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Use of cDNA microarrays to estimate gene modulation profiles induced by zoledronic acid treatment in androgen-resistant prostate cancer cell line (PC3)

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The LNCaP and the PC3 cells are widely used as models for prostate cancer. Aminobisphosphonates have clearly demonstrated to inhibit proliferation and induce apoptosis in these cells by interfering with the mevalonate pathway. The types and pattern of downstream genes modulated by zoledronic acid (ZA) treatment are unknown. We used a cDNA microarray platform to analyse the genetic modulation induced by ZA in the PC3 prostate cancer cell line.

Methods

Cells were grown in RPMI with 5% FCS and treated with ZA at 100 microM for 24 hours. Cells cultured with lipoprotein depleted serum (LPDS) were also included, as control. Gene signatures of untreated vs. ZA-acid treated cells were obtained by Affymetrix HG-U133 chips (including more than 33,000 well-known human genes). Preprocessing methods were performed in two independent examinations at the Insti-

tute for Medical Informatics, Statistics and Epidemiology of Leipzig and of the Max-Planck Molecular Biology Institute. (All the quality controls performed showed no problems).

Results

We considered only the genes with changes > 3 fold after treatment with ZA in PC3 cells. The upregulated and downregulated genes were 73/33.000. The statistical difference of expression of each gene was at least $p < 0.001$. 4 genes were downregulated (-3.82 t -5.58) and 69 genes were upregulated (+3 a +45.52).

Conclusions

ZA induces in PC3 cells at mRNA level (cDNA array) up- and down-regulation of specific genes involved in angiogenesis, tumour growth and, interestingly, in androgen response.