Supplementary Material and Methods

RNA analysis

Total RNA was extracted from untreated and TRAIL-treated cell cultures and from animal frozen tissues by using the Qiagen RNeasy Plus mini kit (Qiagen, Hilden, Germany), according to the supplier's instructions. Integrity of the total RNA preparation was checked by using an Agilent 2100 bioanalyzer. Only RNA samples in which the respective ribosomal RNAs appeared as sharp peaks were used for cDNA microarray and quantitative RT-PCR analyses.

RNA extracted from untreated and TRAIL-treated human PBMC was transcribed into cDNA using GEArray AmpoLabeling-LPR Kit (Superarray Bioscience Corporation, Frederick, MD). An *in vitro* linear polymerase reaction was then performed to generate biotinylated cRNA. Biotinylated labeled cDNA was hybridized with a customized cDNA microarray (GEArray S Series Human Apoptosis & Cell Cycle Gene Array HS-603; http://www.superarray.com/gene_array_product/HTML/HS-603.html), containing an array of stress e toxicity-related genes and genes associated to apoptosis and cell cycle, together with housekeeping genes. Hybridization was revealed by alkaline phosphatase-conjugated streptavidin, using a chemiluminescent detection kit (Superarray Bioscience Corporation). Expression levels were compared between the samples left untreated (controls) or treated with recombinant TRAIL, then data were filtered for the genes whose expression level increased or decreased by at least two fold, that is, filtering the ratio for values ≥ 2.0 or ≤ 0.5.

Validation of array results and investigation of specific gene expression were carried out in RNA samples with the real time thermal analyzer Rotor-Gene^{TM} 6000 (Corbett, Cambridge UK), by using SYBR Green based-technology and the RT-PCR primer set for human SOCS1 cDNA (SABioscience, Frederick, MD) or mouse SOCS1 and VCAM-1 cDNA (Qiagen). Gene expression of the target sequences was normalized in relation to the expression of endogenous controls: POLR2A mRNA for human RNA and Ppia mRNA for mouse RNA, as previously reported (**1**, **2**). Each sample was tested in triplicate.

Supplementary References

1. Radonić A, Thulke S, Mackay IM, Landt O, Siegert W, Nitsche A: Guideline to reference gene selection for quantitative real-time PCR. *Biochem Biophys Res Commun* 313:856-862, 2004

2. Mamo S, Gal AB, Bodo S, Dinnyes A. Quantitative evaluation and selection of reference genes in mouse oocytes and embryos cultured in vivo and in vitro. *BMC Dev Biol* 7:14, 2007