Thyroid hormone T3 acts as a mitogenic and survival factor in rat non tumoral granulosa cells and follicles

Mangialardo Claudia (IT) [1], Verga Falzacappa Cecilia (IT) [2], Cammarata Ilenia (IT) [3], Di Paolo Virginia (IT) [4], Virili Camilla (IT) [5], Canipari Rita (IT) [6], Centanni Marco (IT) [7]

Context: It is clinically evident that thyroid disorders are associated with impaired fertility in women and that these abnormalities are improved by restoring the euthyroid state. The exact mechanisms are not well known; however, it is conceivable that thyroid hormones might act on ovarian physiology via receptors in granulosa cells. Objective: This work aimed at evaluating the T3 effect on non tumoral granulosa cells and follicles.

Methods: We evaluated the effect of thyroid hormone T3 treatment on proliferation, apoptosis and survival of non tumoral rat granulosa cells (rGROV) and freshly isolated follicles. Cells and follicles were treated with T3. Cell growth and viability were evaluated by cell counting and MTT assay, respectively, whether follicles growth was evaluated by volume measuring.

Results: T3 promoted cell growth and viability, inducing a 40% increase in the cell number in rGROV (48h) and a 40% increase in follicle volumes (7 days). In addition, cytotoxicity revealed T3 ability to induce cell cycling in rGROV. In accordance, cell cycle molecules were regulated, as shown by Western Blot analysis. Moreover, as demonstrated by Tunel assay, in serum-free condition, T3 was able to induce a decrease in the cell apoptotic rate of 40%; in addition, the pro-apoptotic molecules Caspase 3 and Bax were downregulated. An increase in pAkt levels was also observed, suggesting that the PI3K pathway might be involved in the survival effect of T3.

Conclusions: These results support our hypothesis that T3 influences cell survival of ovarian granulosa cells, this effect probably participating to T3 induced follicle volume increase.