681Bb , Dem23921681Bc , Dem23921681Bd

Sample description and preparation

N (case)	18
N (control)	6
Disease (case)	RRMS/CIS
Disease (control)	Before treatment (baseline)
Disease induction	IFN-Beta-1b

Sample detection

Array version	TaqMan(r) Array Human MicroRNA A Cards v2.0
Platform	TaqMan GPL13328
Reference source	GSE46282

Molecule list

Show 10 entries

Search:

Molecule ID	ext	External ID	Gene	Name	Source acc	Regulation (case/control)	Scores
BZ187		ENSG00000199059	MIR135B	Homo sapiens miR-135b stem-loop	80.hsa-miR-135b-4395372	ratio: 0.45	p-value: 0.03786
BZ233		ENSG00000207990	MIR182	Homo sapiens miR-182 stem-loop	106.hsa-miR-182-4395445	ratio: 0.45	p-value: 0.02152
BZ349		ENSG00000226380	MIR29A	Homo sapiens miR-29a stem-loop	37.hsa-miR-29a-4395223	ratio: 0.67	p-value: 0.0401
BZ357		ENSG00000249532	MIR302B	Homo sapiens miR-302b stem-loop	156.hsa-miR-302b-4378071	ratio: 14.85	p-value: 0.0179
BZ371		ENSG00000199177	MIR31	Homo sapiens miR-31 stem-loop	42.hsa-miR-31-4395390	ratio: 0.60	p-value: 0.0178
BZ511		ENSG00000207839	MIR33B	Homo sapiens miR-33b stem-loop	44.hsa-miR-33b-4395196	ratio: 0.24	p-value: 0.0182
BZ536		ENSG00000208015	MIR362	Homo sapiens miR-362 stem-loop	182.hsa-miR-362-5p-4378092	ratio: 0.71	p-value: 0.0489
BZE69		ENSG00000208028	MIR616	Homo sapiens miR-616 stem-loop	320.hsa-miR-616-4395525	ratio: 5.18	p-value: 0.04949
BZ199		ENSG00000207807	MIR95	Homo sapiens miR-95 stem-loop	49.hsa-miR-95-4373011	ratio: 0.66	p-value: 0.01686
BZ186		hsa-miR-380-3p		hsa-miR-380-3p	199.hsa-miR-380-4373022	ratio: 0.05	p-value: 0.00512

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Compile date 09-07-2016

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Figure S1 Page-views of the multiple sclerosis database (MuScle). The database is organised and can be accessed by type of study (the study “Exp23921681B” is highlighted in red as an example how the information of the study is stored and displayed in the MuScle database), sample (handles clinical information), tissue/fluid source and by specific queries of molecules. Available at <http://www.padb.org/muscle/>.