**Table 1.** groups' comparison for socio-demographic differences of mothers and children (at the time of birth)

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristics** | **Prenatal methamphetamine exposure children** | **Normal children** | **p value** |
| **Maternal/demographic** |  | | |
| Public insurance | 2498(93.98) | 3466(97.0) | 0.17 |
| No partner | 1776 (66.81) | 2112(60.9) | 0.13 |
| Education  (who didn't completed 12 years of ducation) | 1262(47.5) | 1511(42.3) | 0.14 |
| Maternal age | 22.56±1.3 | 23.34±1.2 | 0.18 |
| Prenatal marijuana use | 422(15.9) | 403(11.3) | 0.08 |
| Joints/d across pregnancy | 0.066± 0.24 | 0.052 ±0.16 | 0.12 |
| Prenatal alcohol use | (15.6) | 23 (8.4) | 0.09 |
| Absolute alcohol/day (oz) across pregnancy | 0.016± 0.29 | 0.011 ±0.08 | 0.05 |
| Prenatal tobacco exposure | 2068 (77.8) | 2443(68.4) | 0.18 |
| Cigarettes/d across pregnancy | 2.94± 6.3 | 1.86 ±4.8 | 0.06 |
| **Neonatal/demographic** |  | | |
| Birth weight, g | 3366±522 | 3596±447 | 0.16 |
| Low birth weight | 760(28.6) | 468(13.1) | 0.04 |
| Length, cm | 50.46±4.4 | 51.06±3.7 | 0.12 |
| Head circumference, cm | 31.23±2.1 | 34.06±1.9 | 0.03 |
| Gestational age, wk | 38.1±2.2 | 39.2±1.2 | 0.22 |

Data are presented as n (%) or mean ± SD.

**Table 2.** Demographic characteristics of subjects who finished the follow up

|  |  |  |
| --- | --- | --- |
| **Variables** | **Prenatal methamphetamine exposure to children** | **Normal children** |
| **Numbers** | 2658 | 3573 |
| **Gender** | 1287 boys / 930 girls | 2064 boys / 1509 girls |

