THE EFFECT OF CALCITRIOL ANALOGUES ON THE PROLIFERATION OF THYROID MEDULLARY CARCINOMA CELLS AND ON THE EXPRESSION OF THE CALCITONIN GENE

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The results of studies have shown that calcitriol (an active form of vitamin D3) and its analogues, acting through a nuclear receptor, exert variable effects on multiple cell types, mainly affecting proliferation, cell differentiation and apoptosis. Moreover, the effects of the compounds on the secretion of calcium metabolism-controlling peptides were demonstrated. We decided to examine the effect of calcitriol and some of its analogues on the proliferation and expression of the calcitonin gene in thyroid parafollicular cells. Alternate splicing of the gene transcript and translation yielded CT (calcitonin) and CGRP (calcitonin gene-related peptide).

The studies were performed on two cell lines: rat MTC 6-23 and human TT. On 24-well plates, cultures of the cell lines were set up (starting at 20,000 cells per well). The culture medium was supplemented with calcitriol and its analogues, PRI-1906 and PRI-2191, to final concentrations of $10^{-9}$, $10^{-8}$, $10^{-7}$, and $10^{-6}$ mol/l. After 5 days of culture, the culture media were collected and the CT and CGRP concentrations were established by RIA techniques. Following fixation, cell proliferation in the wells was estimated using the MTT colorimetric test.

A slight anti-proliferative effect of all the studied analogues on both examined thyroid parafollicular cell lines was noted. In TT cell cultures, correlations were detected between the concentrations of PRI-2191 and the observed peptide levels: a positive correlation for CT and a negative one for CGRP. Also, a significant effect of the analogue was detected on the ratio of secreted CT to CGRP and thus, on the alternate splicing process in the cells. Moreover, an inhibitory effect of calcitriol and of either analogue was noted on CGRP secretion in MTC 6-23 cells. The results indicate differences in the control of expression or secretion in the two examined cell lines.