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Data in Brief

Loss of *Drp1* in the liver leads to an alteration in expression of the genes involved in the immune system

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ABSTRACT

Dynamin-related protein 1 (*Drp1*) is a member of the dynamin family of large GTPase, which cycles between the cytosol and the mitochondrial outer membrane, and mediates mitochondrial fission. Using microarray analysis of gene expression in the livers of wild-type and *Drp1* knockout mice, we have previously identified that endoplasmic reticulum (ER) stress marker genes are significantly increased by the absence of *Drp1* [1]. Here, we provide methodological and analytical details of the microarray data, which have been deposited in the Gene Expression Omnibus as data set GSE64222. We have performed further gene ontology analysis of the data and found the differential expression of a subset of genes that are involved in the immune response in the livers of Drp1 knockout mice versus wild-type controls.

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Specifications	
Organism/cell line/tissue	*Mus musculus*
Sex	*Male*
Sequencer or array type	Agilent 44K mouse 60-mer oligo microarray
Data format	*Raw data: TXT files*
Experimental factors	24 weeks high fat diet *Drp1* knockout and wild-type control liver mRNA
Experimental features	Identify gene expression changes in the liver of mouse that lack *Drp1*
Consent	None necessary, data are publicly available
Sample source location	Fukuoka, Japan

1. Direct link to deposited data

The deposited data can be found at: http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=gse64222.

2. Experimental design, materials and methods

Mitochondria are highly dynamic organelles that frequently fuse and divide in disease, aging, and development [2]. In vertebrates, mitofusin-1 and -2 (MFN1 and MFN2) are involved in mitochondrial fusion, whereas DRP1 and mitochondrial fission factor (MFF) control mitochondrial fission [3]. Recently, it was reported that the ER plays an active role in defining the sites of mitochondrial division [4]. In fact, mitochondria and the ER physically interact by close structural juxtaposition, via the mitochondrial-associated ER membrane (MAM). To clarify the role of mitochondrial fission in this communication, we generated mice lacking the mitochondrial fission protein *Drp1* in the liver (*Drp1*LiKO). When the mice were fed with a high-fat diet (HFD), analysis of gene expression in the liver demonstrated marked elevation of ER stress markers. We also found a second subset of genes, discussed here, that are involved in the immune response.

2.1. Animals

*Drp1*LiKO mice were generated by crossing $Drp1^{flox/+}$ mice with Alb-Cre mice [5]. Mice were fed ad libitum with a normal chow diet (5.4% fat, CRF-1, Orient Yeast Co., Tokyo, Japan) and kept under a light–dark cycle of 12 h. For the HFD study, 4-week-old mice were put on high-fat diet (24% fat, lard fat, 45 kcal % fat, D12451; Research Diets, New Brunswick, NJ) for 24 weeks. All mouse procedures and protocols were in accordance with the Guide for the Care and Use of Laboratory Animals and were approved by the Ethics Committees on Animal Experimentation (Kyushu University, Graduate School of Medicine).

2.2. RNA isolation and microarray

After 24 weeks high fat diet, mice were fasted for 17 h and then sacrificed. Total RNA was isolated from cells using TRIzol Reagent (nitrogen) and purified using SV Total RNA Isolation System (Promega).

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cRNA was amplified and labeled using a Low input Quick Amp Labeling Kit (Agilent Technologies). cRNA was hybridized to a 44K 60-mer oligomicroarray (Whole Mouse Genome Microarray 4 × 44K v2; Agilent Technologies) according to the manufacturer's instructions. The hybridized microarray slides were scanned using an Agilent scanner. The relative hybridization intensities and background hybridization values were calculated using Feature Extraction Software version 9.5.1.1 (Agilent Technologies). The scanned images were analyzed with Feature Extraction Software 9.5.1.1 (Agilent) using default parameters to obtain background subtracted and spatially detrended Processed Signal intensities. The raw signal intensities and flags for each probe were calculated from the hybridization intensities and spot information according to the procedures recommended by Agilent Technologies using the Flag criteria in the GeneSpring Software. In addition, the raw signal intensities of two samples were log2-transformed and normalized by the quantile algorithm with the Bioconductor.

3. Results

Genes were selected using the criterion of a Z score of ≥2, which identified 526 up-regulated and 640 down-regulated genes in Drp1LiKO mice. The top 5 up-regulated genes have been reported in other publications, of these, 3 genes are known to be ER stress response genes, which was the topic of our previously published article [1]. To further investigate these data, we use the DAVID tool to functionally cluster up-regulated and down-regulated genes by similarly annotated gene ontology (GO) biological process terms, respectively. The top ten significantly enriched annotation clusters of up-regulated genes were shown in Fig. 1. We found that seven of the ten clusters were related to the immune system; these clusters included terms such as immune response, phagocytosis, antigen processing and presentation, defense response and response to virus. The remaining clusters were related to 2′-deoxyribonucleotide biosynthetic process, amine biosynthetic process and cell death. Next, to further define connections between immune molecules that were regulated by mitochondrial fission, we list the 32 genes selected by using the term “immune response” in Table 1. The most significant ten clusters for down-regulated genes were presented in Fig. 2, and include lipid biosynthetic process, fatty acid metabolic process, acute inflammatory response, actin filament-based process, cell fate commitment, response to wounding, actomyosin structure organization, complement activation, alternative pathway, actin cytoskeleton organization and brown fat cell differentiation.