**Table 3.** Enriched gene ontology terms calculated using the differentially expressed genes in each sampling.

**Part A.** PME INFANTs

|  |  |  |
| --- | --- | --- |
| **GO term** | **DEGs number** | **p value** |
| **CELULLAR COMPONENT** | | |
| [neuron projection](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043005) | 83 | 2.1E-20 |
| mitochondrial respiratory chain complex I | 26 | 8.8E-16 |
| NADH dehydrogenase complex | 26 | 8.8E-16 |
| respiratory chain complex I | 26 | 8.8E-16 |
| [espiratory chain](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0070469) | 32 | 6.3E-14 |
| synapse | 73 | 2.5E-13 |
| axon | 46 | 3.2E-13 |
| [mitochondrial respiratory chain](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005746) | 28 | 3.7E-12 |
| organelle envelope | 98 | 8.1E-11 |
| organelle membrane | 146 | 7.3E-11 |
| envelope | 98 | 1.0E-10 |
| [plasma membrane part](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0044459) | 243 | 3.6E-10 |
| [mitochondrial envelope](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005740) | 73 | 1.5E-9 |
| [mitochondrial membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0031966) | 70 | 1.8E-9 |
| [cell projection](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042995) | 102 | 3.0E-9 |
| organelle inner membrane | 62 | 2.9E-9 |
| **MOLECULAR FUNCTION** | | |
| [NADH dehydrogenase (quinone) activity](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0050136) | 27 | 2.1E-16 |
| [oxidoreductase activity, acting on NADH or NADPH](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0016651) | 32 | 4.5E-12 |
| gated channel activity | 60 | 4.4E-9 |
| **BIOLOGICAL PROCESS** | | |
| [transmission of nerve impulse](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0019226) | 89 | 5.7E-22 |
| [synaptic transmission](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007268) | 76 | 2.3E-18 |
| [behavior](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007610) | 94 | 1.3E-15 |
| [mitochondrial electron transport, NADH to ubiquinone](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0006120) | 25 | 2.0E-13 |
| [ATP synthesis coupled electron transport](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042773) | 28 | 4.7E-13 |
| [mitochondrial ATP synthesis coupled electron transport](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042775) | 28 | 4.7E-13 |
| [homeostatic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042592) | 29 | 1.4E-12 |
| [neuromuscular process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0050905) | 120 | 1.4E-12 |
| [death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0016265) | 29 | 4.7E-12 |
| [regulation of membrane potential](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042391) | 42 | 5.2E-12 |
| [respiratory electron transport chain](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0022904) | 116 | 5.2E-12 |
| [cell death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0008219) | 114 | 1.9E-11 |
| [adult behavior](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0030534) | 32 | 9.7E-11 |
| [electron transport chain](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0022900) | 37 | 9.1E-11 |
| [leukocyte activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045321) | 56 | 1.1E-10 |
| [regulation of neurological system process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0031644) | 43 | 1.5E-10 |
| [regulation of synaptic transmission](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0050804) | 40 | 2.6E-10 |
| [cell activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0001775) | 61 | 4.0E-10 |
| [dopamine metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042417) | 16 | 4.4E-10 |
| [cellular respiration](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045333) | 33 | 6.5E-10 |
| [response to organic substance](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0010033) | 110 | 8.7E-10 |
| [regulation of transmission of nerve impulse](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0051969) | 41 | 8.3E-10 |
| [regulation of programmed cell death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043067) | 119 | 1.3E-9 |
| [learning or memory](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007611) | 35 | 1.3E-9 |
| [regulation of cell death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0010941) | 119 | 1.7E-9 |
| [lymphocyte activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0046649) | 48 | 2.0E-9 |
| [cellular ion homeostasis](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0006873) | 70 | 3.3E-9 |
| [adult locomotory behavior](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0008344) | 24 | 3.6E-9 |
| [regulation of apoptosis](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042981) | 117 | 3.5E-9 |
| [cellular chemical homeostasis](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0055082) | 70 | 7.2E-9 |
| [chemical homeostasis](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0048878) | 85 | 8.0E-9 |
| [immune system development](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0002520) | 57 | 9.9E-9 |
| [leukocyte differentiation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0002521) | 37 | 9.8E-9 |
| [ion homeostasis](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0050801) | 73 | 1.1E-8 |
| [catechol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0009712) | 19 | 1.1E-8 |
| [catecholamine metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0006584) | 19 | 1.1E-8 |
| [diol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0034311) | 19 | 1.1E-8 |
| [phenol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0018958) | 19 | 2.1E-8 |
| [cell-cell signaling](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007267) | 93 | 3.5E-8 |

**PART B.** PMEs at 12 MONTHs of age

|  |  |  |
| --- | --- | --- |
| **GO term** | **DEGs number** | **p value** |
| **CELLULAR COMPONENT** | | |
| [neuron projection](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043005) | 76 | 1.2E-18 |
| [plasma membrane part](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0044459) | 242 | 1.2E-15 |
| [synapse](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045202) | 72 | 3.1E-15 |
| [organelle membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0031090) | 142 | 4.4E-13 |
| [integral to plasma membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005887) | 146 | 1.3E-11 |
| [intrinsic to plasma membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0031226) | 148 | 1.7E-11 |
| [synapse part](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0044456) | 52 | 4.9E-11 |
| [respiratory chain complex I](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045271) | 21 | 1.2E-10 |
| [NADH dehydrogenase complex](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0030964) | 21 | 1.2E-10 |
| [mitochondrial respiratory chain complex I](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005747) | 21 | 1.2E-10 |
| [axon](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0030424) | 68 | 1.6E-10 |
| [mitochondrial membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0031966) | 40 | 1.5E-10 |
| [mitochondrial envelope](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005740) | 70 | 3.2E-10 |
| [organelle envelope](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0031967) | 60 | 4.4E-10 |
| [postsynaptic membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045211) | 90 | 4.8E-10 |
| [envelope](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0031975) | 36 | 5.2E-10 |
| [organelle inner membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0019866) | 90 | 4.2E-10 |
| [cell projection](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042995) | 95 | 3.7E-9 |
| **MOLECULAR FUNCTION** | | |
| [NADH dehydrogenase activity](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0003954) | 21 | 5.2E-10 |
| [amine binding](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043176) | 32 | 2.5E-9 |
| [oxidoreductase activity, acting on NADH or NADPH, quinone or similar compound as acceptor](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0016655) | 21 | 1.0E-8 |
| **BIOLOGICAL PROCESS** | | |
| [transmission of nerve impulse](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0019226) | 85 | 3.8E-22 |
| [synaptic transmission](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007268) | 72 | 4.2E-18 |
| [leukocyte activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045321) | 59 | 1.8E-14 |
| [behavior](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007610) | 86 | 4.6E-14 |
| [lymphocyte activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0046649) | 63 | 4.6E-13 |
| [cell activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0001775) | 51 | 4.6E-13 |
| [dopamine metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042417) | 17 | 2.3E-12 |
| [B cell activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042113) | 30 | 1.0E-11 |
| [death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0016265) | 108 | 1.3E-11 |
| [homeostatic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042592) | 116 | 2.4E-11 |
| [regulation of programmed cell death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043067) | 110 | 2.4E-11 |
| [regulation of cell death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0010941) | 116 | 3.1E-11 |
| [regulation of membrane potential](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042391) | 39 | 4.1E-11 |
| [cell death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0008219) | 106 | 5.6E-11 |
| [regulation of apoptosis](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042981) | 114 | 7.2E-11 |
| [lymphocyte differentiation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0030098) | 33 | 3.2E-10 |
| [leukocyte differentiation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0002521) | 37 | 6.0E-10 |
| [response to organic substance](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0010033) | 103 | 1.1E-9 |
| [catechol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0009712) | 19 | 2.2E-9 |
| [catecholamine metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0006584) | 19 | 2.2E-9 |
| [diol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0034311) | 19 | 2.2E-9 |
| [immune response](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0006955) | 99 | 2.6E-9 |
| [phenol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0018958) | 19 | 4.2E-9 |
| [cell-cell signaling](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007267) | 89 | 7.2E-9 |
| [immune system development](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0002520) | 54 | 9.7E-9 |
| [neuromuscular process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0050905) | 24 | 1.6E-8 |
| [learning or memory](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007611) | 20 | 1.9E-8 |
| [mitochondrial electron transport, NADH to ubiquinone](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0006120) | 32 | 1.8E-8 |

