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# Data in Brief

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Data Article

# Dataset of mRNA levels for dopaminergic receptors, adrenoceptors and tyrosine hydroxylase in lymphocytes from subjects with clinically isolated syndromes

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A R T I C L E  I N F O

A B S T R A C T

This data article presents a dataset of mRNA levels for dopaminergic receptors, adrenoceptors and for tyrosine hydoxylase, the rate-limiting enzyme in the synthesis of catecholamines, in peripheral blood mononuclear cells as well as in CD4+ T effector and regulatory cells from subjects with clinically isolated syndromes (CIS), which is a first episode of neurological disturbance(s) suggestive of multiple sclerosis. CIS subjects are divided into two groups according to their eventual progression, after 12 months from CIS, to clinically established multiple sclerosis. The data reported are related to the article entitled "Dopaminergic receptors and adrenoceptors in circulating lymphocytes as putative biomarkers for the early onset and progression of multiple sclerosis" (M. Cosentino, M. Zaffaroni, M. Legnaro, R. Bombelli, L. Schembri, D. Baroncini, A. Bianchi, R. Clerici, M. Guidotti, P. Banfi, G. Bono, F. Marino, 2016) [1].

**Specifications Table**

| | |
|---|---|
| Subject area | *Medicine* |
| More specific subject area | *Neurology, Immunology, Neuroimmunology* |
| Type of data | *Tables* |
| How data was acquired | *Real-time PCR, ABI PRISM® 7000 System (Applied Biosystems, Life Technologies Corporation, USA), data statistical analysis (GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com)* |
| Data format | *Analyzed* |
| Experimental factors | *Peripheral blood mononuclear cells (PBMC) isolated by gradient centrifugation from whole blood of subjects with clinically isolated syndromes (CIS), and cultured for 48 h alone or with PHA 10 µg/ml. A sample of freshly isolated PBMC was used to isolate CD4+ T effector (Teff) and regulatory (Treg) cells by means of immunomagnetic sorting.* |
| Experimental features | *Real-time PCR analysis of mRNA levels of dopaminergic receptors, adrenoceptors and tyrosine hydroxylase mRNA levels, following total RNA extraction by PerfectPure™ RNA Cell & Tissue kit (5Prime, Milano, Italy), reverse transcription by a random primer and a high-capacity cDNA RT kit (Applied Biosystems, Life Technologies Corporation, USA), and cDNA amplification by TaqMan® Universal PCR Master Mix (Applied Biosystems), using the TaqMan Gene Expression Assay.* |
| Data source location | *Varese, Gallarate, Como (Italy)* |
| Data accessibility | *Data is within this article* |

**Value of the data**

- These data provide the profile of expression of dopaminergic receptors, adrenoceptors and tyrosine hydroxylase genes in circulating lymphocytes of subjects with clinically isolated syndromes (CIS).
- The data are of value for further experiments on the mechanistic role of dopaminergic and adrenergic pathways in circulating lymphocytes during CIS and multiple sclerosis (MS).
- The data give a basis for longitudinal, prospective clinical studies aimed at validating dopaminergic receptors and/or adrenoceptors gene expression in lymphocytes as early markers of CIS progressing to MS.

## 1. Data

Enclosed are data regarding mRNA levels for dopaminergic receptors (DR), adrenoceptors (AR) and tyrosine hydroxylase (TH), the rate-limiting enzyme in the synthesis of catecholamines, found in peripheral blood mononuclear cells (PBMC) (Tables 1 and 2) and in CD4+ T effector (Teff) cells (Table 3) and regulatory (Treg) cells (Table 4) from subjects with clinically isolated syndromes (CIS), which is a first, usually recovering, episode of neurological disturbance(s) suggestive of multiple sclerosis (MS). Each table provides a comparison between subjects who, after 12 months from CIS, did not progress or progressed to clinically established MS. For further information and discussion about the interpretation and implications of DR, AR and TH mRNA levels in lymphocytes of CIS subjects, please refer to the article [1].