4. Discussion

We described here that lack of DRP1 increased the expression levels of a large number of genes involved in immune response. Within the past several years, a couple of studies have shed light on the connection between mitochondrial dynamics and antiviral innate immunity [6]. Indeed, Castanier and colleague have observed that knockdown of *Drp1* increased innate immune signaling and they have highlighted the importance of the interconnectedness and interdependence of mitochondria fission in antiviral innate immunity in vitro [7]. In this study, we provided the compelling evidence that mitochondrial fission regulates the expression of the genes responsible for the immune system in the liver.

Conflict of interest

The authors declare no conflict of interests.

Acknowledgments

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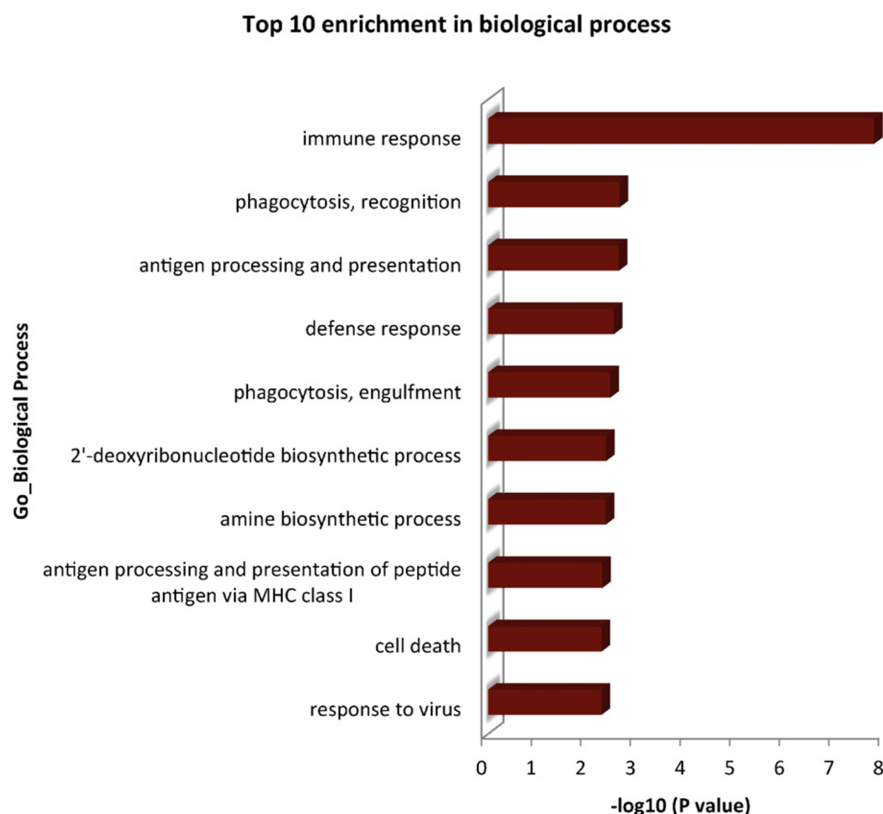

Fig. 1. Microarray functional annotation summary results of the up-regulated genes.

Table 1
Genes involved in the immune response.