**PART C.** PMEs at 24 MONTHS of age

|  |  |  |
| --- | --- | --- |
| **GO term** | **DEGs number** | **p value** |
| **CELLULAR COMPONENT** | | |
| [plasma membrane part](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0044459) | 216 | 8.9E-13 |
| [neuron projection](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043005) | 61 | 3.7E-12 |
| [synapse](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045202) | 60 | 7.3E-11 |
| [integral to plasma membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005887) | 130 | 3.6E-10 |
| **MOLECULAR FUNCTION** | | |
| [amine binding](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043176) | 30 | 2.3E-9 |
| **BIOLOGICAL PROCESS** | | |
| [transmission of nerve impulse](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0019226) | 78 | 1.3E-20 |
| [synaptic transmission](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007268) | 66 | 8.8E-17 |
| [leukocyte activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045321) | 54 | 4.4E-13 |
| [behavior](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007610) | 78 | 1.3E-12 |
| [cell activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0001775) | 58 | 2.2E-12 |
| [lymphocyte activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0046649) | 47 | 4.4E-12 |
| [dopamine metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042417) | 16 | 2.0E-11 |
| [catecholamine metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0006584) | 19 | 3.1E-10 |
| [catechol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0009712) | 19 | 3.1E-10 |
| [diol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0034311) | 19 | 3.1E-10 |
| [B cell activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042113) | 27 | 4.1E-10 |
| [phenol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0018958) | 19 | 5.9E-10 |
| [lymphocyte differentiation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0030098) | 31 | 6.8E-10 |
| [death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0016265) | 96 | 8.8E-10 |
| [regulation of membrane potential](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042391) | 35 | 1.4E-9 |
| [cell-cell signaling](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007267) | 84 | 1.9E-9 |
| [homeostatic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042592) | 97 | 3.1E-9 |
| [leukocyte differentiation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0002521) | 94 | 3.9E-9 |
| [cell death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0008219) | 34 | 3.8E-9 |
| [regulation of apoptosis](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042981) | 99 | 3.1E-8 |