**Table 1**
Levels of DR, AR and TH mRNA in resting PBMC from CIS subjects who, after 12 months from CIS, did not convert (CISnc) or converted (CISc) to clinically established MS. Levels of mRNA are expressed as $2^{-\Delta Ct} \times 10^7$.

| Gene | CISnc | CISc | Ratio CISc/CISnc | P |
|---|---|---|---|---|
| TH | $0.544 \pm 0.469$ | $0.585 \pm 0.643$ | 1.075 | 0.878 |
| DRD2[a] | $0.062 \pm 0.010$ | $0.083 \pm 0.035$ | 1.336 | 0.219 |
| DRD3 | $6.288 \pm 2.273$ | $9.868 \pm 4.232$ | 1.569 | 0.041 |
| DRD5 | $81.073 \pm 134.865$ | $46.128 \pm 42.210$ | 0.569 | 0.390 |
| ADRA1A | $0.076 \pm 0.034$ | $0.082 \pm 0.019$ | 1.077 | 0.618 |
| ADRA1B | $0.991 \pm 0.702$ | $1.418 \pm 0.806$ | 1.431 | 0.232 |
| ADRA1D | $40.271 \pm 10.107$ | $43.439 \pm 13.895$ | 1.079 | 0.583 |
| ADRA2A | $0.075 \pm 0.046$ | $0.116 \pm 0.070$ | 1.559 | 0.151 |
| ADRA2B | undetected | undetected | n/a | n/a |
| ADRA2C | $0.055 \pm 0.023$ | $0.053 \pm 0.033$ | 0.961 | 0.873 |
| ADRB1 | $0.554 \pm 0.329$ | $0.342 \pm 0.180$ | 0.617 | 0.070 |
| ADRB2[b] | $0.659 \pm 0.582$ | $1.180 \pm 1.781$ | 1.790 | 0.438 |
| ADRB3 | $0.149 \pm 0.084$ | $0.186 \pm 0.079$ | 1.244 | 0.329 |

Notes:
n/a=not applicable.
[a] =levels of mRNA below detection limits in 3 CISnc and 3 CISc subjects;
[b] =data from sample of one CISc subject excluded from the analysis due to assay failure.

**Table 2**
Levels of DR, AR and TH mRNA in PHA-stimulated PBMC from CIS subjects who, after 12 months from CIS, did not convert (CISnc) or converted (CISc) to clinically established MS. Levels of mRNA are expressed as $2^{-\Delta Ct} \times 10^7$.

| Gene | CISnc | CISc | Ratio CISc/CISnc | P |
|---|---|---|---|---|
| TH | $17.349 \pm 19.878$ | $21.587 \pm 23.140$ | 1.244 | 0.673 |
| DRD2 | $0.111 \pm 0.044$ | $0.122 \pm 0.096$ | 1.096 | 0.773 |
| DRD3 | $212.251 \pm 102.955$ | $227.008 \pm 146.229$ | 1.070 | 0.806 |
| DRD5 | $615.891 \pm 755.387$ | $447.890 \pm 448.168$ | 0.727 | 0.527 |
| ADRA1A | $0.176 \pm 0.034$ | $0.270 \pm 0.116$ | 1.540 | 0.052 |
| ADRA1B | $149.347 \pm 204.884$ | $153.014 \pm 225.484$ | 1.025 | 0.971 |
| ADRA1D | $212.433 \pm 152.730$ | $199.297 \pm 132.607$ | 0.938 | 0.837 |
| ADRA2A | $0.634 \pm 0.484$ | $1.431 \pm 0.957$ | 2.257 | 0.043 |
| ADRA2B[a] | $0.034 \pm 0.012$ | $0.051 \pm 0.007$ | 1.493 | 0.046 |
| ADRA2C | $0.183 \pm 0.169$ | $0.202 \pm 0.130$ | 1.105 | 0.771 |
| ADRB1 | $1.520 \pm 0.794$ | $1.308 \pm 0.668$ | 0.861 | 0.519 |
| ADRB2[b] | $6.156 \pm 2.782$ | $8.788 \pm 4.242$ | 1.428 | 0.141 |
| ADRB3 | $0.602 \pm 0.369$ | $0.659 \pm 0.295$ | 1.095 | 0.698 |

Notes:
[a] =levels of mRNA below detection limits in 5 CISnc and 8 CISc subjects;
[b] =data from sample of one CISc subject excluded from the analysis due to assay failure.

