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Effects of Cadmium and vitamin D binding protein-derived macrophage activating factor (DBP-MAF) in human breast cancer cells

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We previously demonstrated that chronic exposure of the human breast cancer cell line MCF-7 to non-cytotoxic concentrations of Cadmium reduced viability and angiogenic potential of this cell line. In order to better understand these effects, cells, after Cadmium exposure, were treated with vitamin D binding protein-derived macrophage activating factor (DBP-MAF). DBP-MAF is a potent macrophage-activating factor derived from vitamin D binding protein, a polymorphic serum glycoprotein with multiple functions also known as a group specific component or Gc protein. Besides stimulating macrophages, DBP-MAF has anti-tumour properties.

Our data demonstrate that the decrease of MCF-7 cell viability following Cadmium treatment was completely reversed when DBP-MAF was present in the cell medium. Following this observation, we further investigated the role of DBP-MAF in modulating angiogenesis, morphology and cytoskeleton structure of MCF-7 cell line.

As shown by chorioallantoic membrane assay, DBP-MAF inhibited MCF-7 cancer cell-stimulated angiogenesis.

Concerning cell morphology (studied by contrast phase light microscopy and after Papanicolaou staining), following DBP-MAF treatment, cell shape and growth pattern were significantly modified.

Vimentin expression (studied by immunohistochemistry and Western blot analysis), considered a hallmark of human breast cancer progression, after DBP-MAF treatment, significantly varied. Intermediate filament status changes, consisting in a shift from a keratin-rich to a vimentin-rich network (epithelial-mesenchymal transition), were observed.

In conclusion, we demonstrate that the anti-cancer effects of DBP-MAF can be attributed to multiple actions independent of macrophage stimulation such as reversal of Cadmium effects on cell viability, reversal of morphological malignant phenotype and inhibition of cancer cell-stimulated angiogenesis. For these reasons, DBP-MAF might represent an useful tool to control progression and differentiation of human breast cancer.

Keywords: human breast cancer, macrophages, morphology, angiogenesis, vimentin