**PART D.** PMEs at 36 MONTHs of age

|  |  |  |
| --- | --- | --- |
| **GO term** | **DEGs number** | **p value** |
| **CELLULAR COMPONENT** | | |
| [plasma membrane part](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0044459) | 216 | 1.3E-12 |
| [neuron projection](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043005) | 63 | 7.0E-13 |
| [synapse](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045202) | 62 | 1.5E-11 |
| [integral to plasma membrane](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005887) | 131 | 7.9E-10 |
| **MOLECULAR FUNCTION** | | |
| [amine binding](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0043176) | 31 | 1.3E-9 |
| **BIOLOGICAL PROCESS** | | |
| [transmission of nerve impulse](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0019226) | 78 | 6.0E-20 |
| [synaptic transmission](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007268) | 65 | 1.4E-15 |
| [leukocyte activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0045321) | 53 | 4.0E-12 |
| [behavior](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007610) | 78 | 5.3E-12 |
| [lymphocyte activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0046649) | 47 | 1.1E-11 |
| [dopamine metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042417) | 16 | 2.8E-11 |
| [cell activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0001775) | 57 | 2.8E-11 |
| [cell-cell signaling](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0007267) | 87 | 3.7E-10 |
| [diol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0034311) | 19 | 4.7E-10 |
| [catechol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0009712) | 19 | 4.7E-10 |
| [catecholamine metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0006584) | 19 | 4.7E-10 |
| [B cell activation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042113) | 27 | 7.3E-10 |
| [phenol metabolic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0018958) | 19 | 9.1E-10 |
| [lymphocyte differentiation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0030098) | 31 | 1.3E-9 |
| [regulation of membrane potential](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042391) | 35 | 2.8E-9 |
| [homeostatic process](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0042592) | 98 | 5.5E-9 |
| [leukocyte differentiation](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0002521) | 34 | 7.6E-9 |
| [death](http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0016265) | 95 | 2.3E-8 |

**Part A( infants with PME), partB (PMEs at 12 months of age), part C ( PMEs at 24months of age) and part D (PMEs at 36 months of age)**

**Table 4. KEGG pathway enrichment of DEGs**

|  |  |  |
| --- | --- | --- |
| **PME INFANTS** | | |
| **PATHWAYS** | **P VALUE** | **DEGSs number** |
| [Primary immunodeficiency](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05340$Primary%20immunodeficiency&termId=450038919&source=kegg) | 7.0E-12 | 23 |
| [Alzheimer's disease](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05010$Alzheimer%27s%20disease&termId=450038891&source=kegg) | 1.7E-9 | 48 |
| [Parkinson's disease](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05012$Parkinson%27s%20disease&termId=450038892&source=kegg) | 7.1E-8 | 39 |
| [Huntington's disease](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05016$Huntington%27s%20disease&termId=450038894&source=kegg) | 6.5E-5 | 42 |
| [Apoptosis](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa04210$Apoptosis&termId=450038843&source=kegg) | 2.0E-3 | 24 |
| [T cell receptor signaling pathway](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa04660$T%20cell%20receptor%20signaling%20pathway&termId=450038869&source=kegg) | 3.4E-3 | 27 |
| [Toll-like receptor signaling pathway](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa04620$Toll-like%20receptor%20signaling%20pathway&termId=450038862&source=kegg) | 8.9E-3 | 25 |
| [Oxidative phosphorylation](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa00190$Oxidative%20phosphorylation&termId=450038741&source=kegg) | 1.4E-2 | 29 |
| **PMEs at 12 MONTHS of age** | | |
| **PATHWAYS** | **P VALUE** | **DEGSs number** |
| [Primary immunodeficiency](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05340$Primary%20immunodeficiency&termId=450038919&source=kegg) | 1.7E-12 | 23 |
| [Parkinson's disease](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05012$Parkinson%27s%20disease&termId=450038892&source=kegg) | 1.1E-4 | 32 |
| [Alzheimer's disease](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05010$Alzheimer%27s%20disease&termId=450038891&source=kegg) | 1.2E-3 | 35 |
| [B cell receptor signaling pathway](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa04662$B%20cell%20receptor%20signaling%20pathway&termId=450038870&source=kegg) | 8.9E-3 | 20 |
| [Apoptosis](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa04210$Apoptosis&termId=450038843&source=kegg) | 7.9E-3 | 22 |
| **PMEs at 24 MONTHS of age** | | |
| **PATHWAYS** | **P VALUE** | **DEGSs number** |
| [Primary immunodeficiency](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05340$Primary%20immunodeficiency&termId=450038919&source=kegg) | 4.6E-11 | 21 |
| [Apoptosis](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa04210$Apoptosis&termId=450038843&source=kegg) | 1.4E-3 | 22 |
| [Parkinson's disease](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05012$Parkinson%27s%20disease&termId=450038892&source=kegg) | 1.2E-3 | 28 |
| [T cell receptor signaling pathway](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa04660$T%20cell%20receptor%20signaling%20pathway&termId=450038869&source=kegg) | 1.5E-2 | 23 |
| **PMEs at 36 MONTHS of age** | | |
| [Primary immunodeficiency](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05340$Primary%20immunodeficiency&termId=450038919&source=kegg) | 9.5E-11 | 21 |
| [Parkinson's disease](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa05012$Parkinson%27s%20disease&termId=450038892&source=kegg) | 2.4E-3 | 28 |
| [Apoptosis](https://david-d.ncifcrf.gov/kegg.jsp?path=hsa04210$Apoptosis&termId=450038843&source=kegg) | 8.8E-3 | 21 |