## 2. Experimental design, materials and methods

### 2.1. PBMC isolation and culture

Cells were obtained from venous blood of CIS subjects enrolled at the Centre for research on Multiple Sclerosis, Ospedale S. Antonio Abate of Gallarate (VA) (Investigator in charge: Mauro Zaffaroni), at the Neurology Unit of the "Ospedale di Circolo e Fondazione Macchi", University of Insubria - School of Medicine of Varese (Investigator in charge: Giorgio Bono), and at the Neurological Department, Valduce Hospital, Como (Investigator in charge: Mario Guidotti). Inclusion and exclusion criteria for selection and enrollement of CIS subjects, as well as criteria to define conversion of CIS to

**Table 3**
Levels of DR, AR and TH mRNA in Teff from CIS subjects who, after 12 months from CIS, did not convert (CISnc) or converted (CISc) to clinically established MS. Levels of mRNA are expressed as $2^{-\Delta Ct} \times 10^7$.

| Gene | CISnc | CISc | Ratio CISc/CISnc | P |
|------|-------|------|------------------|---|
| TH | 0.932 ± 0.667 | 1.514 ± 1.680 | 1.625 | 0.367 |
| DRD2[a] | 0.061 ± 0.012 | 0.091 ± 0.037 | 1.495 | 0.083 |
| DRD3 | 71.274 ± 40.127 | 160.645 ± 224.222 | 2.254 | 0.283 |
| DRD5 | 38.986 ± 32.811 | 45.656 ± 25.700 | 1.171 | 0.617 |
| ADRA1A | 0.104 ± 0.027 | 0.136 ± 0.038 | 1.303 | 0.056 |
| ADRA1B | 23.090 ± 20.545 | 40.727 ± 30.437 | 1.764 | 0.170 |
| ADRA1D | 121.840 ± 68.792 | 155.881 ± 73.368 | 1.279 | 0.312 |
| ADRA2A | 0.182 ± 0.116 | 0.229 ± 0.134 | 1.263 | 0.421 |
| ADRA2B[a] | undetected | undetected | n/a | n/a |
| ADRA2C | 0.055 ± 0.034 | 0.085 ± 0.047 | 1.547 | 0.138 |
| ADRB1 | 0.894 ± 0.411 | 0.801 ± 0.581 | 0.896 | 0.700 |
| ADRB2 | 5.479 ± 2.738 | 5.379 ± 4.585 | 0.982 | 0.957 |
| ADRB3 | 0.226 ± 0.140 | 0.243 ± 0.122 | 1.076 | 0.797 |

Notes:
n/a=not applicable.
[a] =levels of mRNA below detection limits in 2 CISnc and 3 CISc subjects.

**Table 4**
Levels of DR, AR and TH mRNA in Treg from CIS subjects who, after 12 months from CIS, did not convert (CISnc) or converted (CISc) to clinically established MS. Levels of mRNA are expressed as $2^{-\Delta Ct} \times 10^7$.

| Gene | CISnc | CISc | Ratio CISc/CISnc | P |
|------|-------|------|------------------|---|
| TH | 6.239 ± 5.575 | 6.029 ± 5.332 | 0.966 | 0.935 |
| DRD2[a] | 0.098 ± 0.044 | 0.162 ± 0.083 | 1.657 | 0.090 |
| DRD3[b] | 524.542 ± 320.649 | 675.012 ± 505.025 | 1.287 | 0.470 |
| DRD5 | 179.094 ± 96.190 | 271.145 ± 87.095 | 1.514 | 0.044 |
| ADRA1A | 0.178 ± 0.084 | 0.228 ± 0.096 | 1.277 | 0.260 |
| ADRA1B | 539.118 ± 634.164 | 685.947 ± 919.180 | 1.272 | 0.703 |
| ADRA1D | 273.060 ± 162.944 | 431.602 ± 273.593 | 1.581 | 0.164 |
| ADRA2A | 0.533 ± 0.401 | 0.708 ± 0.576 | 1.329 | 0.471 |
| ADRA2B[a] | undetected | undetected | n/a | n/a |
| ADRA2C | 0.147 ± 0.152 | 0.168 ± 0.098 | 1.139 | 0.724 |
| ADRB1 | 2.299 ± 2.183 | 1.284 ± 0.734 | 0.558 | 0.166 |
| ADRB2 | 13.974 ± 9.163 | 15.322 ± 9.322 | 1.096 | 0.758 |
| ADRB3 | 0.402 ± 0.228 | 0.470 ± 0.240 | 1.170 | 0.583 |

Notes:
n/a=not applicable.
[a] =levels of mRNA below detection limits in 1 CISnc and 3 CISc subjects;
[b] =data from sample of one CISc subject excluded from the analysis due to assay failure.

MS are detailed elsewhere [1]. Approval of the protocol was obtained from the Ethics Committee of the Ospedale S. Antonio Abate of Gallarate (VA), and all the participants provided a written informed consent.