Gene symbol	Description	WT signal	KO signal	Z score	Ratio	GenBank accession
Oas1a	2′-5′ oligoadenylate synthetase 1A	1602	10,770	5.41	6.72	NM_145211
Oas1f	2′-5′ oligoadenylate synthetase 1F	719	4818	5.40	6.70	NM_145153
Apoa4	Apolipoprotein A-IV	8937	34,821	4.83	3.90	NM_007468
Cxcl10	Chemokine (C-X-C motif) ligand 10	817	3872	4.36	4.74	NM_021274
Rsad2	Radical S-adenosyl methionine domain containing 2	915	4104	4.27	4.49	NM_021384
Ccl5	Chemokine (C-C motif) ligand 5	834	3786	4.24	4.54	NM_013653
Defb1	Defensin beta 1	56	341	4.17	6.14	NM_007843
Oasl2	2′-5′ oligoadenylate synthetase-like 2	277	1088	3.83	3.92	NM_011854
Oas2	2′-5′ oligoadenylate synthetase 2	400	1485	3.68	3.72	NM_145227
Irf7	Interferon regulatory factor 7	829	2906	3.52	3.50	NM_016850
Igh-1a	Immunoglobulin heavy chain 1a	312	1042	3.38	3.34	AK007918
Clec7a	C-type lectin domain family 7, member a	645	2131	3.35	3.31	NM_020008
Sqstm1	Sequestosome 1	3817	12,111	3.28	3.17	NM_011018
Oas3	2′-5′ oligoadenylate synthetase 3	24	332	3.08	13.65	NM_145226
Oasl1	2′-5′ oligoadenylate synthetase-like 1	3388	9930	3.06	2.93	NM_145209
H2-D1	Histocompatibility 2, D region locus 1	34,888	65,382	2.72	1.87	NM_010380
H2-Q2	Histocompatibility 2, Q region locus 2	32,901	59,740	2.59	1.82	NM_010392
Cd14	CD14 antigen	175	541	2.58	3.08	NM_009841
H2-K1	Histocompatibility 2, K1, K region, transcript variant 1	30,325	54,943	2.58	1.81	NM_001001892
Ccl7	Chemokine (C-C motif) ligand 7	12	101	2.57	8.78	NM_013654
Gbp3	Guanylate binding protein 3	593	1450	2.51	2.45	NM_018734
Raet1e	Retinoic acid early transcript 1E	1264	3025	2.48	2.39	NM_198193
C1rb	Complement component 1, r subcomponent B	813	1853	2.31	2.28	NM_001113356
H2-T23	Histocompatibility 2, T region locus 23	39,824	67,056	2.26	1.68	NM_010398
Icosl	ICOS ligand precursor (B7 homolog 2) (B7-H2)	6	126	2.25	21.20	AF394451
Ccl2	Chemokine (C-C motif) ligand 2	204	543	2.24	2.66	NM_011333
Mpa2l	Macrophage activation 2 like	512	1127	2.21	2.20	NM_194336
Ccl4	Chemokine (C-C motif) ligand 4	88	221	2.11	2.51	NM_013652
Spon2	Spondin 2, extracellular matrix protein	987	2080	2.09	2.11	NM_133903
Gm11127	T16 class I MHC gene (exon 5) fragment	21,436	38,601	2.09	1.80	AB359227
LOC676689	Similar to H-2 class I histocompatibility antigen, L–D alpha chain precursor	8739	15,605	2.06	1.79	XM_992161
Igh-VJ558	Immunoglobulin heavy chain V gene segment	6	97	2.01	16.02	AF296435

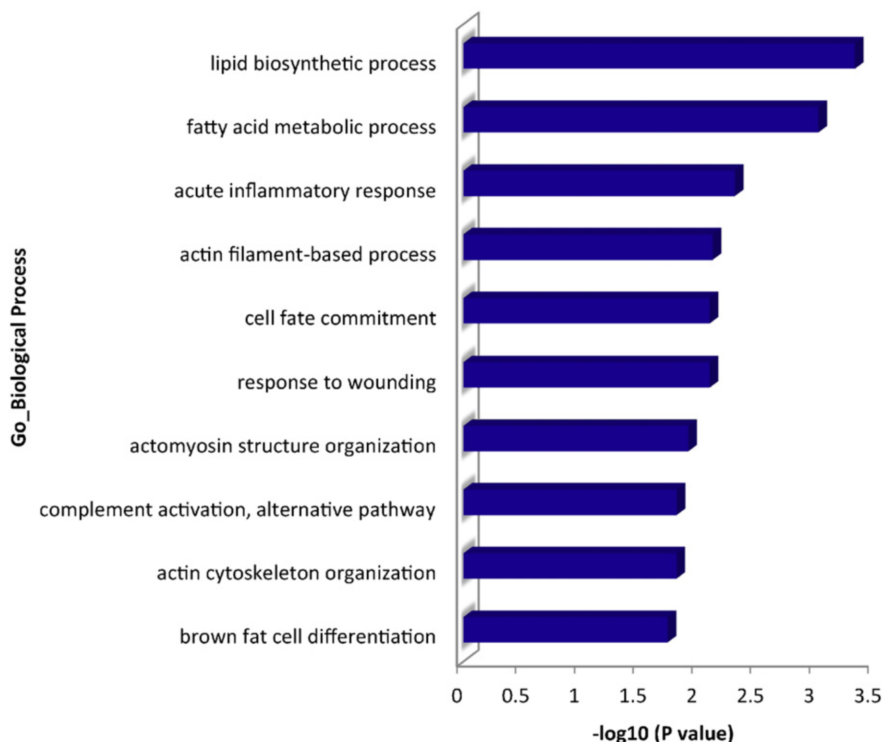

Fig. 2. Microarray functional annotation summary results of the down-regulated genes.

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