**Human Cells Display Reduced Apoptotic Function Relative to Chimpanzee Cells**

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**Supplemental Information File S1**

The resistance of various human cells to mitomycin C (MMC) has been previously associated with decreased expression of genes involved in the conversion of MMC into an active drug (*NQO1, POR*) and/or increased expression of genes involved in glutathione metabolism (*GSTP1, GSR, GPX1, GCLC, GCLM*), nucleotide excision and homologous recombination repair (*ERCC1, XDH*) or multidrug resistance (*ABCB1*) (See below).

To investigate the possibility, that other than apoptosis-related mechanisms were responsible for the observed higher cell viability and lower proportion of apoptotic cells in MMC-treated human cells relative to chimpanzee cells, we compared expression of these genes using repository U95Av2 microarray data for 18 human and 10 bonobo primary fibroblast cultures [1]. At the level of multiplicity adjusted p-value < 0.05, none of the genes known to confer resistance to mitomycin C, except for *GSR*, demonstrated higher expression levels in human compared to bonobo cells (below).

**Differential expression between human and bonobo fibroblasts of genes previously shown to be associated with resistance to MMC**. Microarray data were obtained from Karaman et al. [1]. Probe ID corresponds to U95Av2 3’-expression arrays (Affymetrix). FC (fold change of expression value between humans and bonobo; p-values were multiplicity adjusted using the Benjamini-Hochberg method [2].

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene symbol** | **Probe ID** | **FC (h/b)** | **Adjusted p-value** | **Ref** |
| ERCC1 | 1878\_g\_at | -1.77 | 0.0028 | [3] |
| GSTP1 | 33396\_at | -1.36 | 0.0153 | [4] |
| GSR | 35130\_at | 1.24 | 0.036 | [4] |
| POR | 858\_at | 1.59 | 0.0702 | [5,6] |
| GPX1 | 37033\_s\_at | -1.29 | 0.3195 | [4] |
| GCLM | 33163\_r\_at | -1.28 | 0.3754 | [7] |
| XDH | 33463\_at | -1.15 | 0.4693 | [6] |
| GCLC | 31850\_at | -1.13 | 0.6348 | [7] |
| ABCB1 | 1682\_s\_at | -1.01 | 0.6 | [8] |
| NQO1 | 38066\_at | -1.02 | 0.9527 | [9,10] |

Similarly, genes activating MMC were not differentially expressed between human and bonobo fibroblastic cells. The *GSR* (glutathione reductase) gene was overexpressed in human cells; however, the low fold change value (1.24) and the fact that 6 out of 16 probes in probeset “35130\_at” do not perfectly match with the target chimpanzee sequence (below) suggests that the role of GSR in lower susceptibility of human fibroblasts to MMC is negligible.

**Probeset ID: 35130\_at ( human glutathione reductase, GSR) alignment with chimpanzee sequences from the *Pan troglodytes* genome.** Probe information (top line each box) retrieved from NetAffx (http://www.affymetrix.com/analysis/index.affx) and chimp sequence (bottom line each box). Green color: perfect match; red color: imperfect match.

|  |
| --- |
| Probe sequence 5’3’  Probe-target alignment |
| tcccgaataccaaggacctgagttt  |||||||||||||||||||||||||  tcccgaataccaaggacctgagttt |
| caaactggggattcaaaccgatgac  | |||||||||||||||||||  aatttaggggattcaaaccgatgac |
| aagggtcatatcatcgtagacgaat  |||||||||||||| ||||||||||  aagggtcatatcattgtagacgaat |
| tcatcgtagacgaattccagaatac  |||| ||||||||||||||||||||  tcattgtagacgaattccagaatac |
| gattataacaacatcccaactgtgg  |||||||||||||||||||||||||  gattataacaacatcccaactgtgg |
| acatcccaactgtggtcttcagcca |||||||||||||||||||||||||  acatcccaactgtggtcttcagcca |
| atgtgaagacctattcaacgagctt  |||||||||||||||||||||||||  atgtgaagacctattcaacgagctt |
| atgtatcacgcagttaccaaaagga  ||||||||||||||||||||||||| atgtatcacgcagttaccaaaagga |
| aatgctgcagggttttgctgttgca  |||||||||||||||||| ||||||  aatgctgcagggttttgccgttgca |
| tgctgcagggttttgctgttgcagt  |||||||||||||||| ||||||||  tgctgcagggttttgccgttgcagt |
| ctgcagggttttgctgttgcagtga  |||||||||||||| ||||||||||  ctgcagggttttgccgttgcagtga |
| caccctacctcttcagaagagctgg  ||||||||||||||||||||||||| caccctacctcttcagaagagctgg |
| cctacctcttcagaagagctggtca |||||||||||||||||||||||||  cctacctcttcagaagagctggtca |
| gcgggcagtgggacccatagatctt |||||||||||||||||||||||||  gcgggcagtgggacccatagatctt |
| cagtgggacccatagatcttctgaa  ||||||||||||||||||||||||| cagtgggacccatagatcttctgaa |
| gacccatagatcttctgaaatgaaa  ||||||||||||||||||||||||| gacccatagatcttctgaaatgaaa |

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1. [↑](#footnote-ref-1)