PBMC were isolated from whole blood by using Ficoll–Paque Plus density gradient centrifugation, using standard procedures [2]. PBMC were finally cultured in RPMI 1640/10% heath-inactivated fetal bovine serum, added with 2 mM glutamine and 100 U/ml penicillin/streptomycin, at the concentration of $1 \times 10^6$ cells/ml, at 37 °C in a moist atmosphere of 5% $CO_2$. Cells were cultured for 48 h, alone or in the presence of PHA 10 µg/ml, a concentration which was previously shown to be optimal to trigger mRNA expression of TH [3]. PBMC were finally harvested and assayed for DR, AR and TH mRNA expression by means of real-time PCR.

**Table 5**
Real-Time PCR conditions.

| Gene | UniGene ID | Interrogated sequence *RefSeq/GenBank mRNA* | Protein | | Exon boundary | Assay location | Amplicon length | Efficiency (%) |
|---|---|---|---|---|---|---|---|---|
| TH | Hs.435609 | NM_199292.2 | NP_954986. 2 | | 3–4 | 424–422 | 63 | 94.5 |
| DRD2 | Hs.73893 | NM_000795.3 | NP_000786. 1 | | 2–3 | 524 | 64 | 100.0 |
| DRD3 | Hs.121478 | NM_033663.3 | NP_387512.3 | | 3–4 | 809–725 | 73 | 97.6 |
| DRD5 | Hs.380681 | NM_000798.4 | NP_000789. 1 | 1 | 1–1 | 1092–744 | 88 | 110.2 |
| ADRA1A | Hs. 709175 | NM_033302.2 | NP_150645. 2 | | 1–2 | 1324 | 112 | 100.0 |
| ADRA1B | Hs. 368632 | NM_000679.3 | NP_000670. 1 | | 1–2 | 1126 | 61 | 100.0 |
| ADRA1D | Hs. 557 | NM_000678.3 | NP_000669. 1 | | 1–2 | 1166 | 68 | 100.1 |
| ADRA2A | Hs. 249159 | NM_000681.3 | NP_000672. 3 | | 1–1 | 1960 | 116 | 101.0 |
| ADRA2B | Hs. 247686 | NM_000682.5 | NP_000673. 2 | | 1–1 | 823 | 117 | 100.0 |
| ADRA2C | Hs. 123022 | NM_000683.3 | NP_000674. 2 | | 1–1 | 646 | 93 | 99.1 |
| ADRB1 | Hs. 99913 | NM_000684.2 | NP_000675. 1 | | 1–1 | 863 | 79 | 99.0 |
| ADRB2 | Hs. 2551 | NM_000024.5 | NP_000015.1 | | 1–1 | 778 | 65 | 100.0 |
| ADRB3 | Hs. 2549 | NM_000025.2 | NP_000016.1 | | 1–2 | 1401 | 65 | 99.9 |
| 18S rRNA | X03205.1 | N.A. | N.A. | N.A. | | N.A. | 187 | 98.8 |

## 2.2. Preparation of Teff and Treg

Immunomagnetic sorting of Treg and Teff from freshly isolated PBMC was performed by using the Dynal CD4+CD25+ Treg Kit (Dynal, Oslo, Norway), as previously described [4]. Treg and Teff were directly assayed for DR, AR and TH mRNA expression by means of real-time PCR.

## 2.3. Real-time PCR

Extraction of total RNA was performed with PerfectPure™ RNA Cell & Tissue kit (5Prime, Milano, Italy). RNA was then reverse-transcribed to cDNA using a random primer, high-capacity cDNA RT kit (Applied Biosystems, Life Technologies Corporation, USA), and finally amplified by *Taq*Man® Universal PCR Master Mix (Applied Biosystems), using the *Taq*Man Gene Expression Assay (Table 5). Assayed of cDNA was accomplished on an ABI PRISM® 7000 System (Applied Biosystems). Gene expression levels were finally expressed as $2^{-\Delta Ct}$ where $\Delta Ct = [Ct \text{ (sample)} - Ct \text{ (housekeeping gene)}]$, and normalized to 18S cDNA, using the AB Prism 7000 SDS software™. Annealing temperature was 60 °C for all the genes.

## 2.4. Statistics

Data are reported as means $\pm$ standard deviation (SD). The D'Agostino & Pearson normality test was used to assess the distribution of values. The two-tailed Student's *t* test for unpaired data or the Mann–Whitney test for continuous variables were used to assess differences between groups. Calculations were performed using a commercial software (GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com).

## Conflict of Interest

All the authors declare that they have no conflict of interest.

## Acknowledgments

## Transparency document. Supporting information

Transparency data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.dib.2016.08.067.

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