**TABLE S1**

**TOP TEN GENES DIFFERENTIALLY EXPRESSED BETWEEN NORMAL AND CML HSCs**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene Symbol | Gene name | Fold change | p-Value | FDR |
| GAS2 | growth arrest-specific 2 | **29.11** | 0.000001 | 0.002113 |
| RXFP1 | relaxin/insulin-like family peptide receptor 1 | **19.5** | 1.24E-07 | 0.000758 |
| MAMDC2 | MAM domain containing 2 | **13.39** | 9.97E-07 | 0.002113 |
| PIEZO2 | piezo-type mechanosensitive ion channel component 2 | **13.15** | 2.22E-07 | 0.001076 |
| HPGDS | hematopoietic prostaglandin D synthase | **11.16** | 0.000157 | 0.020181 |
| CPA3 | carboxypeptidase A3 (mast cell) | **9.17** | 0.00024 | 0.023154 |
| DPP4 | dipeptidyl-peptidase 4 | **8.52** | 0.000002 | 0.003124 |
| PTPRD | protein tyrosine phosphatase, receptor type, D | **8.28** | 0.000091 | 0.017957 |
| CACNA1D | calcium channel, voltage-dependent, L type, alpha 1D subunit | **8.05** | 0.000151 | 0.02005 |
| MSMO1 | methylsterol monooxygenase 1 | **7.66** | 0.00002 | 0.010612 |
| ETV3 | ets variant 3 | **-7.03** | 0.000044 | 0.013483 |
| PCDH9 | protocadherin 9 | **-7.05** | 0.000012 | 0.008027 |
| NR4A1 | nuclear receptor subfamily 4, group A, member 1 | **-7.39** | 0.00985 | 0.110612 |
| METTL24 | methyltransferase like 24 | **-7.77** | 0.006062 | 0.088629 |
| PLAG1 | pleiomorphic adenoma gene 1 | **-8.69** | 4.34E-07 | 0.001403 |
| SKIL | SKI-like oncogene | **-10.62** | 0.000869 | 0.037752 |
| FIGN | Fidgetin | **-10.91** | 0.00784 | 0.099114 |
| FAM19A2 | family with sequence similarity 19 (chemokine (C-C motif)-like), member A2 | **-12.68** | 0.000006 | 0.007243 |
| EMP1 | epithelial membrane protein 1 | **-13.37** | 0.000066 | 0.015424 |
| ABI3BP | ABI family, member 3 (NESH) binding protein | **-14.06** | 0.000003 | 0.004017 |

Top ten genes upregulated and downregulated between CML and NBM HSCs, according to the analysis performed with Affymetrix transcriptome analysis console. Fold Change > 2; p <0.05.

**TABLE S2**

**TOP TEN GENES DIFFERENTIALLY EXPRESSED BETWEEN NORMAL AND CML HPCs**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene Symbol | Gene name | Fold change | p-Value | FDR |
| KYNU | kynureninase (L-kynurenine hydrolase) | **4.78** | 0.000016 | 0.022009 |
| MSMO1 | methylsterol monooxygenase 1 | **4.45** | 0.000068 | 0.036407 |
| RXFP1 | relaxin/insulin-like family peptide receptor 1 | **4.45** | 3.20E-07 | 0.009322 |
| CFH | complement factor H | **4.24** | 0.000006 | 0.020357 |
| HDC | histidine decarboxylase | **4.17** | 0.001673 | 0.091594 |
| DHCR24 | 24-dehydrocholesterol reductase | **4.13** | 0.000012 | 0.020357 |
| SCN9A | sodium channel, voltage-gated, type IX, alpha subunit | **3.69** | 0.000004 | 0.017817 |
| CCL5 | chemokine (C-C motif) ligand 5 | **3.51** | 0.002565 | 0.103662 |
| PIEZO2 | piezo-type mechanosensitive ion channel component 2 | **3.46** | 0.000546 | 0.061798 |
| ANGPT2 | angiopoietin 2 | **3.43** | 0.000065 | 0.036407 |
| ZFP36 | ZFP36 ring finger protein | **-3.69** | 0.000154 | 0.045739 |
| ID2 | inhibitor of DNA binding 2, dominant negative helix-loop-helix protein | **-3.82** | 0.000387 | 0.059006 |
| HCAR3 | hydroxycarboxylic acid receptor 3 | **-3.92** | 0.020908 | 0.212205 |
| NBPF14 | neuroblastoma breakpoint family, member 14 | **-4.15** | 0.041335 | 0.258699 |
| CRHBP | corticotropin releasing hormone binding protein | **-5.18** | 0.009848 | 0.160345 |
| ARHGAP32 | Rho GTPase activating protein 32 | **-5.2** | 0.014604 | 0.189113 |
| ELANE | elastase, neutrophil expressed | **-5.22** | 0.003229 | 0.113648 |
| KCNA3 | potassium voltage-gated channel, shaker-related subfamily, member 3 | **-5.65** | 0.000057 | 0.036407 |
| SKIL | SKI-like oncogene | **-6.96** | 0.00096 | 0.073001 |
| IRF8 | interferon regulatory factor 8 | **-7.04** | 0.002576 | 0.103682 |

Top ten genes upregulated and downregulated between CML and NBM HPCs, according to the analysis performed with Affymetrix transcriptome analysis console. Fold Change > 2; p <0.05.