*P* values were calculated via hypergeometric tests and go with a correction. DEGs Indicated number of differentially expressed genes.

**Table 5**: List of genes selected as potential bimarkers with significantly different expression in each comparison

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Comparisons** | **Genes** | **microarray p-value** | **False discovery rate** | **microarray log2 fold change** | **Real-time PCR log2 fold change** |
| **PME infants**  **Vs.**  **Normal infants** | DRD1 | 0.00004 | 0.0045 | 2.64 | 2.67 |
| DRD2 | 0.00005 | 0.0042 | 2.87 | 2.74 |
| DRD3 | 2.26E-04 | 0.0031 | 2.92 | 2.63 |
| BDNF | 0.000004 | 0.0023 | 3.72 | 3.32 |
| FOXP2 | 0.00003 | 0.0031 | -2.39 | -2.41 |
| TGFB1 | 0.00004 | 0.0035 | -2.46 | -2.48 |
| IL-1B | 0.00006 | 0.004 | 2.44 | 2.32 |
| IL8 | 0.00003 | 0.0013 | 2.48 | 2.4 |
| CDK4 | 0.00003 | 0.0016 | 2.55 | 2.52 |
| UPF3B | 0.000002 | 0.0017 | -2.58 | -2.63 |
| EGR2 | 0.00002 | 0.0049 | -2.65 | -2.66 |
| CREB1 | 0.000003 | 0.0021 | -2.68 | -2.72 |
| CYP2E1 | 0.00002 | 0.0028 | -2.62 | -2.65 |
| **twelve months of age PMEs**  **Vs.**  **twelve months of age Normal's** | DRD3 | 0.00004 | 0.0031 | 2.42 | 2.49 |
| BDNF | 0.000003 | 0.0022 | 2.57 | 2.54 |
| FOXP2 | 0.000004 | 0.0038 | -3.4 | -3.45 |
| TGFB1 | 0.000002 | 0.0028 | -2.56 | -2.62 |
| IL-1B | 0.000004 | 0.0079 | 3.38 | 3.36 |
| IL8 | 0.00007 | 0.0032 | 3.29 | 3.24 |
| CDK4 | 0.00003 | 0.0018 | 2.88 | 2.82 |
| UPF3B | 0.000004 | 0.002 | -4.65 | -4.66 |
| EGR-2 | 0.000002 | 0.004 | -3.78 | -3.81 |
| CREB1 | 0.00003 | 0.0022 | -3.83 | -3.86 |
| MECP2 | 0.00001 | 0.0028 | -2.84 | -2.83 |
| MAOA | 0.000003 | 0.0039 | -3.73 | -3.76 |
| twenty-four months of age PMEs  Vs.  twenty-four months of age Normal's | DRD3 | 0.00003 | 0.0016 | 2.54 | 2.47 |
| BDNF | 3.00E-06 | 0.0025 | 4.16 | 3.96 |
| FOXP2 | 3.00E-06 | 0.0018 | -3.58 | -3.63 |
| TGFB1 | 0.00002 | 0.0033 | -2.57 | -2.58 |
| IL-1B | 3.00E-05 | 0.0065 | 2.35 | 2.39 |
| IL8 | 0.000001 | 0.0024 | 3.54 | 3.56 |
| CDK4 | 3.00E-06 | 0.0022 | 2.61 | 2.57 |
| EGR2 | 2.00E-06 | 0.0028 | -3.77 | -3.79 |
| CREB1 | 0.00003 | 0.0013 | -3.82 | -3.83 |
| UPF3B | 2.00E-06 | 0.0017 | -3.63 | -3.66 |
| MECP2 | 0.00001 | 0.0015 | -2.74 | -2.77 |
| MAO-A | 0.000005 | 0.0027 | -3.71 | -3.72 |
| DLG-4 | 4.48E-05 | 0.0035 | 3.5 | 3.49 |
| SHANK-2 | 0.0015339 | 0.0013 | -2.75 | -2.78 |
| thirty-six months of age PMEs  Vs.  thirty-six months of age Normal's | DRD3 | 0.00006 | 0.0029 | 2.44 | 2.38 |
| BDNF | 0.00001 | 0.003 | 3.19 | 3.12 |
| FOXP2 | 0.00003 | 0.0015 | -3.61 | -3.64 |
| TGFB1 | 0.000003 | 0.0027 | -2.6 | -2.62 |
| IL-1B | 0.000003 | 0.0062 | 2.42 | 2.36 |
| IL8 | 0.00002 | 0.0016 | 2.6 | 2.61 |
| CDK4 | 0.00003 | 0.0026 | 2.64 | 2.67 |
| EGR2 | 0.000001 | 0.0029 | -2.75 | -2.78 |
| CREB1 | 0.000003 | 0.0036 | -2.83 | -2.85 |
| UPF3B | 0.000002 | 0.0024 | -2.67 | -2.71 |
| MECP2 | 0.00003 | 0.0046 | -2.76 | -2.78 |
| MAO-A | 0.000002 | 0.0041 | -3.72 | -3.74 |
| DLG-4 | 0.00001 | 0.002 | 3.46 | 3.44 |
| SHANK-2 | 0.000005 | 0.0015 | -2.79 | -2.8 |

