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PROGRAMME & ABSTRACTS

The regulation of the human cumulus-oocyte complex: The MicroRNAs

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An enormous amount of knowledge about the human oocyte and CCs have been generated over the last years, due in part to the recent advances in gene expression technologies using microarray, CGH array and high-fidelity RNA amplification.
Numerous small endogenous non-coding transcripts, termed microRNAs (miRNAs), have been found to execute key functions in silencing expression of specific target genes in plant, animal and human systems.

Changes in miRNA expression profiles have been linked to pathologies such as cancer and infertility: female mice with global miRNA deficiency are sterile from several causes, including defects in oocyte function. In addition, the messenger RNA (mRNA) expression in mice and bovine during oogenesis shows that a large proportion of maternal genes are under the control of miRNAs. Thus, miRNA profiling offers an effective means of acquiring novel and valuable information regarding the regulation of transcripts involved in human reproduction.

The miRNAs study of oocyte-cumulus complex offers a promising opportunity, by a non-invasive method, to evaluate ovarian failure and pregnancy outcome

Azole fungicides in zebrafish: new effects for old molecules

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Azole is a class of diverse compounds discovered several decades ago and essentially used as antifungals in agriculture and medicine. Their primary mode of action is to inhibit the fungal enzyme 14α-demethylase, which produces ergosterol, an important component of the cell membranes of fungi. Despite this specific mode of action, azoles are also characterized by their capacity to disrupt the endocrine system of vertebrate through multiple mechanisms notably by altering steroidogenesis, a key physiological process responsible for the biosynthesis of steroidal hormones. For instance, azole compounds affect both expression and enzymatic activities of several steroidogenic enzymes in vertebrate models, including fish, leading to reproductive disorders. Because of their uses, their presence in the aquatic environment (surface waters of rivers, lakes and estuaries; sewage sludge) has been recently reported in different industrialized countries raising the need to assess hazard and risk posed to aquatic organisms. In this context, several experiments have been performed to explore the effects of the pharmaceutical azole, clotrimazole, on the endocrine system in the zebrafish. In males, we found that clotrimazole was able to affect the testicular physiology by affecting steroidogenesis, androgen release and spermatogenesis (Hinfray et al., 2011, Baudiffier et al. 2012, 2013). However, the most striking effect was observed in females. Indeed, we found that exposure of adult female zebrafish to clotrimazole led to a dramatic masculinisation as revealed by the complete sex-reversal of the phenotypic sex. Remarkably, this sex-reversal occurred rapidly leading to well-differentiated testicular tissue after 42 days of exposure. By using *cyp19a1a*-GFP transgenic zebrafish, we further demonstrated that clotrimazole led to a time-dependent inhibition of GFP expression in ovary which preceded the histological differentiation of testis demonstrating the crucial role played by aromatase in the process of masculinisation. Altogether, our study demonstrates that clotrimazole significantly affect the gonad endocrinology and physiology of fish revealing new and striking effects on its ability to reverse the phenotypic sex of adult female. Based on our data, it is clear that further studies are needed to address the issue raised by the presence of azoles in the aquatic environment as regards to their potential impact on wild population of fish.

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