**TABLE S3**

**TOP TEN GENES DIFFERENTIALLY EXPRESSED BETWEEN NORMAL HPCs BEFORE AND AFTER IN VITRO CULTURE WITHOUT IM**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene Symbol | Gene name | Fold change | p-Value | FDR |
| MMP12 | matrix metallopeptidase 12 | **28.57** | 0.000491 | 0.006669 |
| DHCR24 | 24-dehydrocholesterol reductase | **19.47** | 4.23E-08 | 0.000103 |
| IL7R | interleukin 7 receptor | **15.15** | 0.000111 | 0.002865 |
| CYP1B1 | cytochrome P450, family 1, subfamily B, polypeptide 1 | **14.39** | 0.000002 | 0.000535 |
| GYPA | glycophorin A (MNS blood group) | **13.91** | 0.000078 | 0.002359 |
| MRC1 | mannose receptor, C type 1 | **13.31** | 0.000638 | 0.007906 |
| HBG1; HBG2 | hemoglobin, gamma A; hemoglobin, gamma G | **10.89** | 7.52E-08 | 0.000103 |
| MSMO1 | methylsterol monooxygenase 1 | **10.79** | 1.57E-07 | 0.000148 |
| S100A8 | S100 calcium binding protein A8 | **10.53** | 0.005526 | 0.033125 |
| CCL2 | chemokine (C-C motif) ligand 2 | **8.84** | 0.0001 | 0.002704 |
| KLF4 | Kruppel-like factor 4 | **-13.56** | 0.000012 | 0.001006 |
| NR4A2 | nuclear receptor subfamily 4, group A, member 2 | **-14.63** | 0.000002 | 0.000515 |
| NR4A1 | nuclear receptor subfamily 4, group A, member 1 | **-15.84** | 3.26E-07 | 0.000207 |
| RGS1 | regulator of G-protein signaling 1 | **-15.93** | 0.000004 | 0.000674 |
| TNFAIP3 | tumor necrosis factor, alpha-induced protein 3 | **-17.39** | 0.000009 | 0.000847 |
| DUSP1 | dual specificity phosphatase 1 | **-19.88** | 5.03E-08 | 0.000103 |
| FOS | FBJ murine osteosarcoma viral oncogene homolog | **-20.12** | 0.000011 | 0.000961 |
| AREG | amphiregulin | **-34.22** | 0.000258 | 0.004609 |
| FOSB | FBJ murine osteosarcoma viral oncogene homolog B | **-36.01** | 1.86E-07 | 0.000159 |
| JUN | jun proto-oncogene | **-62.62** | 8.58E-08 | 0.000104 |

Top ten genes upregulated and downregulated between NBM HPCs cultured without IM for 48 hrs vs HPCs at time 0 (before culture), according to the analysis performed with Affymetrix transcriptome analysis console. Fold Change > 2.0; p <0.05.

**TABLE S4**

**TOP TEN GENES DIFFERENTIALLY EXPRESSED BETWEEN NORMAL HPCs BEFORE AND AFTER IN VITRO CULTURE WITH IM**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene Symbol | Gene name | Fold change | p-Value | FDR |
| MMP12 | matrix metallopeptidase 12 | **25.5** | 0.000243 | 0.006535 |
| DHCR24 | 24-dehydrocholesterol reductase | **19.31** | 2.01E-08 | 0.000065 |
| IL7R | interleukin 7 receptor | **17.33** | 0.000465 | 0.009341 |
| CYP1B1 | cytochrome P450, family 1, subfamily B, polypeptide 1 | **16.89** | 2.82E-07 | 0.000256 |
| HBG1 | hemoglobin, gamma A; hemoglobin, gamma G | **14.74** | 1.64E-08 | 0.000065 |
| GYPA | glycophorin A (MNS blood group) | **14.28** | 0.000015 | 0.001585 |
| MRC1 | mannose receptor, C type 1 | **13.38** | 0.000851 | 0.013032 |
| S100A8 | S100 calcium binding protein A8 | **13.08** | 0.007049 | 0.049329 |
| MSMO1 | methylsterol monooxygenase 1 | **12.12** | 1.61E-07 | 0.000203 |
| GYPB | glycophorin B (MNS blood group) | **9.77** | 0.000039 | 0.002496 |
| KLF4 | Kruppel-like factor 4 (gut) | **-13.98** | 0.00001 | 0.001335 |
| NR4A2 | nuclear receptor subfamily 4, group A, member 2 | **-14.16** | 0.000002 | 0.00057 |
| ZFP36 | ZFP36 ring finger protein | **-14.31** | 4.54E-07 | 0.000266 |
| RGS1 | regulator of G-protein signaling 1 | **-15.75** | 0.000005 | 0.000982 |
| TNFAIP3 | tumor necrosis factor, alpha-induced protein 3 | **-16.85** | 0.000005 | 0.000982 |
| FOS | FBJ murine osteosarcoma viral oncogene homolog | **-17.97** | 0.00001 | 0.001335 |
| DUSP1 | dual specificity phosphatase 1 | **-20.64** | 1.12E-08 | 0.000065 |
| FOSB | FBJ murine osteosarcoma viral oncogene homolog B | **-26.17** | 2.27E-08 | 0.000066 |
| AREG | Amphiregulin | **-41.61** | 0.000228 | 0.006325 |
| JUN | jun proto-oncogene | **-48.37** | 9.53E-07 | 0.000391 |