list of genes after meeting 0.01 FDR criteria and confirmation data with Real-time PCR.

**Table 6.** Primer sequences of 17 differentially genes (and GAPDH gene) that confirmed by Real time PCR

|  |  |  |
| --- | --- | --- |
| **Gene** | **Forward Primer** | **Reverse Primer** |
| *DRD1* | 5'GGCTCTCGAAAGGAAGCCAA3' | 5'ACTAGACCCCGGCTAAGGG3' |
| *DRD2* | 5' CATGGACCACTCACACCCC 3' | 5' GAACGAACAAACACACACGGG 3' |
| *DRD3* | 5' GAACCCCACGAATGTTTCAGG 3' | 5' GAGTTGTCAGGTCCCCATCAG 3' |
| *BDNF* | 5'AAGCTCCGTAGTGCAGGAAG3' | 5' ACATCCAGTTGTCCTTCGGG 3' |
| *FOXP2* | 5'CCTAGGACTCCGTTTCAAGGT3' | 5'TCTGTCGCAGATTCCTGCAT3' |
| *TGFB1* | 5'ACCTCATCCAGGAAGTCCCC3' | 5'CAGAGGAACGTCAATGCAGG3' |
| *IL1B* | 5'CCAAACCTCTTCGAGGCACA3' | 5'TTCAGACACCTAGTTGTAAGGAAGA3' |
| *IL8* | 5'AGCACTCCATAAGGCACAAACT3' | 5'TGGTTCCTTCCGGTGGTTTC3' |
| *CDK4* | 5'GGAGTCTGTGATTGTAGGGTCTC3' | 5'TAGGCACCGACACCAATTTCA3' |
| *UPF3B* | 5'CAGGTCGATTCTGGTGGCAA3' | 5' CCTTCCTGGAGAGGGTACACA3' |
| *EGR2* | 5'AATAACACTACACCAGCAACTCC3' | 5'CCCAACTCCCTCGCTACTC3' |
| *CREB1* | 5'GCTTGAAATTCTGTGACTCTTCCC3' | 5'TGGACTTGAACTGTCTGCCC3' |
| *CYP2E1* | 5'TTCCGATGTTGAATTTTCCTTCTGG3' | 5'GGTGACTCCGAGGGCAGA3' |
| *MECP2* | 5'TATAGTTCCCATCAGGAGCCGT3' | 5'CACATCAAAGCAGGAACTGGTG3' |
| *MAOA* | 5'TAGAAGGGTCCTTCCCACCC3' | 5'CACCTCCGATCACGACTACG3' |
| *DLG4* | 5'CCATCCCCAGAAATACCGCT3' | 5'CTCGGTCCCGTTCACATATCC3' |
| *SHANK2* | 5'TTGTACCCCTTGTGCCAACC3' | 5'TCCAAGTTGCAAGACTGGGC3' |
| *GAPDH* | 5'CACTAGGCGCTCACTGTTCTC3' | 5'AAATCCGTTGACTCCGACCT3' |