

# **Identification of commonly regulated genes in HPV18- and HPV16-infected cervical cancer cells treated with the curcumin analogue 1,5-bis(2-hydroxyphenyl)-1,4-pentadiene-3-one**

## **ABSTRACT**

### **Objective:**

To identify commonly regulated genes in HPV-infected HeLa and CaSki cervical cancer cells treated with curcumin analogue 1,5-bis(2-hydroxyphenyl)-1,4-pentadiene-3-one (MS17) and to explore potential mechanisms that underlie its cytotoxic, anti-proliferative and apoptotic activity.

### **Methods:**

HeLa and CaSki cells were treated with  $2 \times EC_{50}$  and  $3 \times EC_{50}$  doses of MS17 for 24 h and the RNA extracts were subjected to one-colour microarray-based gene expression profiling. Pairwise significant genes (false discovery rate-corrected,  $P < 0.05$ ) were analysed for fold change (FC) compared to control samples. Differentially expressed genes with  $FC \geq 2.0$  (up-regulated;  $FC \geq 2.0$  and down-regulated;  $FC \leq -2.0$ ) compared to the control samples were filtered through and analysed to create a global gene expression profile. Mutually regulated genes were ranked by FC and categorised by gene ontology.

### **Results:**

Our data indicated dose-dependent regulation by MS17 and identified top 20 mutually up and down-regulated genes each in HeLa and CaSki cells. Amongst these 17 were commonly regulated in both cell lines. These include the up-regulation of CCL26, DEFB103B, IL1RL1, LY96, GCNT3, MMP10, MMP3, GADD45G and HSPA6, and the down-regulation of TENM2, NEBL, KIFC1, CTDSP1, IGFBP5, LTBP1, NREP and MXD3. These genes were associated with key biological functions that were proposed to mediate the anticancer activity of MS17 in cervical cancer cells such as immune response, metabolic processes, proteolysis, programmed cell death, unfolded protein response, cell adhesion, cytoskeletal organisation, phosphatase activity, signal transduction and transcription regulator activity.

### **Conclusions:**

Identification of seventeen common genes modulated by MS17 could be used as potential therapeutic targets in both cervical cancer cell lines and the findings of this study could be used to present an insight into the potential antitumor activity of MS17 in cervical cancer.

**Keyword:** Diarylpentanoic acid; Cervical cancer; Gene expression profiling; Microarray; Curcumin analogue