Thyroid hormones T3 and T4 as survival factors for human Granulosa Luteal Cells: a possible role in the ovulatory follicle

Context
Hyperthyroidism and hypothyroidism have adverse effects on female reproductive capacity and cause menstrual disorders. Thyroid dysfunctions in women are related to ovulation and fertilization problems and to abortion. However, the precise mechanisms underlying the relation between thyroid and ovarian function are still lacking.

Follicular development is finely regulated by the cross talk between survival and cell death promoters, including endocrine, paracrine and autocrine factors. Whether a follicle grows or not depends on the expression and action of factors-promoting proliferation, growth, differentiation and apoptosis of different cell populations within the follicle.

Objective
Aim of this work was to analyze the action of thyroid hormones on human granulosa luteal (hGL) cells, in order to highlight a possible effect of thyroid hormones on the apoptosis of these cells.

Methods
Human GL cells, obtained from follicular aspirates of women undergoing IVF treatment, were cultured in the absence of serum and the effect of T3 and T4 on cell apoptosis/survival was evaluated by TUNEL analysis and MTT assay.

Results
Once verified the presence of TH machinery genes by RT-PCR, and the presence of receptors by immunofluorescence microscopy, we evaluated the role of both T3 and T4 on apoptosis in hGL cells. T3 and T4 (100 nM) were able to significantly inhibit apoptosis induced by serum deprivation, while preserving cell viability. This effect was accompanied by Akt activation.

Conclusions
In conclusion T3 and T4 appear to play a role in maintenance of follicle viability because of their antiapoptotic effect. Although further studies are warranted to elucidate the roles of thyroid hormones in ovarian physiology and their mechanism of action, our data strenthen the idea that thyroid function should be included in the panel of ovarian function evaluation.