Top ten genes upregulated and downregulated between NBM HPCs cultured with IM for 48 hrs vs HPCs at time 0 (before culture), according to the analysis performed with Affymetrix transcriptome analysis console. Fold Change > 2.0; p <0.05

**TABLE S5**

**TOP TEN GENES DIFFERENTIALLY EXPRESSED BETWEEN CML HPCs BEFORE AND AFTER IN VITRO CULTURE WITHOUT IM**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene Symbol | Gene name | Fold change | p-Value | FDR |
| GYPA | glycophorin A (MNS blood group) | **13.25** | 0.000454 | 0.008921 |
| HBA2 | hemoglobin, alpha 2 | **12.39** | 0.000296 | 0.00678 |
| CYP1B1 | cytochrome P450, family 1, subfamily B, polypeptide 1 | **11.29** | 0.000828 | 0.012972 |
| PLK1 | polo-like kinase 1 | **10.43** | 0.00001 | 0.001091 |
| PSAT1 | phosphoserine aminotransferase 1 | **7.92** | 0.000043 | 0.002338 |
| KIF20A | kinesin family member 20ª | **7.41** | 0.000001 | 0.00046 |
| DLGAP5 | discs, large (Drosophila) homolog-associated protein 5 | **6.75** | 0.000006 | 0.0009 |
| CDK1 | cyclin-dependent kinase 1 | **6.33** | 9.33E-07 | 0.000431 |
| HMMR | hyaluronan-mediated motility receptor (RHAMM) | **6.24** | 0.000002 | 0.000582 |
| PBK | PDZ binding kinase | **5.84** | 0.000002 | 0.000576 |
| CD40LG | CD40 ligand | -8.1 | 0.00004 | 0.002259 |
| NR4A3 | nuclear receptor subfamily 4, group A, member 3 | **-10.27** | 0.002228 | 0.023754 |
| CXCL8 | chemokine (C-X-C motif) ligand 8 | **-10.92** | 0.000023 | 0.001653 |
| AREG | Amphiregulin | **-11.49** | 0.011381 | 0.072177 |
| ARRDC3 | arrestin domain containing 3 | **-14.68** | 0.000006 | 0.000922 |
| DUSP1 | dual specificity phosphatase 1 | **-18.47** | 0.000001 | 0.000455 |
| NR4A2 | nuclear receptor subfamily 4, group A, member 2 | **-28.35** | 0.000134 | 0.004402 |
| FOS | FBJ murine osteosarcoma viral oncogene homolog | **-29.67** | 2.21E-07 | 0.000189 |
| FOSB | FBJ murine osteosarcoma viral oncogene homolog B | **-31.4** | 7.45E-07 | 0.000364 |
| JUN | jun proto-oncogene | **-39.23** | 0.000005 | 0.000807 |

Top ten genes upregulated and downregulated between CML HPCs cultured without IM for 48 hrs vs HPCs at time 0 (before culture), according to the analysis performed with Affymetrix transcriptome analysis console. Fold Change > 2.0; p <0.05

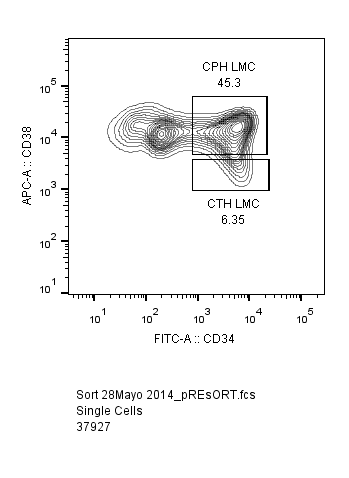
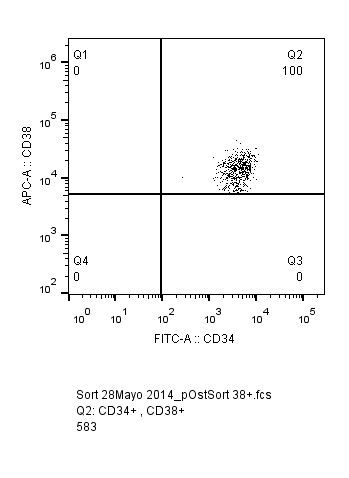
**TABLE S6**

**TOP TEN GENES DIFFERENTIALLY EXPRESSED BETWEEN CML HPCs BEFORE AND AFTER IN VITRO CULTURE WITH IM**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Gene Symbol | Gene name | Fold change | p-Value | FDR |
| CYP1B1 | cytochrome P450, family 1, subfamily B, polypeptide 1 | **17.87** | 0.000142 | 0.007406 |
| GYPA | glycophorin A (MNS blood group) | **13.79** | 0.000183 | 0.008253 |
| HBA2 | hemoglobin, alpha 2 | **12.02** | 0.00016 | 0.007808 |
| PLK1 | polo-like kinase 1 | **7.42** | 0.000023 | 0.003116 |
| HBG1 | phosphoserine aminotransferase 1 | **7.39** | 0.009897 | 0.084269 |
| GYPB | glycophorin B (MNS blood group) | **6.22** | 0.005267 | 0.057451 |
| KIF20A | kinesin family member 20A | **6.17** | 0.000007 | 0.001821 |
| CDK1 | cyclin-dependent kinase 1 | **6.12** | 0.000016 | 0.002696 |
| SLC7A11 | solute carrier family 7 (anionic amino acid transporter light chain, xc- system), member 11 | **5.62** | 0.000896 | 0.020311 |
| DLGAP5 | discs, large (Drosophila) homolog-associated protein 5 | **5.54** | 0.000027 | 0.003283 |
| NFKBIZ | nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta | **-7.71** | 0.000051 | 0.004559 |
| NR4A3 | nuclear receptor subfamily 4, group A, member 3 | **-7.71** | 0.005117 | 0.056423 |
| NFKBIA | nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha | **-8.54** | 3.23E-07 | 0.000588 |
| AREG | amphiregulin | **-10.64** | 0.019226 | 0.127539 |
| ARRDC3 | arrestin domain containing 3 | **-11.47** | 0.000005 | 0.00155 |
| NR4A2 | nuclear receptor subfamily 4, group A, member 2 | **-20.32** | 0.000304 | 0.011273 |
| DUSP1 | dual specificity phosphatase 1 | **-21.31** | 0.000003 | 0.001166 |
| FOS | FBJ murine osteosarcoma viral oncogene homolog | **-22.95** | 7.31E-07 | 0.000787 |
| FOSB | FBJ murine osteosarcoma viral oncogene homolog B | **-32.17** | 0.000001 | 0.000808 |
| JUN | jun proto-oncogene | **-37.32** | 0.000025 | 0.003227 |

Top ten genes upregulated and downregulated between CML HPCs cultured with IM for 48 hrs vs HPCs at time 0 (before culture), according to the analysis performed with Affymetrix transcriptome analysis console. Fold Change > 2.0; p <0.05.

**FIGURE S1**



CD34

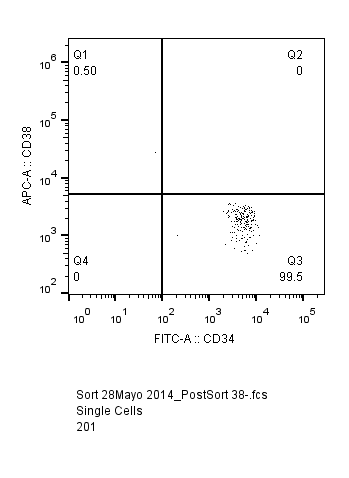
CD38

CD38

CD34

CD38

CD34



**Purification of HSCs and HPCs**. FACS plots showing the strategy followed for the purification of cell fractions enriched for HSCs (CD34+ CD38- Lin- cells; bottom panel on the right) and HPCs (CD34+ CD38+ Lin- cells; top panel on the right) obtained from CML bone marrow. The same strategy was followed for obtaining both cell populations from normal bone marrow.

**FIGURE S2**

**Effect of IM on the proliferation of HPCs derived from normal (NBM) and CML bone marrow**. Results correspond to the percentage of the total nucleated cell number after 48 hrs of culture in Serum-Free Expansion Media supplemented with a mixture of recombinant cytokines (SCF, TPO, FL, IL-6, IL-3, GM-CSF, G-CSF, and EPO) in the absence (C) or in the presence (IM) of 2.5 µM IM. Total cell number before culture corresponded to 100%.